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Letter

The Distance Between Us and Community Pharmacies: A Commentary on The Needs of Zoning Policy in Malaysia

Alan Miao Thong Tan, Chee Ping Chong*

The community pharmacy sector in Malaysia has seen substantial growth in recent years. In 2021, there were 5,271 community pharmacists in the country, making up over a quarter of all pharmacists in Malaysia, second only to those in government-funded hospitals and clinics. This number has risen significantly since 2019, with a similar increase in community pharmacy stores, totalling 3,835 in 2021 [1]. Despite the economic downturn caused by the COVID-19 pandemic, the number of registered community pharmacists reached approximately 7,000 by 2023 [2].

Community pharmacists operate privately owned stores within their local communities, offering both prescription and over-the-counter medications. They also provide crucial advice on medication use and maintaining optimal health. These pharmacies generate employment opportunities for pharmacists, pharmacy assistants, logisticians, accountants, and others, contributing to a robust pharmaceutical industry.

Imbalanced distribution: A cause for concern

The growth of the community pharmacy sector has raised concerns about an imbalanced distribution of pharmacists. The majority of the community pharmacies are concentrated in urbanized areas of Kuala Lumpur, Selangor, Penang, and Johor. This creates a significant disparity in pharmacy-to-population ratios, with urban areas enjoying ratios of 1:3,000 to 1:5,000, while rural areas in Pahang and Sabah have much higher ratios, such as 1:9,000 and 1:13,000, respectively [2].

This imbalance has several implications. In urban areas, the high density of pharmacies leads to intense competition. With no regulations on the proximity of new pharmacies, owners may find new competitors setting up shop right next door, leading to price wars and diminished profits for all involved. Meanwhile, rural areas suffer from limited access to medicines, forcing residents to rely on distant government clinics or hospitals, which can lead to time loss and even endanger lives during emergencies due to overcrowding [3].

Another concern is the growing competition between chain and independent pharmacies. The top 10 corporate pharmacy brands now account for around 25% of all community pharmacies and 33% of pharmacists in Malaysia [1]. Chain pharmacies have the advantage of capital for expansion and bulk purchasing power, allowing them to dominate price wars. This competition threatens the survival of small and medium-sized independent pharmacies, which are crucial for fostering innovation and ensuring quality pharmacy services. A monopoly by chain pharmacies could potentially lead to reduced competition, lower service quality, and increased unemployment as independent pharmacies close.

Zoning: A suitable legislation?

The challenges facing the community pharmacy sector stem from a lack of regulation regarding the establishment of new pharmacies. Implementing zoning policies could help address these issues by designating specific areas for certain economic activities, including the distribution of pharmacies. This approach would promote balanced economic growth and ensure that all regions have adequate access to pharmaceutical services [3].

Zoning for community pharmacies is not widely discussed in the Western Pacific region, except in Australia. In the 1990s, Australia faced a similar problem and introduced laws to regulate the distance between new and existing pharmacies [4]. Incentives were provided to pharmacies in less urbanized regions through the Pharmaceutical Benefits Scheme (PBS), which helped increase the number of pharmacies in rural and suburban areas and improved medicine accessibility [4].

Zoning policies include laws to restrict new pharmacies from opening stores within proximity of existing community pharmacies [5]. With a set distance between stores, there is a decrease in competitive pressure for price wars and provide pharmaceutical services in greater quantity and quality. Zoning policies also provide job opportunities in areas that are in greater need for medicine accessibility. With the restrictions

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of new outlets within urbanized districts, community pharmacists may turn to the suburban and rural districts [3]. If the zoning policy includes provisions for incentives for these actions, pharmacists will be able to break even and maintain a respectable profit margin within these districts.

The cost of zoning: An issue of health economics

If zoning policies are to be implemented in Malaysia, the government will need to conduct extensive dialogues on the type of restrictions tabled in the policy. It would be wise to consider a middle ground, allowing zoning policies to affect only new pharmacies or branches rather than the existing ones. Such a policy would prevent further competition stress in urban areas, even though it will not eliminate it completely. Various dialogues would need to be conducted to ensure that both individual pharmacies and chain pharmacies do not suffer significant losses due to adjustments made to store locations through these policies, especially for the former.

Another factor for consideration is the rapid digitalization of healthcare, leading to a borderless healthcare system in the country. The concept of digital health clinics has already begun to pick up momentum in Malaysia. Talks on digitalizing pharmacies will be inevitable, especially considering the emphasis on product-based profit. In a digitalized world, the effect of any geographical zoning is reduced, as consumers do not even need to leave their homes to purchase medicines. Nevertheless, digital healthcare is still far from being a reality in the country. Much of Malaysia's landmass consists of towns and villages, with some areas struggling to obtain sufficient necessities – let alone luxuries such as phone lines and internet access. As such, it is logical to ensure that the geographical need for physical medicines available for purchase is met first before any considerations on digital healthcare are made.

Conclusion

Zoning policies are essential for the equitable distribution of pharmacies across Malaysia, improving access to medicines and reducing competitive pressures in urban areas. By encouraging the expansion of pharmacies in underserved regions, zoning can help ensure that all Malaysians have access to the pharmaceutical services they need. While the implementation of such policies will require careful consideration and dialogue, the potential benefits for public health and economic stability make zoning a justified proposal for discussion among pharmacists and government stakeholders.

CONFLICT OF INTEREST

No conflict of interest declared.

REFERENCE

[1] Chu KE, Goh M. Malaysia Community Pharmacies Report. 2022; https://aipharm.xyz/articles/malaysia-community-pharmacies-report-2022

[2] Pharmaceutical Services Programme, Ministry of Health Malaysia. Register of Licenses. 2023; https://www.pharmacy.gov.my/v2/en/information/register-licences.html

[3] Leong PC, Chong CP. Community pharmacists' opinions of zoning policy in community pharmacy: A qualitative study in Malaysia. J Appl Pharm Sci. 2024;14(02):093–101. https://dx.doi.org/10.7324/JAPS.2024.151337

[4] Nissen L, Singleton J. Explainer: What is the Community Pharmacy Agreement? The Conversation. 2015; https://theconversation.com/explainer-what-is-the-community-pharmacy-agreement-38789

[5] Australian Government, Department of Health and Aged Care. Pharmacy Location Rules. Applicant's Handbook. 2018; https://www.health.gov.au/sites/default/files/documents/2022/08/pharmacy-location-rules-applicant-s-handbook.pdf

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Original Research Article

Effect of *Annona muricata* (Soursop) on Patients with Cancer: A Systematic Review

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ABSTRACT

Introduction: *Annona muricata* is among the most commonly used herbal remedies by cancer patients. Most previous systematic reviews on *Annona muricata* have reported studies performed in-vitro and in-vivo. However, no systematic review has been conducted solely to compile studies on humans with cancer. **Objective:** We aimed to summarise the effects of *Annona muricata* and explore its potential mechanisms of action and safety for cancer patients. **Method:** A systematic search was performed in the following electronic databases from inception until February 2022: MEDLINE, Cochrane library, EMBASE, ClinicalTrials.gov, WHO Trials Portal, Google scholar, and grey literature reports. The papers were then reviewed and assessed for eligibility based on the inclusion and exclusion criteria. **Results:** From the 475 abstracts, 11 were extracted for a full review, with five included in the final analysis. All studies included had a high or critical risk of bias, along with varying outcome measures; thus, caution is required when interpreting the results. *Annona muricata* has shown to inhibit cancer cell growth, enhance caspase activity, and provide anti-inflammatory effects. It was found to be safe, with minimal side effects in cancer patients. *Annona muricata* does not interfere with bone marrow, liver, and kidney function and may even improve nutritional status. **Conclusion:** *Annona muricata* could offer potential anticancer benefits while being safe for cancer patients. However, the absence of high-quality studies and incomplete evidence pose challenges in drawing a conclusive statement. More research is required to validate the efficacy and safety of *Annona muricata*, enabling more definitive evidence-based recommendations.

INTRODUCTION

The growth of cancer has become a significant health problem globally. The number of new cases reported in patients with cancer has been increasing recently, and it is expected to rise even more over time [1, 2]. The increase in new cases will eventually elevate the burden on patients due to heightened health and social costs, especially in low- and middle-income countries. A data-based study in Pakistan found substantial and noticeable differences in price among different anti-cancer brands sold in the country, with variations ranging from 4.01% to 19,912.25% observed across 115 different formulations of anticancer drugs [3]. As a result, the self-usage of alternative medicines such as herbal medicines, may increase among cancer patients in these countries due to their lower cost and availability.

Herbal medicine, as an adjuvant to the standard therapy, has been practised in some Asian countries to enhance therapeutic benefits and quality of life while reducing the side effects of the conventional treatments [4]. A cross-sectional study on the use of herbal medicines among multiethnic secondary care patients in Malaysia (n= 250) found that 42.4% of participants used herbal medicines, with over a third using herbs and conventional treatments concurrently (67.9%). In addition, those with higher education were more inclined to use herbal medicines (OR: 4.06, 95% CI 1.47 – 11.23, p=0.007) [5]. Although current standard cancer therapies are effective, growing evidence highlights substantial side effects, which restrict their use [4]. There is a lay belief that herbal medicine is likely to be safer and associated with fewer side effects.

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Annona muricata, also referred to as soursop or graviola, is a tropical plant species belonging to the *Annonaceae* family [7]. It is a small and slender tree with glossy evergreen leaves that produce spiny heart-shaped fruit, the largest group in the genus [7, 8]. *Annona muricata* most likely originates from Central America and can be found in tropical areas of Central and South America, as well as lowlands of Africa and South-East Asia [7].

Annona muricata is among the most commonly used herbal remedies by cancer patients. A cross-sectional study on herbal medicines used by cancer patients in Trinidad (n= 150) reported that 80.7% of participants use *Annona muricata*, especially in prostate, breast and colorectal cancer (CRC) patients [9]. In addition, another similar cross-sectional study in Jamaica reported that nearly 60% (n = 100) of participants used *Annona muricata* as a complement to standard therapy mainly in breast and prostate cancer, as well as other types of cancer [10].

Annona muricata has shown promising potential in the treatment of cancer. Its leaves are also known as "cancer killers" due to their possible anticancer effects [11]. Annonaceous acetogenins, which are derivatives of long-chain fatty acids, are the major bioactive components in *Annona muricata* that exhibit selective toxicity to cancer cells, including those that are multidrug-resistant [12]. Acetogenins are natural compounds that exert anticancer effects by inducing tumour cell death via various mechanisms such as controlling the cell cycles (causing cell arrest in the G1 phase), and promoting apoptosis by inhibiting multiple proteins while also inducing autophagy [13].

Most previous systematic reviews on *Annona muricata* have reported studies performed *in-vitro* and *in-vivo*. These systematic reviews have addressed the anticancer, antibacterial, anti-inflammatory, and hypoglycaemic properties of *Annona muricata*. Although studies have been done on the effects of *Anonna muricata* on cancer patients, no systematic review has been solely dedicated to compiling studies on humans with cancer. Thus, the goal of this review is to summarise the effects of *Annona muricata* and explore its potential mechanisms of action and safety for cancer patients.

MATERIALS AND METHODS

The protocol for this systematic review has been registered on PROSPERO with the registration number CRD42022315081. This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [14]. The Population, Intervention, Control, and Outcomes (PICO) framework was utilised to provide a structured framework for the review [15]. The population of interest is all adult patients with cancer, and the intervention of interest is the administration of *Annona muricata*. Studies must report a control arm receiving usual therapy or placebo and any reported outcomes are of interest.

Literature search

A systematic search was performed in the following electronic databases from inception until February 2022: 1) Medical Literature Analysis and Retrieval System Online (MEDLINE), 2) Cochrane library, 3) Excerpta Medica Database (EMBASE), 4) ClinicalTrials.gov, and 5) World Health Organisation (WHO) Trials Portal. Searches were also done in Google scholar, OpenGrey (www.opengrey.eu) and grey literature reports (www.greylit.org). The keywords applied were ("*Annona muricata*" OR Soursop OR Graviola OR Guyabano OR Guanabana OR Sirsak OR "Durian Belanda") AND (Cancer OR Tumor OR Tumour OR Malignancy OR Malignant OR Neoplasm). One reviewer (MTA) conducted the systematic search, and two reviewers (MTA and KA) reviewed the included articles. Study authors were not contacted for additional non-published data.

Study eligibility

Studies were included if they met the following inclusion criteria: 1) Human intervention studies (including clinical trials and observational studies), 2) Participants over 18 years old with any type of cancer, 3) Intervention using *Annona muricata* in any form, at any dose, and in a single formulation or combination, 4) Published in English, and 5) Published from inception until the current date (February 2022).

Data extraction

Two reviewers (MTA and KA) independently reviewed the titles and abstracts of the potentially eligible studies to assess if they fulfilled the selection criteria. During each stage of reviewing and assessing eligibility, papers that met any of the following criteria were excluded: 1) Non-clinical trials, 2) Review papers, conference abstracts, book chapters, and duplicate studies, and 3) Studies examining the effect of *Annona muricata* not related to cancer. Any disagreements were resolved through discussion with a third reviewer (NJ). Relevant data from the included studies were extracted by two reviewers (MT and KA), including the following details: 1) Study details (first author, year of publication, country), 2) Study design, 3) Population, 4) Intervention group details (form, dosage), 5) Control group details, and 6) Outcome measures.

Risk of bias

Each study's quality was assessed using the revised Cochrane Risk of Bias (RoB-2) Tools [16] for randomised controlled trial, with bias assessed as high, low, or some concern. For non-randomised studies of intervention, the ROBINS-I tool was

used, with bias assessed as low, moderate, serious, critical, or no information [17].

Data analysis

Sufficient data could not be obtained to permit a meta-analysis, as no similar outcome was reported twice. Thus, only a narrative synthesis was conducted for the systematic review. Reported study outcomes were extracted and discussed according to similar subthemes: 1) Effect of *Annona muricata* in different types of cancer, 2) Possible mechanisms of action of *Annona muricata* on cancer, 3) Safety of *Annona muricata* for patient with cancer, and 4) Limitations of the included studies.

RESULTS AND DISCUSSION

Result of search

The electronic databases searches resulted in 516 relevant papers under consideration. Forty-one were duplicates, and were excluded from further review. The titles and abstracts of 475 papers were screened for potential relevance, excluding 464 for being irrelevant to the review. Eleven full-text papers were obtained and evaluated, resulting in exclusion of six papers (two case reports [12, 38], two non-human trials [39, 40], one not involving cancer patients [41], and one ongoing trial [42]. Five studies fulfilled all eligibility criteria and were included in the review. Meta-analyses could be conducted due to the differences in the outcome measures.

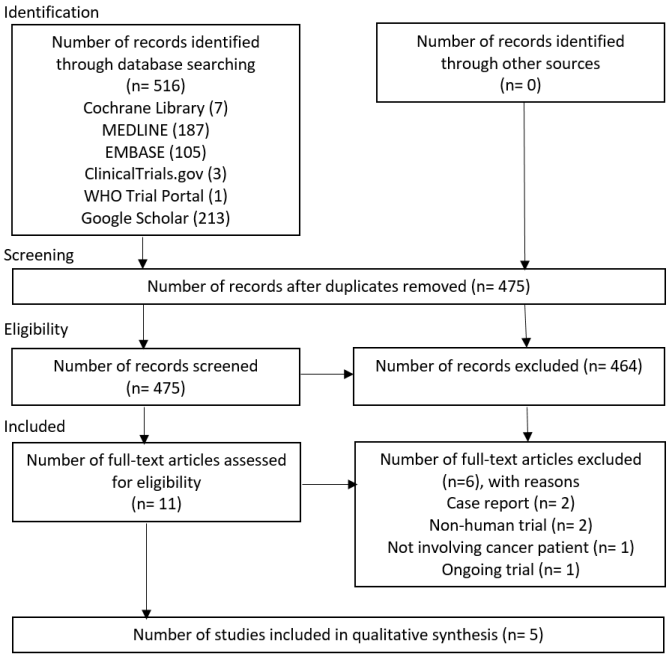

Figure I. Flow diagram of study selection.

Characteristics of Included Studies

The five trials were included a total of 273 participants [18-22]. Table I provides additional details on the characteristics of the studies included.

All four randomised controlled trials were conducted in Indonesia, whereas one observational study was conducted in Italy. Participants in all trials were enrolled from outpatient clinics and included both sexes. Baseline demographic characteristics were balanced between the intervention and comparison groups in three randomised controlled trials [19-21] and one observational study [22], whereas one randomised controlled trial [18] did not report demographic characteristics.

Four of the studies included were randomised double-blind controlled trials [18-21], which involved patients with colorectal cancer. In contrast, one study was a prospective observational, non-randomised study which included patients with invasive bladder cancer [22].

For all five studies, the intervention was *Annona muricata* extract given orally. In one trial with 162 participants [22], the intervention group received a combination of *Annona muricata* and ellagic acid with a dose of 100 mg per day, whereas 111 participants in other four trials received an ethanol-soluble fraction of *Annona muricata* (ESFAM) leaves in the form of capsules at a dose of 300 mg per day [18-21]. Among the five trials, one was conducted over a period of six months [22] and four trials lasted for eight weeks [18-21]. Four of the five trials used a placebo in the capsule form containing maltose [18-21], whereas one trial did not have a placebo in the control group [22].

Risk of Bias in Included Studies

The risk of bias assessment for randomised controlled trials is shown in Figure II(a) and II(b). Figure II(a) presents studies assessed as having low, some concern or high risk of bias for each indicator. Figure II(b) shows the risk of bias indicators for individual studies. The assessment of the risk of bias for the observational study is shown in Table II which is assessed as low, moderate, serious, critical or no information.

Four trials were assessed using RoB-2 tools, and the overall risk of bias for all four trials was high, as there were domains judged as high risk of bias [18-21].

All four trials were judged as high risk of bias for the randomisation process due to inadequate concealment of the allocation sequence, as there were no details provided on the randomisation process. Additionally, three of the trials exhibited an unusually high degree of similarity in baseline characteristics that is unlikely to occur by chance [19-21]. One

Table I. Characteristics of included studies

Authors	Country	Study Design	Population	*Annona muricata* form/ route/ dose	Control	Outcome Measure
Indrawati et al., (2016a) [18]	Indonesia	Randomised Double-Blind Placebo-Controlled Trial	30 patients with colorectal cancers; 15 in treated group, 15 in control group	Form: Capsule Route: Oral Dose: 300mg ethanol-soluble fraction of *Annona muricata* Leaves (ESFAM) after breakfast daily Duration: 8 weeks	Maltose in the form of capsule	1. Cytotoxicity 2.Caspase activity
Indrawati et al., (2016b) [19]	Indonesia	Randomised Double-Blind Placebo-Controlled Trial	30 patients with colorectal cancers; 15 in treated group, 15 in control group	Form: Capsule Route: Oral Dose: 300mg ethanol-soluble fraction of *Annona muricata* Leaves (ESFAM) after breakfast daily Duration: 8 weeks	Maltose in the form of capsule	Organ function by measuring metabolic profile and blood count test
Indrawati et al., (2017) [20]	Indonesia	Randomised Double-Blind Placebo-Controlled Trial	30 patients with colorectal cancers; 15 in treated group, 15 in control group	Form: Capsule Route: Oral Dose: 300mg ethanol-soluble fraction of *Annona muricata* Leaves (ESFAM) after breakfast daily Duration: 8 weeks	Maltose in the form of capsule	1. Cytotoxicity 2. Nutritional status
Surono et al., (2017) [21]	Indonesia	Randomised Double-Blind Placebo-Controlled Trial	30 patients with colorectal cancers; 15 in treated group, 15 in control group	Form: Capsule Route: Oral Dose: 300mg ethanol-soluble fraction of *Annona muricata* Leaves (ESFAM) after breakfast daily Duration: 8 weeks	Maltose in the form of capsule	1. Concentration of TNF-a, IFN-y, and interleukin-IO (IL-10). 2. Concentration of Cyclooxygenase-2 (COX-2) level serum concentration
Serretta et al., (2022) [22]	Italy	Prospective observational non-randomised study	162 patients with non-invasive muscle bladder; 90 in treated group, 72 in control group	Form: Not mentioned Route: Oral Dose: Ellagic Acid 100mg and *Annona muricata* 100mg Duration: 6 months	No placebo	1. Recurrence-Free Rate 2. Recurrence-Free Survival

of the trials did not mention the baseline characteristics [18]. Three trials were judged as having high risk of bias for deviation from intervention and missing outcome data, as two trials provided data that did not match with the total data [18, 20], and one trial had discrepancies in the number of dropouts [21]. All four trials [18-21] were assessed as having some concerns of bias in the selection of reported results, as there were no details provided on whether the reported results were chosen from several eligible outcome measures within the outcome domain or from various eligible analyses of data.

One study [22] was assessed using ROBIN-I tools, and the overall risk of bias was assessed as critical, as one domain being judged as critical.

Cytotoxicity effect: Inhibitory effects on cancer cells

Possible mechanism of action

Annona muricata is capable of inhibiting cancer cell growth possibly through several pathways, such as inhibiting the signaling pathways of the eGFR receptor and disrupting the regulation of the cell cycle, which leads to cell cycle arrest and inhibits cell proliferation [22]. Active component of *Annona muricata*, including ethyl acetate and n-butanol fractions, exhibit activity that inhibits pancreatic lipase, α-amylase, and α-glucosidase. In addition, acetogenins can inhibit mitochondrial ATP formation and suppress cancer cell growth by facilitating the nuclear translocation of apoptosis-inducing factor (AIF) and promoting AIF-dependent cell death [44].

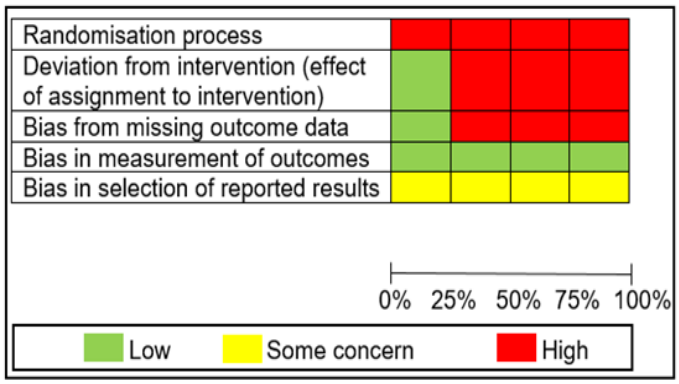

Figure II(a). Risk of bias graph for randomised controlled trial (RCT)s Presented as percentages across all studies

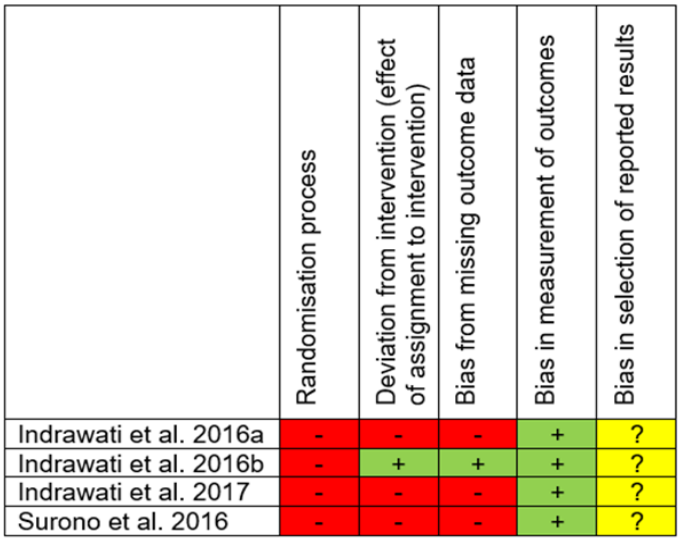

Figure II(b). Assessment of study quality of (RCT)s

Table II. Assessment of study quality for the observational study (N= 11 Patients)

Details	Impact
Author	Serretta et al., (2022) [22]
Confounding	Serious
Selection of participants	Serious
Classification of intervention	Moderate
Deviation from intended interventions	Low
Missing data	Serious
Measurement of outcomes	Critical
Selection of reported results	Low
Overall	Critical

Findings from included studies

Two randomised controlled trials [18, 20] demonstrated cytotoxicity effect, as the ethanol-soluble fraction of *Annona muricata* (ESFAM) leaves extract had a lower IC_{50} than fluorouracil (5-FU) and placebo [18]. In addition, ESFAM demonstrated significant reduction in the growth of the DLD-1 colorectal cancer cell line (p=0.013) after ESFAM administration, compared to before the treatment, whereas no significant changes in growth inhibition were observed in the placebo group before and after administration (p= 0.86). 97% of serum from the ESFAM group inhibited one or more of the colorectal cell lines, in contrast to 58.3% in the placebo group [20].

Findings from previous studies

These results are similar to several previous *in-vitro* and *in-vivo* studies showing significant inhibition of growth in other cancer cell lines, such as HT-29 cells [24] and A549 cells [25].

Cytotoxicity effect: Apoptosis of cancer cells

Possible mechanism of action

Caspases are regulatory factors responsible for the cell's apoptosis and are classified based on their function. Caspases -2, -8, -9, and -10 play a central role in regulating the initiation of apoptosis, while caspases -3, -6, and -7 function as executioners in the apoptosis process [25]. Caspase-9 plays a crucial role in the intrinsic pathway, namely the mitochondrial-mediated pathway, whereas caspase -8 and -10 work through the extrinsic pathway, namely the death receptor-mediated pathway. These caspase trigger caspases -3, -6, and -7, leading to apoptosis [26].

The active component Annomuricin E in *Annona muricata* has been reported to induce apoptosis through a cascade of caspases. Annomuricin E causes a reduction in mitochondrial membrane potential (MMP), which results in the opening of mitochondrial permeability transition pores and the subsequently release of pro-apoptotic proteins like cytochrome C. This process results in the formation of the apoptosome and the activation of caspase -9 and caspase -3 or -7, which are implicated in the mitochondrial death pathway [45].

Findings from included studied

One trial measured the caspase activity of *Annona muricata* on cancer cell [18] and reported that caspase activity in the DLD-1 cell line was higher when treated with ESFAM extracts compared to 5-FU. Their *ex vivo* experiments showed ESFAM extract significantly enhanced caspase-9 activity (p= 0.001) of DLD-1 cell line.

Findings from previous studies

A similar *in-vitro* study found that *Annona muricata* elevated caspase-3 activity compared to leucovorin and placebo [27].

Cytotoxicity effect: Selective cytotoxicity against cancer cells

Possible mechanism of action

Annona muricata exhibits selective cytotoxicity against cancer cells by blocking ATP production in mitochondria. Cancer cells generate more ATP than normal cells;, therefore *Annona*

muricata limits the ability of cancer cells to grow without affecting healthy cells [28].

Acetogenin activity in the mitochondrial complex I electron transport chain inhibits ATP production, thereby inhibiting the growth of cancer cells. This molecular mechanism effectively targets cancer cells, which produce more ATP than normal cells, therefore inhibiting cancer cell growth [44, 46].

Findings from included studies
One of the trials [20] reported that the ESFAM group showed a significant increase in HEK cells (p=0.006) compared to the placebo group, exhibiting significant selective cytotoxic activity against HEK cells compared to baseline (p=0.04). Serum from the ESFAM group resulted in a 72% increase in normal HEK cells, compared to just 14.3% in the placebo group.

Findings from previous studies
These findings correspond with previous systematic reviews of *in-vitro* and *in-vivo* studies, which also found that *Annona muricata* selectively inhibits growth against various cancer cells, leaving normal host cells unaffected [29]. One mouse study reported that *Annona muricata* significantly inhibited the growth of MDA-MB-468 cell lines, with an IC_{50} of 4.8 µg/ml, while showing no effect on MCF-10 cell lines [30].

Anti-inflammatory effect

Possible mechanism of action
Annona muricata also exhibit potent anti-inflammatory effects by activating the anti-inflammatory pathway through the prostaglandin synthesis pathway [31]. Chronic exposure to inflammatory markers can have pleiotropic effects on cancer development, facilitating carcinogenesis, tumour growth, and metastatic spread [32].

Inflammation is triggered through cyclooxygenase (COX) and lipoxygenase (LOX) pathways when a cell responds to mechanical trauma, cytokines, or other stimuli. Ethanolic and hydroalcoholic extracts of *Annona muricata* have been shown to produce an antinociceptive effect in both neurogenic and inflammatory phases, likely through inhibition of COX and LOX. Other than that, the seeds of *Annona muricata* contain amide N-p-coumaroyl tyramine and cyclopeptides, which have anti-inflammatory properties [45].

Findings from included studies
Annona muricata shows anti-inflammatory response, as Tumour Necrosis Factor-a (TNF-a) and Interleukin-10 (IL-10) showed a significant moderate linear correlation in the *Annona muricata* group after administration of the extract (R 0.64, p= 0.01) but not in the placebo group (p= 0.12). Furthermore, IFN-y and IL-10 showed a significant low linear correlation in *Annona muricata* group (R 0.47, p= 0.05) but not in placebo group (p= 0.07) [21].

Findings from previous studies
Similarly, *in-vitro* studies on RAW264.7 cell lines reported that the *Annona muricata* group had lower levels of TNF-a, IL-1B, IL-6, and nitric oxide levels than untreated cells [32],showing *Annona muricata* can inhibit inflammatory mediators.

Effect on cancer recurrence

Findings from included studies
One of the studies [22] examined the effect of *Annona muricata* on recurrence-free rate and recurrence-free survival. The recurrence-free rate (RFR) was better in participants consuming a combination of ellagic acid and *Annona muricata* (EA+AM) at 3 and 6 months: 96.5% versus 84.6% (p=0.003) and 85.4% versus 64.8% (p=0.005), respectively. In contrast, the recurrence-free survival (RFS) was better at 12 months in patients consuming EA+AM. (63.0% versus 34.5% , p<0.0001).

Finding from previous studies
These results are similar to a mouse study [34] that reported *Annona muricata*'s ability to significantly reduce croton oil-induced mice skin papillomagenesis in a dose-dependent manner (p< 0.05), suggesting that *Annona muricata* can suppress cancer cells initiation and promotion.

Safety and adverse effect of Annona muricata on patients with cancer

Effect on bone marrow function

Finding from included studies
Baseline and end-line haematological parameters, such as platelets, erythrocytes, leukocytes, and haemoglobin, showed no significant differences between the *Annona muricata* group and the placebo group before and after administration, with all parameters remaining within the normal range (p>0.05 for all parameters) [19, 21]. Haemoglobin concentrations before and after consuming *Annona muricata* were within a normal range, with no statistical difference between them (p= 0.582). There were also no statistically difference in haemoglobin concentration when comparing the *Annona muricata* group with the placebo group from baseline to endpoint (p= 0.88) [20]. Thus, *Anonna muricata* did not reduce bone marrow function.

Findings from previous studies
These findings were similar to an *in-vivo* study on mice, which showed no significant difference in haematological parameters between the *Annona muricata* group (with dose up to 2500mg/kg) and the placebo group [35].

Effect on liver and kidney function

Findings from included studies

Baseline and end-line biochemical parameters, such as ALT, AST, albumin, and C-reactive protein, were within the normal range, with no significant differences between the *Annona muricata* group and the placebo group before and after administration ($p > 0.05$ in all parameters) [19, 21], showing that *Annona muricata* did not induce hepatotoxicity and nephrotoxicity.

Findings from previous studies

The findings were consistent with a previous systematic review involving *in-vitro* and *in-vivo* studies, where most studies investigating the effects on liver and kidney function reported the hepatoprotective and nephroprotective effects of *Annona muricata* [36].

Effect on nutritional status

Supplementation with *Annona muricata* showed no body weight loss or decrease in nutritional intake, indirectly suggesting an absence of detrimental effects. Energy intake in the *Annona muricata* group showed a significant increase at week 8 (1787.55±620.2 kcal) compared to week 4 (1544.31±560.43 kcal, $p = 0.04$) and week 6 (1596.6±531.11 kcal, $p = 0.02$). The placebo group showed no statistical difference in energy intake throughout the eight weeks [20].

Adverse effect

The 300mg ESFAM dose was found to be safe and highly tolerable, with only 6.7% participants experiencing severe adverse effects [19]. In addition, one study [22] reported that no grade 3 – 4 toxicity associated with *Annona muricata*. However, two patients (2.2%) suffered from grade 2 gastrointestinal disorders, and three patients (3.3%) complained of grade 2 headache.

Limitation of included studies

While all the studies show promising potential effects of *Annona muricata*, many were at high or critical risk of bias, warranting caution in interpreting the result. Thus, the evidence is neither complete nor universally applicable, making it challenging to draw definitive conclusions.

All controlled trials recruited small study population (range, N= 25-162), which may not be sufficient for solid conclusions. The studies included [18-21] did not report on the sample size required. increasing the risk of bias and potentially affecting the precision and power of the results. Thus, more extensive studies are required to confirm the findings, with sample sizes reflecting the broader population.

In addition, the randomisation processes were not adequately explained in all four randomised controlled trials [18-21]. One trial [18] did not declare baseline characteristics, raising doubt about the asequacy of the blinding process. In one observational study [22], the selection criteria for the intervention group posed a serious risk of bias, as participants were selected solely based on their acceptance, with no maintenance of the control group, which might affect the overall results.

Other than that, most studies did not report matched data from the recruited samples, raising concerns about the risk of bias in the reported results [18-21]. There were also no explanations provided for participants who did not complete the studies.

All four randomised controlled trials [18-21] used *ex-vivo* studies to extract serum from the samples and measure the effects using a cell lines, which might not accurately reflect the actual effects on the human body. Information on the phytochemical bioavailability and pharmacodynamics of the compounds in the human body is also limited. Further pharmacodynamics studies are needed to understand better how *Annona muricata* act on the body.

There are no studies on the optimal dose of *Annona muricata* in humans. The doses used were extrapolated from traditional consumption amount. In addition, one study [22] used a much lower dose than the others. Even though all included studies reported that the doses given were safe with minimal side effects and demonstrated positive effects, the dosage might not be sufficient to achieve maximal therapeutic effects. One randomised clinical trial [18] reported that the serum concentration might have been too low to significantly increase caspase-8 activity, accounting for only 10% in the cell culture media, which may have contributed to the reported results, indicating that the provided dose might be insufficient. A systematic review on the safety and tolerability of *Annona muricata* leaf extract found that chemopreventive effects of *Annona muricata* were observed in four in-vivo studies using ethanolic and methanolic leaf extracts administered at doses ranging from 30–400 mg/kg [36]. In addition, *in-vivo* studies showed that the LD_{50} of ethanolic extract of *Annona muricata* ranged from 1000mg/kg to 1670mg/kg [36]. Considering the tolerable doses used in *in-vivo* studies, future studies should explore the optimal dose of *Annona muricata* in humans to ensure maximal therapeutic effect with minimal side effects.

Besides, all studies were conducted over a short period. The safety effects of *Annona muricata* should be evaluated across various types of cancers over a duration longer than the lifespan of human cells, such as red blood cells, which survive in circulation for approximately 115 days [37]. Thus, more accurate results regarding the safety of *Annona muricata* can

be obtained if studies were done over a period extending beyond the lifespan of human cells.

Limitation of this review

Regarding this systematic review, the major strength is its adherence to systematic review guidelines and a thorough quality assessment of the selected studies. However, the limitations of our systematic review include the inclusion of only studies published in English with full-text availability. Expanding the search to non-English literature might have yielded additional relevant studies.

In addition, even though the search was thorough, involving 516 initial abstracts from 6 primary databases, it is a possiblr that articles published in foreign languages or less accessible journals were missed.

The high or critical risk of bias in all included studies, along with the inability to perform a meta-analysis due to differences in outcome measures, makes it challenging to draw conclusions from the current evidence.

CONCLUSION

Annona muricata, known traditionally as an anticancer agent, has only recently been the subject of appropriate scientific research regarding its effects.

This systematic review has identified that *Annona muricata* extracts exhibits beneficial effect on cancer, demonstrating cytotoxicity effect through inhibitory effect, apoptosis, and selective killing of cancer cells without affecting normal cells. Additionally, it has anti-inflammatory effects by activating the anti-inflammatory pathway through the prostaglandin synthesis pathway. *Annona muricata* extracts are considered safe for cancer patient, as they do not interfere with bone marrow, liver or kidney function, and may even improve nutritional status, with few adverse effects, none exceeding than grade 2 toxicities. However, the absence of high-quality studies, and incomplete evidence pose challenges in drawing conclusive statements. More research is required to validate the efficacy and safety of *Annona muricata*, enabling more definitive evidence-based recommendations.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

REFERENCE

[1] Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018 Nov;68(6):394-424. Epub 2018 Sep 12; Erratum in: CA Cancer J Clin. 2020 Jul;70(4):313. https://doi.org/10.3322/caac.21492

[2] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021 May; 71(3): 209-249. https://doi.org/10.3322/caac.21660

[3] Mohd Baidi Bahari and Saw June Tze. Predictors of Herbal Utilization by Multiethnic Secondary Care Patients in Malaysia: a Cross Sectional Survey. Mal J Pharm 2011; 325-335. http://dx.doi.org/10.52494/LEML5968

[4] Yin SY, Wei WC, Jian FY, Yang NS. Therapeutic applications of herbal medicines for cancer patients. Evid Based Complement Alternat Med. 2013;302426. Epub 2013 Jul 11. https://doi.org/10.1155/2013/302426

[5] Sulaiman. Amal, Ayub. Fiza, Rabbani. Imtiaz, Lee. Kah, Goh. Khang Wen, Nadeem. Muhammad Faisal et al. Price variation among registered brands of anti-cancer medicines available in Pakistan. Mal J Pharm. 2022; 8:42-56. http://dx.doi.org/10.52494/EXVW6975

[6] Liu W, Yang B, Yang L, Kaur J, Jessop C, Fadhil R, et al. Therapeutic Effects of Ten Commonly Used Chinese Herbs and Their Bioactive Compounds on Cancers. Evid Based Complement Alternat Med. 2019. https://doi.org/10.1155/2019/6057837

[7] Badrie, N., & Schauss, A. G. Chapter 39 - Soursop (*Annona muricata* L.): Composition, Nutritional Value, Medicinal Uses, and Toxicology. Bioactive Foods in Promoting Health. Academic Press. 2010; 621-643 http://dx.doi.org/10.1016/B978-0-12-374628-3.00039-6

[8] Pinto AC de Q (ed.). Annona species. International Centre for Underutilised Crops, University of Southampton, 2005; ISBN: 0854327851.

[9] Clement YN, Mahase V, Jagroop A, Kissoon K, Maharaj A, Mathura P, et al. Herbal remedies and functional foods used by cancer patients attending specialty oncology clinics in Trinidad. BMC Complement Altern Med. 2016 Oct 21;16(1):399. https://doi.org/10.1186/s12906-016-1380-x

[10] Foster K, Younger N, Aiken W, Brady-West D, Delgoda R. Reliance on medicinal plant therapy among cancer patients in Jamaica. Cancer Causes Control. 2017 Nov;28(11):1349-1356. https://doi.org/10.1007/s10552-017-0924-9

[11] Yajid AI, Ab Rahman HS, Wong MPK, Wan Zain WZ. Potential Benefits of *Annona muricata* in Combating Cancer: A Review. Malays J Med Sci. 2018 Feb;25(1):5-15. https://doi.org/10.21315/mjms2018.25.1.2

[12] Hansra, D., Silva, O., Mehta, A., & Ahn, E. Patient with Metastatic Breast Cancer Achieves Stable Disease for 5 Years on Graviola and Xeloda after Progressing on Multiple Lines of Therapy. Adv. Cancer Res, 2014; 03, 84-87. http://dx.doi.org/10.4236/abcr.2014.33012

[13] Jacobo-Herrera N, Pérez-Plasencia C, Castro-Torres VA, Martínez-Vázquez M, González-Esquinca AR, Zentella-Dehesa A. Selective Acetogenins and Their Potential as Anticancer Agents. Front Pharmacol. 2019 Jul 18;10:783. https://doi.org/10.3389/fphar.2019.00783

[14] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated

guideline for reporting systematic reviews. BMJ. 2021 Mar 29;372:n71. https://doi.org/10.1136/bmj.n71

[15] Schardt C, Adams MB, Owens T, Keitz S, Fontelo P. Utilization of the PICO framework to improve searching PubMed for clinical questions. BMC Med Inform Decis Mak. 2007 Jun 15;7:16. https://doi.org/10.1186/1472-6947-7-16

[16] Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019. https://doi.org/10.1136/bmj.l4898

[17] Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, er al: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016. https://doi.org/10.1136/bmj.i4919

[18] Indrawati, L., Purwantyastuti, A., Budiman, B., Abdullah, M., Surono, I. S., & Suwijiyo, P. Antiproliferative activity and caspase enhancement properties of *Annona muricata* leaves extract against colorectal cancer cells [Academic Journal]. Med. J. Indones, 2016; 25(3), 136-142. https://doi.org/10.13181/mji.v25i3.1449

[19] Indrawati, L., Purwantyastuti, P., Abdullah, M., Surono, I. S., & Basir, I. Safety of *Annona muricata* extract supplementation for colorectal cancer patients. The Indonesian Journal of Gastroenterology, Hepatology, and Digestive Endoscopy, 2016; 17(3), 170-175. http://dx.doi.org/10.24871/1732016170-175

[20] Indrawati, L., Ascobat, P., Bela, B., Abdullah, M., & Surono, I. S. The effect of an *Annona muricata* leaf extract on nutritional status and cytotoxicity in colorectal cancer: a randomized controlled trial [Journal Article; Randomized Controlled Trial]. Asia Pac J Clin Nutr, 2017; 26(4), 606-612. https://doi.org/10.6133/apjcn.062016.02

[21] Surono, I. S., Lienggonegoro, L. A., Indrawati, L., & Wibowo, H. Inflammatory response of *Annona muricata* Linn leaves extract in colorectal cancer patients. J Global Pharma Technol, 2017; 9(7 Suppl), 150-157.

[22] Serretta V, Berardinis E, Simonato A, Guarneri A, Dispensa N, Pavone C, et al. A prospective observational study on oral administration of Ellagic Acid and *Annona muricata* in patients affected by non-muscle invasive bladder cancer not undergoing maintenance after 6-week intravesical prophylaxis. Urologia. 2022 Feb;89(1):49-52. https://doi.org/10.1177/03915603211022285

[23] Rady I, Bloch MB, Chamcheu RN, Banang Mbeumi S, Anwar MR, Mohamed H, et al. Anticancer Properties of Graviola (*Annona muricata*): A Comprehensive Mechanistic Review. Oxid Med Cell Longev. 2018 Jul 30; 2018:1826170. https://doi.org/10.1155/2018/1826170

[24] Zorofchian Moghadamtousi S, Rouhollahi E, Karimian H, Fadaeinasab M, Firoozinia M, Ameen Abdulla M, Abdul Kadir H. The chemopotential effect of *Annona muricata* leaves against azoxymethane-induced colonic aberrant crypt foci in rats and the apoptotic effect of Acetogenin Annomuricin E in HT-29 cells: a bioassay-guided approach. PLoS One. 2015 Apr 10;10(4). https://doi.org/10.1371/journal.pone.0122288

[25] Moghadamtousi SZ, Kadir HA, Paydar M, Rouhollahi E, Karimian H. *Annona muricata* leaves induced apoptosis in A549 cells through mitochondrial-mediated pathway and involvement of NF-κB. BMC Complement Altern Med. 2014 Aug 15;14:299. https://doi.org/10.1186/1472-6882-14-299

[26] Olsson M, Zhivotovsky B. Caspases and cancer. Cell Death Differ. 2011 Sep;18(9):1441-9. https://doi.org/10.1038/cdd.2011.30

[27] Pistritto G, Trisciuoglio D, Ceci C, Garufi A, D'Orazi G. Apoptosis as anticancer mechanism: function and dysfunction of its modulators and targeted therapeutic strategies. Aging (Albany NY). 2016 Apr;8(4):603-19. https://doi.org/10.18632/aging.100934

[28] Abdullah M, Syam AF, Meilany S, Laksono B, Prabu OG, Bekti HS, et al. The Value of Caspase-3 after the Application of *Annona muricata* Leaf Extract in COLO-205 Colorectal Cancer Cell Line. Gastroenterol Res Pract. 2017;2017:4357165.

[29] Waechter, A.-I., Hocquemiller, R., Laurens, A., & Cavé, A. Glaucafilin, an acetogenin from Annona glauca. Phytochemistry, 1997, 44(8), 1537-1540. https://doi.org/10.1155/2017/4357165

[30] Ioannis, P., Anastasis, S., & Andreas, Y. Graviola: A Systematic Review on Its Anticancer Properties. Am. J. Cancer Prev, 2015, 3(6), 128-131. https://pubs.sciepub.com/ajcp/3/6/5

[31] Dai Y, Hogan S, Schmelz EM, Ju YH, Canning C, Zhou K. Selective growth inhibition of human breast cancer cells by graviola fruit extract in vitro and in vivo involving downregulation of EGFR expression. Nutr Cancer.2011;63(5):795-801. https://doi.org/10.1080/01635581.2011.563027

[32] Abdul Wahab SM, Jantan I, Haque MA, Arshad L. Exploring the Leaves of *Annona muricata* L. as a Source of Potential Anti-inflammatory and Anticancer Agents. Front Pharmacol. 2018 Jun 20;9:661. https://doi.org/10.3389/fphar.2018.00661

[33] Multhoff G, Molls M, Radons J. Chronic inflammation in cancer development. Front Immunol. 2012 Jan 12;2:98. https://doi.org/10.3389/fimmu.2011.00098

[34] Laksmitawati, D., Prima, A., Larasinta, N., Syauta, G., Hilda, R., Ramadaniati, H., et al. Anti-Inflammatory Potential of Gandarusa (Gendarussa vulgaris Nees) and Soursoup (*Annona muricata* L) Extracts in LPS Stimulated-Macrophage Cell (RAW264.7). J. Nat. Remedies, 2016; 16: 73-81. http://dx.doi.org/10.18311/jnr/2016/5367

[35] Hamizah S, Roslida AH, Fezah O, Tan KL, Tor YS, Tan CI. Chemopreventive potential of *Annona muricata* L leaves on chemically-induced skin papillomagenesis in mice. Asian Pac J Cancer Prev. 2012;13(6):2533-9. https://doi.org/10.7314/apjcp.2012.13.6.2533

[36] Arthur, F., Terlabi, B., Larbie, C., & Woode, E. Evaluation of acute and subchronic toxicity of *Annona muricata* (Linn.) aqueous extract in animals. European Journal of Experimental Biology, 1, 115. 2015

[37] Chan WJ, McLachlan AJ, Hanrahan JR, Harnett JE. The safety and tolerability of *Annona muricata* leaf extract: a systematic review. J Pharm Pharmacol. 2020 Jan;72(1):1-16. https://doi.org/10.1111/jphp.13182

[38] Franco RS. Measurement of red cell lifespan and aging. Transfus Med Hemother. 2012 Oct;39(5):302-7. https://doi.org/10.1159/000342232

[39] Gunasekaran SS, Emmadi R, Landers LA, Gaba RC. Regression of Hepatocellular Carcinoma Lung Metastases after Guyabano Fruit Extract Consumption. J Diet Suppl. 2016;13(3):237-44. https://doi.org/10.3109/19390211.2015.1008613

[40] Lee M-S. Evaluation of Antioxidant and Anticancer Activity of Guarana and Graviola in Human Colon Cancer. Journal of KOEN. 2019;13(1):217-23. http://doi.org/10.21184/jkeia.2019.1.13.1.217

[41] Yuniarti, L., Sastramihardja, H. S., Purbaningsih, W., Tejasari, M., Respati, T., Hestu, E., et al, A. Soursop effect in cervical cancer apoptosys mechanism. Glob. Health Commun. 2014;2(1):6-14. https://doi.org/10.29313/gmhc.v2i1.1524

[42] Morosetti G, Criscuolo AA, Santi F, Perno CF, Piccione E, Ciotti M. Ellagic acid and *Annona muricata* in the chemoprevention of HPV-related pre-neoplastic lesions of the cervix. Oncol Lett. 2017 Mar;13(3):1880-1884. https://doi.org/10.3892/ol.2017.5634

[43] Study of Guanábana Leaves for The Treatment of Patients With Gastric, Gastroesophageal Junction, Pancreatic and Colorectal Adenocarcinomas; Hepatocellular Carcinoma, and Low Grade Lymphomas. Clinical Study ID: NCT04773769, CCAM 18-01

[44] Ilango S, Sahoo DK, Paital B, Kathirvel K, Gabriel JI, Subramaniam K, et al. A Review on *Annona muricata* and Its Anticancer Activity. Cancers (Basel). 2022 Sep 19;14(18):4539. https://doi.org/10.3390/cancers14184539

[45] Gavamukulya Y, Wamunyokoli F, El-Shemy HA. *Annona muricata*: Is the natural therapy to most disease conditions including cancer growing in our backyard? A systematic review of its research history and future prospects. Asian Pac J Trop Med. 2017 Sep;10(9):835-848. https://doi.org/10.1016/j.apjtm.2017.08.009

[46] Mutakin M, Fauziati R, Fadhilah FN, Zuhrotun A, Amalia R, Hadisaputri YE. Pharmacological Activities of Soursop (*Annona muricata* Lin.). Molecules. 2022 Feb 10;27(4):1201. https://doi.org/10.3390/molecules27041201

MALAYSIAN Journal of Pharmacy

Original Research Article

Caregivers' Involvement in Medication Management of Elderly in Hospital Tuanku Fauziah, Kangar Perlis

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ABSTRACT

Introduction: The ageing population, defined as individuals aged 60 years or older, often manages multiple chronic conditions requiring complex medication regimens. Due to physical, cognitive, and functional limitations, many older adults rely on caregivers for medication management and healthcare assistance. Caregivers' involvement is crucial in ensuring treatment adherence and positive health outcomes. However, managing complex regimens can be challenging for caregivers, especially those balancing other responsibilities. Despite the importance of caregivers in medication management, limited research exists on their roles and challenges in supporting older adults. **Objective:** To explore caregivers' involvement in medication management of elderly patients with multiple chronic conditions and to identify the challenges faced by caregivers in managing older adult medications. **Method:** A qualitative study using semi-structured interview was conducted. 10 subjects were interviewed. Each interview session lasted between 30 to 45 minutes. Interviews were audio-recorded, transcribed verbatim and then coded according to themes. **Results:** Ten caregivers (mean age 43 years, 80% female) were interviewed, along with 11 elderly patients (mean age 83 years, 90% female). Caregivers' roles included general assistance, emotional support, and active involvement in health management, such as attending medical appointments and managing medications. Most caregivers reported challenges in administering medications due to patient emotions, medication taste, and the complexity of regimens. Strategies to overcome these challenges included preparing medications in advance and providing reminders. Financial difficulties were not a major barrier for most, though some caregivers cited occasional financial constraints. **Conclusion:** This study highlights the critical role of caregivers in managing older adults' medication, categorizing their involvement into active and peripheral roles. Caregivers provided essential support in medication management, healthcare visits, and emotional well-being, often adapting their schedules to accommodate caregiving responsibilities. Key challenges included managing the complexities of multiple medications, emotional distress in older adults, and balancing caregiving with work. Despite these challenges, caregivers played a pivotal role in ensuring medication adherence and optimizing therapy outcomes. The findings emphasize the need for better support systems and policies to assist caregivers in their multifaceted roles.

INTRODUCTION

Background

The elderly or ageing population is defined as individuals aged 60 years or older [1]. Most elderly take more than five medications [2] to manage multiple chronic diseases such as hypertension, diabetes mellitus, and orthopaedic problems. Chronic diseases limit older adult self-care abilities and other functions leading to decrease in health-related quality of life over time [3]. Moreover, restriction in physical health, functional abilities, mental health, and cognitive functioning are the primary reasons why older adults need help from others [4].

Almost 8 million older adults with significant disabilities live in the community with help from family and unpaid caregivers. Caregivers provide not only assistance with daily activities but

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also support with a range of health care activities, including physician visits, transitions between care settings, medical decisions, and medical tasks, such as injections, medication management, and wound care [4].

A study by Ferreira, J.M. et al., (2015) found higher Medication Regimen Complexity Index (MRCI) scores among older patients and those with multiple chronic conditions [5]. In reality, the majority of elderly are prescribed complex regime of medication, but have limited capabilities in managing them [6]. A.G.K. Beckman et al. (2004) reported that in a study assessing abilities related to medication adherence in the elderly population, 9.4% could not read instructions on a medicine container, and 14.6% had difficulty opening a plastic flip-top medicine bottle. 31.8% of the sample who did not pass all tests lived alone with no home-help [6]. Therefore, close contact or family members have been shown to play a significant role in this context. Caregivers' involvement in medication and health-related management lead to a positive treatment outcome and improved medication adherence [7]. However, healthcare providers should not assume that all caregivers are actively involved in medication administration but caregivers did take part in medication management and other activities of older adults. Given that many caregivers have other responsibilities, managing these complex regimens can be difficult and stressful [8].

Overall, there are limited studies on caregivers' involvement in medication management among older adults; however, some studies have explored the correlation between caregiver and older adult. A previous study by O'Conor et al., (2021) demonstrated that many elderly have difficulty performing the tasks, leading them to seek assistance from caregivers [7]. This qualitative study focused on the caregivers' involvement from several aspects in the medication management of elderly with multiple medications. More specifically it is aimed to (1) identify the roles carried out by caregivers when managing the patients, and (2) understand the challenges faced by caregivers in managing medications for older adults.

METHODS

This study adhered to and reported findings according to the Consolidated Criteria for Reporting Qualitative Research (COREQ) guidelines [9].

Design

A descriptive qualitative study was conducted using semi-structured interviews. The interview guide was adapted with permission from a previous study by O'Conor et al. (2021) to fit the research context [7]. To ensure linguistic and cultural accuracy, the semi-structured interview guide was translated into Malay by an English educator who holds a Bachelor's degree in Education with Honours in Teaching English as a Second Language (TESL) and has credentials in English proficiency.

Before the main study, a pilot study was conducted using the translated semi-structured questions with a senior pharmacist at Hospital Tuanku Fauziah. This was done to ensure the clarity and comprehensibility of the questions. Participants were recruited until saturation was reached, meaning no new information or themes emerged during the interviews, and participants began providing repeated answers regarding their involvement in managing elderly medications.

Sampling and recruitment

The study adopted a purposive sampling technique to select caregiver encounters at dispensing counters, medication therapy adherence clinics and during ward rounds. The purposes of conducting the research was explained prior to participation. Purposive sampling ensured that participants who were likely to provide rich information on the topic were included in the study [10]. Participants recruited met the inclusion criteria 1) Malaysian citizen, 2) over 18 years of age, 3) provided care for ≥ 6 months, 4) assisted with at least one activity of daily living, instrumental activity of daily living, or health management task. The sample size was determined based on data saturation, the point at which no new themes emerged from the data [11].

Data collection

The interviews were done face-to-face in a counselling room inside the outpatient pharmacy department of Hospital Tuanku Fauziah, Kangar, Perlis during operating hours of pharmacy and on weekend, as well as via phone as requested by participants. The semi-structured interview format allowed for flexibility in gathering the required data. Each interview was conducted in Malay and lasted between 30 to 45 minutes. Interviews were done both face-to-face and via phone, based on the participants' preferences.

Written consent was obtained from each participant before the interview. In the case of phone interviews, participants were informed about the study, and verbal consent was obtained during the first encounter. Three investigators, including two provisionally registered pharmacists and one fully registered pharmacist, attended the interviews with the participants. Appointments were set based on the participants' schedules, and reminders (via phone calls or text messages) were sent a day before the interviews.

All interviews were audio-recorded with the participants' consent. Field notes were taken to capture non-verbal cues and contextual information, ensuring a comprehensive

understanding of the responses. In-depth interviews were employed as the primary data collection tool, as they allowed for honest and detailed responses from participants, fostering transparent interpretations [12].

Data analysis

The interview audio was transcribed verbatim using Microsoft Word and translated into English. Data were analyzed using thematic analysis, a method for identifying, analyzing, and reporting patterns within data [13], which provides flexibility in identifying both explicit and implicit themes. To ensure a systematic and rigorous approach to data management, coding was conducted using NVivo software [14]. Investigators thoroughly read the text to familiarize themselves with the data, generated codes to capture key points, and independently identified and classified recurring patterns into themes. The themes were then reviewed, named, and discussed among the investigators to reach a consensus.

This research was approved by the Medical Research and Ethics Committee, Ministry of Health, NMRR ID-22-00102-N9X.

RESULTS

Demographic profiles

The demographic characteristics of caregivers interviewed consisted of age, gender, race, education level, relationship with patient, and monthly income. Ten caregivers were interviewed. Their ages ranged from 26 to 61, with a mean age of 43 years; 80% were female, and 100% of the sample were Malay. See Table I for a full description.

The demographic characteristics of the patients under care of the caregivers consisted of age, gender, race, patient's condition/disease and live/ not live with caregiver. Eleven patients were documented. Their age ranged from 69 to 82, with a mean age of 83 years; 90% were female, 100% of the sample were Malay. See Table II for a full description.

Roles carried out by caregivers when managing the patients

Caregiver's comments about their roles in managing the patients fell into three major themes. Each of these are presented below.

Table I. Demographics data of the caregivers. (N= 10 Caregivers).

CHARACTERISTIC	NUMBER (%)
GENDER	
Male	2(20)
Female	8(80)
RACE	
Malay	10(100)
AGE	
Min	26
Mean	43
Max	61
EDUCATION LEVEL	
Secondary School	1(10)
SPM	3(30)
STPM	1(10)
Diploma	4(40)
Degree	1(10)
INCOME (RM)	
Min	1200
Mean	3525
Max	6000
RELATIONSHIP WITH PATIENT	
Daughter	7(70)
Son	2(20)
Daughter in law	1(10)

Table II. Demographics data of the patient. (N= 11 Patients).

CHARACTERISTIC	NUMBER (%)
GENDER	
Male	2(18)
Female	9(81)
RACE	
Malay	11(100)
AGE	
Min	69
Mean	83
Max	82
PATIENT'S CONDITION/ DISEASE	
Heart Disease	4
Dyslipidaemia	2
Hypertension	8
Stroke	2
Diabetes Mellitus	7
Chronic Kidney Disease	3
Joint Pain	1
Broken on the right thigh	1
LIVE WITH CAREGIVERS	
Yes	5
Yes (when not well)	1
No	5

Theme 1: General and health-related assistance

Our findings demonstrated that most caregivers were actively involved in providing general and health-related assistance.

Subtheme 1.1: General assistance

Most caregivers provided transportation for hospital visits and helped with house chores.

- "I did house chores, washed clothes, and tidied up the house. For food, in the past, my mother was healthy; she cooked because I worked. Sometimes, I bought the food and went to the market in the morning." C6
- "She dragged a chair beside the stove, and I helped her get everything she needed for her cooking. For the laundry, we helped with washing, drying and folding." C8
- "We transported by renting an ambulance or by car since my father was a stroke patient and bedbound." C3

Few caregivers were involved in providing emotional support to the patients.

- "I spent a lot of time with her, communicated with her, and brought her for walks to relieve her stress. I opened the radio for her because she liked to listen to it." C4
- "I gave emotional support because she lived with me." C5

From the study, we found that involvement of caregivers in patient medication for the elderly started when they helped to take prescribed medications from the pharmacy, met with the prescribers during appointments, asked the prescribers or pharmacists for any ambiguities, and helped to administer or prepare the medications for the elderly. The caregivers admitted that they faced challenges while administering medications to the elderly sometimes due to the taste of the medications, and the quantity of medications to be taken at one time.

Subtheme 1.2: Health management

Most caregivers helped by taking prescribed medications from pharmacies.

- "Yes, I took the prescriptions myself and informed her how to take medications. I took care of everything by myself." C2
- "If the doctor gave the prescription, I would go take the medication." C5
- "If she went to see a doctor, she would take medicine herself. For follow-up medication, I would take it." C7

The majority of caregivers met the prescribers during consultations or appointments.

- "I entered the doctor's room along with my mother as long as I am allowed to because I was worried she might not understand what the doctor said, as my mother was an old woman." C1
- "I met the doctor face-to-face. But due to COVID-19 pandemic, caregivers could not enter and meet doctors; only the patient could enter. If there was anything, the doctor would call me." C5
- "I entered with the patient to meet the doctor." C10

Theme 2: Interaction with healthcare providers

Based on our interviews, we found that most caregivers preferred direct interaction with healthcare providers during the hospital visits.

- "I never called the pharmacy or hospital to ask regarding medication/patient condition because I will ask everything thoroughly during the visit." C1
- "I interacted face-to-face with a healthcare provider. Especially during fasting month, I went to the pharmacy counter and asked about diabetic medication on how to adjust the dose for insulin." C8
- "I never called pharmacies or hospitals to ask about medication or patient conditions. During the visits to the doctor or pharmacy, everything was explained clearly; besides, the medications had their own labels. If there was any doubt, I asked face-to-face the healthcare provider at that time." C9

Theme 3: Medication assistance

Most caregivers were involved in medication management activities but were not directly involved during medication taking and experienced challenges in providing the medications.

Subtheme 3.1: Medication management

Most caregivers were involved with medication management activities such as preparing and providing medications but did not directly administer them.

- "She took the medication by herself. I told her when and how many to take." C2
- "I prepared one container for medication only. In the container, I separated the morning and night medications. I prepared the medication and then my mother took it. I put it beside her table; when she woke up, she took the medication." C4

Meanwhile, some caregivers were directly involved in administering medications to the patient.

- "I gave one by one to her what she should take. She took the medication in front of me." C5
- "I prepared the medicine for her now. In the past, she could take her medicine by herself." C6

Some caregivers stated that patients knew how to take the medication themselves but required assistance with insulin injections.

- "She knew all about her medicine; she just did not want to inject insulin herself." C7
- "The patient was able to manage her own medication; however, for the insulin part, we helped her every time with the injection as she was not good at it." C9

One caregiver mentioned that the patient was able to manage her own medication.

- "She understood her medicine more than I did." C10

Challenges faced by caregivers in managing older adult medications

Caregivers' comments about their challenges in managing older adult medications fell into three major themes. Each of these was presented below.

Theme 1: Challenges in providing medications

The majority of the caregivers faced different challenges in providing medications to the patient. The most commonly cited challenges were the patient's emotional state when given the medications.

- "Sometimes, she was emotionally unstable, so I needed to entertain her first then slowly persuaded her." C4
- "She was afraid of medication; sometimes she got angry and did not want to take it." C5
- "She did not want to take medication, but I forced her to take it." C6

Some caregivers stated that the patient refused medications due to their taste.

- "My mother complained that she was tired of taking medication and said her tongue tasted bitter after she took it." C9
- "The taste of the medication was not good, sometimes she got tired of it." C10

One caregiver had issues with the smell of the medication, leading them to find alternatives.

- "Patients disliked Neurobion as it had a smell; however, she never missed medication. We bought a medication named Neutrovils as a substitute for Neurobion." C8

Meanwhile, a caregiver stated that the quantity of medication posed a challenge but was overcame by giving the patient some time.

- "There was a lot of medicine to take, so it was difficult when we wanted to give painkillers for knee pain. As it became too much, she would not take the medicine. I persuaded her and gave her some time." C7

Theme 2: Successful strategies/Activities

Most caregivers had their own successful experiences with the patient when providing the medication assistance by ensuring the patient did not miss their medications.

- "I never missed taking warfarin medication every day at 6pm." C1
- "I reminded her to take her medication and brought her to see the doctor." C2
- "Physiotherapy, giving medication, feeding and taking care of my father's hygiene." C3
- "From a medication perspective, we missed monthly top up one or 2 days, but we made sure the medication was still there to take every day." C8

Theme 3: Difficult strategies/ Activities

Subtheme 3.1: Challenges in providing medication and methods to overcome

The findings observed that the majority of caregivers faced difficulties in providing health and medication management but managed to overcome these challenges. Most caregivers had issues with their working schedules, leading them to prepare the medication before leaving for work.

- "I went to her house before work to give her medication and after work to check if she took it." C1
- "I prepared early before I went to work. Then, I called her to take medication. Kind of giving a reminder for her to take medication." C4
- "I am busy with my work. I worked at night, so for medication that needed to be taken at night, I gave it in the evening before I went to work." C6

Subtheme 3.2: Financial issue

The majority of caregivers stated that financial status did not interfere with their ability to provide health assistance.

- "So far, there was no financial issue while taking care of my mother, as taking medication from the hospital did not cost a lot of money." C1
- "No, because taking medicine did not cost any money." C7

Meanwhile, some caregivers mentioned that their financial status may affect the care provided.

- "Financially, it was normal; sometimes it was enough, and sometimes it was not." C4
- "Yes, finances were quite limited." C5

DISCUSSION

This qualitative study explored the caregivers' involvement, their roles and the challenges faced when managing older adult medications. We divided the caregiver roles into two categories: actively involved and peripherally involved. Actively involved was defined as caregivers who provided medications and general health-related assistance. Meanwhile, peripherally

involved was defined as caregivers' involvement in either medication assistance or general health-related assistance. From the medication management perspective in this study, caregivers were considered involved if they participated in any activities such as medications administration, preparing, and providing the medications.

Roles carried out by caregivers when managing the patients

A. Caregivers involvement in healthcare visits and medication management

The finding that caregivers provided transportation for hospital visits and assisted in managing medications aligned with research by Wolff et al. (2016), which highlighted that family caregivers frequently accompanied older adults to medical appointments and participated in medication management activities such as filling prescriptions and discussing medication plans with healthcare providers [15]. Caregivers often took responsibility due to the cognitive or physical decline of older adults, which limited their ability to manage their medications effectively. This finding was also consistent with a previous study that stated the physical aspects of managing medications could compromise visits to collect prescriptions and medications from pharmacies [16]. Most caregivers performed this task instead of older adults themselves. Caregivers were worried that older adults might not understand what the healthcare provider said, leading them to accompany older adults during consultations. A study among incapacitated adults mentioned that they might be overwhelmed by receiving difficult information during the visits with prescribers [17].

B. Emotional support by caregivers

Caregivers also mentioned that they were involved by providing emotional support to the patients. This agrees with a previous study where family caregivers for the elderly provided care and support in health, social, emotional, and financial domains, particularly for those who were delicate or suffered from chronic illness [18]. Another study also mentioned that emotional support could be regarded by an older adult as experiencing good health [19]. Furthermore, Brodaty and Donkin (2009), found that caregivers played a vital role in the emotional well-being of the elderly by providing reassurance, reducing anxiety, and helping them cope with their medical conditions [20]. Emotional support was identified as crucial for maintaining the elderly's sense of security and health. In another study, Mendes, R. et al., (2019) challenged the assumption that caregiving always had a positive emotional impact on older adults. Their study found that while some caregivers provided essential emotional support, others inadvertently increased stress by becoming overly controlling or by projecting their own anxieties onto the patient [21]. This highlights the complexity of the caregiver-older adult relationship.

C. Direct versus indirect interaction with healthcare providers

For the theme of interaction with healthcare providers, we categorised the interaction into direct and indirect interaction. Direct interaction was defined as a caregiver interacting with a healthcare provider in person, while indirect interaction referred to communication with a healthcare provider done through other mediums, such as telephone calls. Our study reported that most caregivers preferred direct interaction with healthcare providers during the hospital visits. The majority mentioned that they never called healthcare providers to ask about medication or health conditions, as they would ask or listen to information explained during the visit themselves. This could be a good situation, as the doctor and pharmacist could explain directly to the caregivers regarding the patient's condition and medication. Inperson interaction could guarantee that correct information was delivered and increased confidence level for both healthcare providers delivering and caregivers receiving the information. While our study found that most caregivers preferred direct interaction with healthcare providers, Jaglal et al. (2014) reported that many caregivers, particularly those in rural or remote areas, relied on indirect interactions such as phone calls or telehealth consultations due to barriers like distance and time constraints [22]. This finding suggests that preferences for direct in-person interaction might vary based on caregivers' circumstances.

D. Medication assistance by caregivers

Regarding medication assistance, we observed that most caregivers were involved with medication assistance, even though they might not directly administer the medication to older adults themselves. Given that most caregivers had to juggle with other responsibilities, such as work, while handling older adults with chronic conditions who took more than five medications, they provided medication assistance to varying extents. A previous study stated that caregiving impacted caregivers' work and family finances, requiring them to balance their job and the care provided to family members [18]. Some caregivers prepared the medication beside the older adults' beds to make it easy for them to get it. Although they did not directly administer the medication, they ensured that the medication was arranged according to the time of administration by putting it in a pill box and reminding them to take it. There were also caregivers who directly administered the medication to older adults when they required specific assistance, such as insulin injections. One older adult that was capable of managing her medication herself, and the caregiver stated that the patient knew her medication better than the caregiver did. The finding that caregivers help ensure medication adherence is supported by Riffin, Wolff, and

Pillemer (2021) [23], who concluded that active involvement by caregivers in medication management leads to improved adherence to prescribed treatments among older adults, reducing the likelihood of adverse outcomes related to medication non-compliance. Elliott et al. (2017) contradicted the notion that most caregivers are actively involved in medication management [24]. Their study revealed that a significant proportion of caregivers, particularly those who are not immediate family members, felt unprepared or uncomfortable managing medications, leading them to adopt a more passive role or rely on professional healthcare providers for guidance. Meanwhile Golberstein et al. (2017) found that many older adults, especially those who are cognitively intact, prefer to maintain autonomy over their medication regimens and only seek assistance when absolutely necessary [25]. This contrasts with the assumption that caregivers must always intervene in medication management.

E. Challenge while providing medications

Caregivers faced difficulties with the patients' emotion while providing the medications. Most older adults experienced unstable emotions complicated by their chronic conditions. A study documented that from emotional perspectives, taking medication was perceived as a negative cue of their illness and a burden. Subjects mentioned that they felt negative when taking medication, such as frustration and embarrassment [26]. Meanwhile, another challenge was the taste of the medication that led older adults to refuse to take it. Some drugs have an unpleasant taste and may leave a bitter taste second to minutes after absorption. A study reported that the bitter taste of a drug may be affected by active substances, and some drugs may alter taste and smell sensation [27]. Another challenge was the smell of medications, which led caregivers to find alternative medications. It was important to note that caregivers should refer to healthcare providers if patients could not tolerate the medication and seek alternatives after discussing them with healthcare providers. Older adults with multiple chronic conditions were often prescribed with large quantities of medication. Another study mentioned that with more pills, it was more difficult to adhere to medication regimens and some expressed their fear that the number of medications would increase with increase with age [28]. Roth et al. (2017) found that caregivers commonly experienced difficulties managing complex medication regimens for elderly patients, particularly those with multiple chronic conditions [29]. They emphasized that the sheer number of medications can overwhelm both patients and caregivers, a challenge also highlighted in our discussion. In our study, caregivers opted to give older adults time to take their medications. Caregivers could arrange the timing of administration to reduce the amount of medication taken at the same time while ensuring older adults took the medication as prescribed. This was also important, as certain medications should not be taken together to reduce drug interactions.

F. Successful events while providing medications

The majority of caregivers stated their successful events as being able to ensure that the patients did not miss the medications. Involving caregivers in medication management had a positive impact in improving medication adherence among older adults and optimising medication therapy. Successful caregiver assistance has been associated with positive results for older adults, including better adherence to treatment plans and enhanced physical functioning [23]. Another finding reported thatassistance and support from companions and family have been linked to promoting patient adherence [30].

G. Caregivers' Burden and Impact on Employment

This study reveals that most caregivers mentioned their working schedules required them to adjust medication management activities accordingly. A study reported that a common problem faced by caregivers was blending working administration timetables into caregiving routines, where most caregivers handled by planning medication schedules [31]. The finding that caregivers faced challenges balancing caregiving responsibilities with work is supported by Lai (2012) and Schulz and Sherwood (2008) [18, 32]. These studies found that caregiving often disrupted work routines and impacted caregivers' financial and social lives. Many caregivers experienced stress, financial strain, and fatigue due to the dual responsibility of caregiving and maintaining employment, which negatively affected their quality of life. However, they still ensured that older adults took their medications as prescribed. Other related caregiving expenses such as transportation, nonprescription medications, medical supplies, prescription medications, equipment, and homemaking supplies could also affect financial sufficiency [33]. However, there was not much burden regarding medication costs, as hospitals provided medications for free. In Malaysia, medical care is heavily subsidised by the public healthcare system. All Malaysian citizens, nonetheless of their salaries, have access to medical care at government hospitals and clinics, where they need to pay a minimum of Ringgit Malaysia (RM) 1 to RM5 (USD 0.25 to 1.24) per visit [34]. However, these financial challenges and impacts, if unaddressed, will further hinder caregivers' capacity and endurance to support the elders in their communities. Policies and programs are needed to address the financial needs and security of these family caregivers [18].

Our result demonstrates that the majority of caregivers can be classified as actively involved, as they provided both medications and general health- related assistance to older adults. However, a caregiver fell into the peripherally involved category, as there was one older adult who was able to perform

medication management activities without assistance from the caregiver.

Limitations

The strength of this study was the in-depth interviews, which allowed participants to openly express their honest opinions and experiences without bias. However, there were several limitations when conducting this study, including a small sample size of caregivers who could speak both English and Malay, as well as the complexity of medication regimens for individuals aged 65 years and above who regularly attended routine check-ups in Hospital Tuanku Fauziah, Perlis. Therefore, the results cannot be generalised. We only interviewed caregivers, whose responded based on their experiences or opinions without considering any perspectives from older adults. Furthermore, there are limited previous studies related to caregivers' involvement in medication management among older adults. Future studies should be carried out to determine the correlation between caregivers' involvement in medication management and older adults' perspectives, providing a better understanding among healthcare professionals of caregivers' roles in improving older adult treatment and optimising the medication therapy.

CONCLUSION

In conclusion, this study highlights the significant involvement of caregivers in managing older adults' medications, identifying both active and peripheral roles. Most caregivers were actively involved, providing both medication-related and general healthcare assistance, often compensating for the physical and cognitive decline in older adults. Caregivers played crucial roles during healthcare visits, in medication preparation, and in providing emotional support, helping to ensure adherence to treatment plans and improving patient outcomes. However, challenges such as managing complex medication regimens, dealing with patient emotions, and balancing caregiving with employment responsibilities were common. These challenges sometimes strained caregivers' ability to maintain both their personal and professional lives. While caregivers were generally successful in supporting medication adherence, they also faced difficulties with financial and emotional burdens, underscoring the need for policies and programs to support them. Overall, this study demonstrates the critical role caregivers play in ensuring the well-being of older adults, despite the challenges they face in their dual responsibilities.

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CONFLICT OF INTEREST

No conflict of interest declared.

REFERENCE

[1] Karim, H.A., The elderly in Malaysia: demographic trends. Med J Malaysia, 1997. 52(3): 206-12. https://www.e-mjm.org/1997/v52n3/Elderly.pdf

[2] Weng, M.-C., et al., The impact of number of drugs prescribed on the risk of potentially inappropriate medication among outpatient older adults with chronic diseases. QJM: An Int. J. Med, 2013. 106(11): 1009-1015. https://doi.org/10.1093/qjmed/hct141

[3] Alqahtani, J. and I. Alqahtani, Self-care in the older adult population with chronic disease: concept analysis. Heliyon, 2022. 8(7): e09991. https://doi.org/10.1016/j.heliyon.2022.e09991

[4] Wolff, J., et al., A National Profile of Family and Unpaid Caregivers Who Assist Older Adults With Health Care Activities. JAMA Intern. Med, 2016. 176. https://doi.org/10.1001/jamainternmed.2015.7664

[5] Ferreira, J.M., D. Galato, and A.C. Melo, Medication regimen complexity in adults and the elderly in a primary healthcare setting: determination of high and low complexities. Pharm Pract (Granada), 2015. 13(4): 659. https://doi.org/10.18549/pharmpract.2015.04.659

[6] Beckman, A.G.K., M.G. Parker, and M. Thorslund, Can elderly people take their medicine? Patient Educ Couns, 2005. 59(2): 186-191. https://doi.org/10.1016/j.pec.2004.11.005

[7] O'Conor, R., et al., Caregiver involvement in managing medications among older adults with multiple chronic conditions. J Am Geriatr Soc, 2021. 69(10): 2916-2922. https://doi.org/10.1111/jgs.17337

[8] Kuharic, M., et al., Care recipient self-perceived burden: Perspectives of individuals with chronic health conditions or personal experiences with caregiving on caregiver burden in the US. SSM - Qual Health Res, 2024. 5: 100398. https://doi.org/10.1016/j.ssmqr.2024.100398

[9] Tong, A., P. Sainsbury, and J. Craig, Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care, 2007. 19(6): 349-357. https://doi.org/10.1093/intqhc/mzm042

[10] Patton, M.Q., Qualitative Research & Evaluation Methods. 2001: SAGE Publications. https://aulasvirtuales.files.wordpress.com/2014/02/qualitative-research-evaluation-methods-by-michael-patton.pdf

[11] Guest, G., A. Bunce, and L. Johnson, How Many Interviews Are Enough?:An Experiment with Data Saturation and Variability. Field Methods, 2006. 18(1): 59-82. http://dx.doi.org/10.1177/1525822X05279903

[12] Svend Brinkmann, S.K., Interviews: Learning the Craft of Qualitative Research Interviewing. Third ed. 2014. http://dx.doi.org/10.1002/nha3.20251

[13] Braun, V. and V. Clarke, Using thematic analysis in psychology. Qual. Res. Psychol, 2006. 3:77-101. http://dx.doi.org/10.1191/1478088706qp063oa

[14] International, Q., NVivo (Version 12) [Software]. 2020.

[15] Wolff, J.L., J. Feder, and R. Schulz, Supporting family caregivers of older Americans. N. Engl. J. Med., 2016. 375(26): 2513-2515. https://doi.org/10.1056/nejmp1612351

[16] Wilson, E., G. Caswell, and K. Pollock, The 'work'of managing medications when someone is seriously ill and dying at home: A longitudinal qualitative case study of patient and family perspectives'. Palliat Med, 2021. 35(10): 1941-1950. https://doi.org/10.1177/02692163211030113

[17] Robben, S., et al., Preferences for receiving information among frail older adults and their informal caregivers: a qualitative study. Fam Pract, 2012. 29(6): 742-747. https://doi.org/10.1093/fampra/cms033

[18] Lai, D.W., Effect of financial costs on caregiving burden of family caregivers of older adults. Sage Open, 2012. 2(4): 2158244012470467. https://doi.org/10.1177/2158244012470467
[19] Pejner, M.N., K. Ziegert, and A. Kihlgren, Trying to cope with everyday life—Emotional support in municipal elderly care setting. Int J Qual Stud Health Well-being, 2012. 7(1): 19613. https://doi.org/10.3402/qhw.v7i0.19613
[20] Brodaty, H. and M. Donkin, Family caregivers of people with dementia. Dialogues Clin. Neurosci, 2009. 11(2): 217-228. https://doi.org/10.31887/dcns.2009.11.2/hbrodaty
[21] Mendes, R., S. Martins, and L. Fernandes, Adherence to Medication, Physical Activity and Diet in Older Adults With Diabetes: Its Association With Cognition, Anxiety and Depression. J Clin Med Res, 2019. 11(8): 583-592. https://doi.org/10.14740/jocmr3894
[22] Jaglal, S.B., et al., Increasing access to chronic disease self-management programs in rural and remote communities using telehealth. Telemed E-Health, 2013. 19(6): 467-473. https://doi.org/10.1089/tmj.2012.0197
[23] Riffin, C., J.L. Wolff, and K.A. Pillemer, Assessing and addressing family caregivers' needs and risks in primary care. J Am Geriatr Soc, 2021. 69(2): 432-440. https://doi.org/10.1111/jgs.16945
[24] Cross, A.J., et al., Interventions for improving medication-taking ability and adherence in older adults prescribed multiple medications. Cochrane Database Syst Rev, 2020. 5(5): Cd012419. https://doi.org/10.1002/14651858.cd012419.pub2
[25] Golberstein E, Grabowski DC, Langa KM, Chernew ME. Effect of Medicare home health care payment on informal care. Inquiry. 2009 Spring;46(1):58-71. https://doi.org/10.5034/inquiryjrnl_46.01.58
[26] Easthall, C., N. Taylor, and D. Bhattacharya, Barriers to medication adherence in patients prescribed medicines for the prevention of cardiovascular disease: a conceptual framework. Int J Pharm Pract, 2019. 27(3): 223-231. https://doi.org/10.1111/ijpp.12491
[27] Schiffman, S.S., Influence of medications on taste and smell. WJOHNS, 2018. 4(01): 84-91. https://doi.org/10.1016/j.wjorl.2018.02.005
[28] O'Quin, K.E., T. Semalulu, and H. Orom, Elder and caregiver solutions to improve medication adherence. Health Educ Res, 2015. 30(2): 323-35. https://doi.org/10.1093/her/cyv009
[29] Roth, D.L., et al., Family caregiving and emotional strain: Associations with quality of life in a large national sample of middle-aged and older adults. Qual Life Res, 2009. 18: 679-688. https://doi.org/10.1007/s11136-009-9482-2
[30] DiMatteo, M.R., Social support and patient adherence to medical treatment: a meta-analysis. Health Psychol, 2004. 23(2): 207. https://doi.org/10.1037/0278-6133.23.2.207
[31] Travis, S.S., L.S. Bethea, and P. Winn, Medication administration hassles reported by family caregivers of dependent elderly persons. The J. Gerontol Series A: Biological Sciences and Medical Sciences, 2000. 55(7): p. M412-M417. https://doi.org/10.1093/gerona/55.7.m412
[32] Schulz, R. and P.R. Sherwood, Physical and mental health effects of family caregiving. Am J Nurs, 2008. 108(9 Suppl): 23-7. https://doi.org/10.1097/01.NAJ.0000336406.45248.4c
[33] Hollander, M.J., G. Liu, and N.L. Chappell, Who cares and how much. Healthc. q, 2009. 12(2):42-49. https://doi.org/10.12927/hcq.2009.20660
[34] Aziz, H., et al., Qualitative exploration of the modifiable factors for medication adherence among subsidised and self-paying patients in Malaysia. BMC Health Serv. Res, 2018. 18:1-8. https://doi.org/10.1186/s12913-018-3417-y

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Original Research Article

Association Between Parental Asthma Knowledge and Perceptions of Asthma Control in Children: A Cross-Sectional Study in a Malaysian Tertiary Hospital

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ABSTRACT

Introduction: Parental knowledge and perceptions about asthma are core factors influencing the better management and control of their children's asthma, as parents are the primary caretakers. The association between these factors and childhood asthma control is not well characterised in Malaysia. **Objective:** This study aimed to investigate the association between asthma knowledge and perceptions among parents of asthmatic children and their children's asthma control level. **Method:** A cross-sectional study with a sample size of 131 participants was conducted in the paediatric medical outpatient clinic of Sarawak General Hospital from January to March 2019. Face-to-face interviews were conducted with parents of asthmatic children using a validated questionnaire to determine socio-demographic characteristics of both parents and children, as well as parental asthma knowledge and perceptions. The internal consistency (Cronbach's α) of the knowledge and perception constructs were 0.631 and 0.647, respectively. Children's asthma control levels were assessed using two rating systems: the C-ACT score and the GINA-defined asthma control questionnaire. Data were analysed using non-parametric tests (Mann-Whitney U and Kruskal-Wallis tests) and Spearman's correlation. **Results:** Parents averaged an asthma knowledge score of 8.8 out of 15, with those aged between 41-50 years old ($p=0.006$), those with tertiary education ($p=0.001$), and families with an income of ≥RM5000 ($p<0.001$) achieving significantly higher scores. The knowledge score was positively correlated with parental perceptions regarding the timeline of childhood asthma ($r=0.184$, $p=0.035$), but did not significantly correlate with their children's asthma control level ($r=0.024$, $p=0.783$). C-ACT scores were significantly higher among parents living in urban areas ($p=0.029$) and those who were well educated ($p=0.001$), but negatively correlated with parental perceptions regarding the timeline of childhood asthma ($r=-0.285$, $p=0.001$). **Conclusion:** Despite a positive correlation between asthma knowledge scores and the education level of parents, their asthma knowledge and perceptions did not significantly influence the control of their children's asthma. Other factors should be investigated.

INTRODUCTION

Asthma is a common respiratory disease affecting around 300 million individuals worldwide [1]. According to the 2006 National Health and Morbidity Survey (NHMS), the overall asthma prevalence among children (below 18 years) was 7.1% in Malaysia [2]. Additionally, 32.3% of those with asthma sought care at the emergency department (ED) due to exacerbations, 14.3% required hospitalisation, and 82.1% had clinic visits for asthma exacerbations [2]. Consequently, asthma is associated with significant morbidity, resulting in increased hospitalisation rates and ED visits among the paediatric population. Conversely, asthma symptoms and treatment can impact the daily lives of individuals with asthma and their families, leading to missed school days, reduced quality of sleep, and limitations in physical and social activities

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[3-4]. Therefore, managing childhood asthma should involve the implementation of asthma action plans, suitable pharmacological treatments, and asthma education for both parents and children with asthma [5].

Most asthma management guidelines emphasise the crucial role of families in handling childhood asthma. Caregivers must closely monitor symptoms and address them daily due to the condition's variable nature [6-7]. Numerous studies have stated that the control of childhood asthma can be greatly affected by family factors [7-8]. Factors like parental knowledge, attitudes, education, income, healthcare access, and medications influence asthma management for parents of asthmatic children. Adherence to asthma treatment plans is a primary family responsibility in asthma management [9]. A study by Faber HJ et al. revealed that parental misunderstanding of inhaled corticosteroids correlated with reduced daily usage [10]. Moreover, asthma management is often influenced by parents' perceptions of their children's symptoms. Some studies have shown that many parents struggle to accurately assess the severity of their children's asthma, relying on the frequency of symptoms and the use of bronchodilator inhalers [11-12]. This misunderstanding can eventually lead to uncontrolled asthma and severe consequences. Thus, understanding the importance of asthma knowledge and perceptions for parental asthma management is essential for improving asthma control in children.

In Malaysia, a study evaluated parental knowledge of childhood asthma and its management in an outpatient setting at a state hospital. The findings revealed that parents had adequate knowledge of asthma's causes and symptoms but were less informed about its management [13]. In contrast, another local study conducted in 1998 at Hospital Kuala Lumpur reported a low asthma knowledge level and its association with steroid use and economic status [14].

Given the conflicting results from local studies and the scarcity of research on the relationship between parental knowledge of asthma and perceptions of asthma control in children, this study aims to investigate the association between parental asthma knowledge and perceptions among parents of asthmatic children, as well as their children's levels of asthma control.

METHOD

Study type and design

This was a cross-sectional study that assessed the parent's asthma knowledge and perceptions, along with asthma control assessment via a validated questionnaire in Sarawak General Hospital (SGH).

Study population and sampling method

A convenience sampling method was used in this study, targeting all the parents aged 18 years old and above who have at least one child with a doctor-confirmed diagnosis of asthma, aged between 4 and 11 years, and followed up in the paediatric medical clinic at SGH during the period from 28 January 2019, to 8 March 2019. Children with significant developmental delays or other chronic conditions requiring extensive medical care were excluded from this study.

Sample size

The required sample size for this study was determined based on a study conducted by Zhao J et al. [15]. The monthly average number of asthma patients following up in SGH paediatric medical clinic was 168, which served as a guide to estimate the minimum effective sample size needed for this study. Using a 95% confidence interval and a 5% error margin, the estimated sample size was 98 participants. However, the final sample size should be at least 108 participants to account for a 10% non-response rate. The sample size required for a given significance level and margin was calculated by using the formula below [16]:

$$n = \frac{NZ^2P(1-P)}{d^2(N-1) + Z^2P(1-P)}$$

Where,
N = Population size (168),
p = Expected proportion (18.3%),
d = Precision (5%),
Z = Z statistic for a confidence level of 95% (Z = 1.96)

Data collection

The questionnaires were divided into five sections: (1) parent's and children's socio-demographic information, (2) parental perceptions of childhood asthma, (3) asthma knowledge questionnaire (AKQ) with 15 items, (4) Childhood Asthma Control Test (C-ACT) scores in the past 4 weeks (assessed by research investigators), and (5) asthma control level in the past 4 weeks according to GINA guidelines (assessed by doctors). The self-administered questionnaires were then answered by the participants under the supervision of the researchers to ensure clarity and limit response bias. After that, all of the participants' children were assessed by the researchers based on C-ACT to determine their asthma control level before being reviewed by the doctors in the paediatric medical clinic. Finally, the doctors evaluated the asthma control level of the children based on GINA guideline criteria. The doctors were blinded to the C-ACT scores assessed by the researchers to avoid any forms of bias.

Parental asthma knowledge questionnaires

The parental asthma knowledge questionnaire was used to measure components of parental asthma knowledge particularly relevant for paediatric asthma management, including knowledge about aetiology, symptoms, and asthma management. This questionnaire was adapted from previously published questionnaires, with modifications made to suit the local population [13-14,17-20]. The questionnaire was written in the Malay language and consisted of 15 items requiring answers of "True", "False," or "Don't Know". Each correct answer was allocated 1 point, whereas a wrong answer or an item with no response (don't know) was given 0 points. The total score was 15, with higher scores indicating better knowledge of asthma. The questionnaire was reviewed by a panel of experts in the clinical pharmacy field for face validation and modifications were made based on their feedback. The reliability of the questionnaire was assessed using the internal consistency reliability test.

Parental asthma perceptions questionnaires

Parental asthma perceptions questionnaire was used to assess the perceptions of childhood asthma among parents with asthmatic children. The questionnaire was adapted from the Malay version of a brief illness perceptions questionnaire (MBIPQ), with permission granted by the authors [21-22]. A total of 8 items are rated using a 0-to-10 scale. This questionnaire was divided into 3 sections: (1) Five items assessing cognitive illness aspects: consequences, timeline (acute or chronic), parental control, treatment control, and presence of asthma symptoms. (2) Two items assessing emotional aspects: concern and emotions regarding asthma. (3) One item assessing asthma comprehensibility. The reported test-retest reliability correlation coefficients of the MBIPQ ranged from 0.39 to 0.70 at 2 weeks and from 0.58 to 0.78 at 4 weeks [22].

Asthma control assessment tools

The C-ACT was designed to assess asthma control in asthmatic children aged 4 to 11 years. It comprised 4 child-reported and 3 parent-reported items, and requiring both parent and child presence simultaneously [23-24]. The total score of C-ACT ranged from 0 to 27, with higher scores representing better asthma control. The validity and reliability study of C-ACT scores showed a Cronbach's alpha coefficient of 0.79, indicating high internal consistency [23]. On the other hand, the asthma control level of participants determined by doctors was based on GINA guidelines. According to GINA guidelines, the level of asthma symptom control can be categorized into three categories: "well controlled," "partly controlled," or "uncontrolled," based on the frequency of daytime and nocturnal asthma symptoms, limitations of activities, and the use of rescue medication [1].

Statistical analysis plan

The collected data were tabulated and analysed using the Statistical Package for Social Sciences (SPSS, version 24, Chicago, IL, US). A descriptive analysis was conducted to show the distribution of participants' socio-demographic characteristics. In addition, the results of each item in the asthma knowledge questionnaire were presented in percentages and frequencies, whereas the parental asthma perception scales were presented in the median ± interquartile range (IQR).

As AKQ's total scores followed a non-parametric distribution, Mann-Whitney U and Kruskal-Wallis tests were utilized to assess the influence of demographic characteristics on the AKQ's total scores and C-ACT scores. On the other hand, Spearman's Rank-Order correlation was used to assess the association among correlations of AKQ's total scores with parents' variables and C-ACT scores. Moreover, the relationship between parental asthma perceptions scores and AKQ's total scores and C-ACT scores were also examined. A statistically significant difference was defined at $p < 0.05$.

Ethical considerations

The ethical approval of this study was obtained from the Medical Research Ethics Committee (MREC), Ministry of Health Malaysia (NMRR Registration Number: NMRR-18-2999-44497). Moreover, written informed consent was obtained from all participants who met the inclusion criteria of this study when the questionnaire was distributed.

RESULTS

One hundred thirty-one of 135 respondents completed the questionnaires, resulting in a response rate of 97%. The socio-demographic characteristics of the participants are summarized in Table I. More than half of the respondents were in the age group of 31-40 years, contributing about 57.3 % (n=75) of the total respondents, while parents aged 50 years and above constituted only 1.5% (n=2). Most respondents were mothers (80.9%; n=106), whereas fathers made up 19.1% (n=25) of the total respondents. Regarding education level, almost two-thirds of the respondents had education up to secondary school (64.9%; n=85), followed by 27.5% (n=36) who received tertiary education. Most respondents reported a household income of less than RM 2000 per month (46.6 %; n=61), despite 61.8% (n=81) being employed. More than half of the respondents' children with asthma were boys (55%; n=72), and almost half of the respondents' children were diagnosed at the age of 2 to 5 years (51.9%; n=68). Nevertheless, nearly 40% of

asthmatic children did not have any episodes of hospitalisation due to asthma exacerbations in 2018(≥3; n=13, 9.9%).

Table II displays the median scores of parental perceptions of childhood asthma. The parental perception of treatment control (ranging from zero to ten scores) had the highest median ± interquartile range scores (9.0 ± 2.0) among parental asthma perceptions. Whereas, the parental perception of asthma timeline had the lowest median ± interquartile range scores (4.0 ± 2.0), as most perceived that their children's asthma condition would recover in a short period. The overall Cronbach's alpha coefficient of the parental asthma perceptions questionnaire was 0.647, indicating moderate internal consistency and an acceptable level.

Table III illustrates the 15 statements of asthma knowledge. Overall, parents averaged an asthma knowledge score of 8.8 out of 15, indicating a moderate level of knowledge. When asked whether smoking at home would worsen their child's asthma, a vast majority (97%; n=127) answered correctly. Similarly, most respondents (94.7%; n=124) agreed that inhalation of paint fumes, gasoline, smoke, or haze would trigger an asthma attack. However, half of the respondents (51.1%; n=67) failed to recognize coughing as one of the asthma symptoms, although three-quarters agreed that asthma can be inherited from parents and that asthma is due to inflammation in the lungs. On the other hand, the majority (90.1%; n=118) had a misconception about the roles of rescue inhalers in managing asthma attack, believing that rescue inhalers reduce inflammation in the lungs instead of dilating the bronchial airways. Furthermore, only 24.4% of the respondents (n=32) were aware that the side effects of asthma inhalers are lesser than the oral form of anti-asthmatic medications. The overall Cronbach's alpha coefficient of the parental asthma knowledge questionnaire was 0.631, indicating moderate internal consistency and an acceptable level.

Table IV shows the differences in total asthma knowledge scores related to the parents' socio-demographic characteristics. At a significance level of 5%, median asthma knowledge scores differed among in these groups: parents' age, education level, and family income. Higher asthma knowledge scores were achieved by parents aged 41–50 years, those with tertiary education level, and those with a family income of more than RM5,000.

Table V outlines the differences in C-ACT scores related to the parents' socio-demographic characteristics. At a significance level of 5%, median C-ACT scores differed in two groups: places of living ($p = 0.029$) and education level ($p = 0.001$). Parents living in urban areas and those with tertiary education had higher C-ACT scores.

Table I. Socio-demographic Characteristics of Participants (n=131)

Socio-demographic information	n (%)
Age	
20-30 years old	29 (22.1)
31-40 years old	75 (57.3)
41-50 years old	25 (19.1)
> 50 years old	2 (1.5)
Parents	
Father	25 (19.1)
Mother	106 (80.9)
Marital status	
Married	123 (93.9)
Divorced	2 (1.5)
Widow/ Widower	2 (1.5)
Single parent	4 (3.1)
Races	
Malay	59 (45.0)
Chinese	14 (10.7)
Sarawak Dayak	52 (39.7)
Others	6 (4.6)
Place of living	
Rural	23 (17.6)
Urban	108 (82.4)
Education level	
No formal education	2 (1.5)
Primary school	8 (6.1)
Secondary school	85 (64.9)
Tertiary school	36 (27.5)
Employment status	
Employed	81 (61.8)
Unemployed	50 (38.2)
Family income	
Less than RM 2000	61 (46.6)
RM 2000 – RM 5000	49 (37.4)
RM 5000 – RM 8000	13 (9.9)
More than RM 8000	8 (6.1)
Family history of asthma	
Yes	63 (48.1)
No	68 (51.9)
Children age	
4-6 years old	70 (53.5)
7-9 years old	43 (32.8)
10-11 years old	18 (13.7)
Children gender	
Male	72 (55.0)
Female	59 (45.0)
Age diagnosed with asthma	
< 2 years old	45 (34.4)
2-5 years old	68 (51.9)
6-10 years old	18 (13.7)
No. of hospitalisation due to asthma exacerbation (in last year)	
None	53 (40.5)
1	43 (32.8)
2	22 (16.8)
≥3	13 (9.9)

Table II. Median Scores of Parental Childhood Asthma Perceptions

Parental Asthma Perceptions	Median Scores	Interquartile range (IQR)
How much does your child asthma affect your life?	5.0	3.0
How long do you think your child asthma will continue?	4.0	2.0
How much control do you feel you have over your child asthma?	8.0	4.0
How much do you think your child treatment can help in his or her asthma?	9.0	2.0
How much do your child experience symptoms of asthma?	5.0	3.0
How concerned are you about your child asthma?	8.0	3.0
How well do you feel you understand your child asthma?	8.0	3.0
How much does your child asthma affect you emotionally? (e.g.: does it make you angry, scared, upset or depressed?)	6.0	5.0

Table III. Correct and Incorrect Answers to the Asthma Knowledge Test

Statements	Correct Response	Frequency; n (%)	
		Correct Answer	Incorrect Answer
1. Asthma can be inherited from parents to children.	T	99 (75.6)	32 (24.4)
2. Coughing is not one of the symptoms of asthma.	F	64 (48.9)	67 (51.1)
3. Asthma is due to inflammation in the lungs.	T	99 (75.6)	32 (24.4)
4. Smoking at home can make a child's asthma worse.	T	127 (97)	4 (3.0)
5. Inhalation of paint fumes, gasoline, smoke or haze will trigger an asthma attack.	T	124 (94.7)	7 (5.3)
6. Asthmatic attack is more common at night time than daytime.	T	102 (77.9)	29 (22.1)
7. Anger, crying or laughing can cause an asthma attack.	T	41 (31.3)	90 (68.7)
8. Most of the asthmatic children have to go to the hospital for the management of asthma attacks.	F	105 (80.2)	26 (19.8)
9. Wheezing after exercise suggests a sign of asthma.	T	97 (74.0)	34 (26.0)
10. Asthmatic children should not play sports in which involved a lot of running.	F	51 (38.9)	80 (61.1)
11. Asthma can be treated with antibiotics.	F	59 (45.0)	72 (55.0)
12. Inhalers for asthma have lesser side effects than tablets/ syrup form of medications for asthma.	T	32 (24.4)	99 (75.6)
13. A rescue inhaler (i.e.: reliever inhaler) is used to reduce inflammation in the lungs.	F	13 (9.9)	118 (90.1)
14. You don't need to shake most of the asthma medication inhalers before using them.	F	123 (93.9)	8 (6.1)
15. A preventer inhaler (i.e.: steroid inhaler) doesn't work unless you use them every day.	T	105 (80.2)	26 (19.8)

As shown in Table VI, there was a significant positive correlation between asthma knowledge, measured by AKQ, and the parental perception of the timeline of childhood asthma ($r = 0.184$, $p = 0.035$). However, other parental perceptions regarding childhood asthma were not significantly correlated with asthma knowledge scores.

In addition, another correlation analysis was conducted to examine the association between the C-ACT scores and the mean scores of parental perceptions of childhood asthma. Based on the correlations analysis shown in Table VII, the p-value was less than 0.05, indicating a significant association between the C-ACT scores and perceptions of the timeline of asthma, parental control over asthma, and asthma symptoms. However, the C-ACT scores were found to be negatively correlated with perceptions of the timeline of asthma ($r = -0.285$, $p = 0.001$) and asthma symptoms ($r = -0.383$, $p < 0.001$). On the other hand, there was a significant positive correlation between C-ACT scores and parental perception on parental of asthma control ($r = 0.186$, $p = 0.033$), indicating that C-ACT scores moderately increased as parents perceived themselves to have better control over their children's asthma at home.

As presented in Table VIII, there was a significant positive correlation between asthma knowledge scores and the education level of parents ($r = 0.338$, $p < 0.001$). Additionally, parents with higher monthly family incomes had better knowledge of the disease ($r = 0.394$, $p < 0.001$). Surprisingly, an analysis of the association between parents' asthma knowledge and asthma control level demonstrated that AKQ scores were not significantly correlated with C-ACT scores ($r = 0.024$, $p = 0.783$). On the other hand, parents of children with a longer duration of asthma diagnosis were not significantly associated with AKQ total scores ($r = 0.045$, $p = 0.607$).

Table IV. Total Asthma Knowledge Scores Differences between Parents' Socio-demographic Characteristics

Socio-demographic information	n (%)	Median (IQR)	Z-statistics* χ^2-statistics (df)#	p-value
Age			12.593 (3)	0.006
20-30 years old	29 (22.1)	8.00 (2.50)		
31-40 years old	75 (57.3)	9.00 (3.00)		
41-50 years old	25 (19.1)	10.00 (2.50)		
> 50 years old	2 (1.5)	6.00		
Parents			-1.250	0.211
Father	25 (19.1)	8.00 (2.50)		
Mother	106 (80.9)	9.00 (2.00)		
Marital status			3.493(3)	0.322
Married	123 (93.9)	9.00 (2.00)		
Divorced	2 (1.5)	6.50		
Widow/ Widower	2 (1.5)	7.00		
Single parent	4 (3.1)	8.50 (8.00)		
Races			5.898 (3)	0.117
Malay	59 (45.0)	9.00 (3.00)		
Chinese	14 (10.7)	9.00 (5.25)		
Sarawak Dayak	52 (39.7)	9.00 (2.00)		
Others	6 (4.6)	11.00 (3.00)		
Places of living			-0.844	0.398
Rural	23 (17.6)	8.00 (3.00)		
Urban	108 (82.4)	9.00 (2.00)		
Education level			17.067 (3)	0.001
No formal education	2 (1.5)	8.50		
Primary school	8 (6.1)	8.00 (2.50)		
Secondary school	85 (64.9)	8.00 (2.50)		
Tertiary school	36 (27.5)	10.00 (3.00)		
Employment status			-0.347	0.728
Employed	81 (61.8)	9.00 (4.00)		
Unemployed	50 (38.2)	9.00 (2.00)		
Family income			21.761 (3)	<0.001
Less than RM 2000	61 (46.6)	8.00 (2.00)		
RM 2000 – RM 5000	49 (37.4)	9.00 (3.00)		
RM 5000 – RM 8000	13 (9.9)	11.00 (3.00)		
More than RM 8000	8 (6.1)	10.00 (3.75)		
Family history of asthma			-0.829	0.407
Yes	63 (48.1)	9.00 (2.00)		
No	68 (51.9)	9.00 (2.75)		

*Mann-Whitney U, #Kruskal-Wallis, $p < 0.05$
Multivariable analysis (i.e.: ANCOVA) was not conducted due to violation some of the assumptions.
IQR - Interquartile range

Table V. C-ACT Scores Differences between Parents' Socio-demographic Characteristics

Socio-demographic information	n (%)	Median (IQR)	Z-statistics* χ^2-statistics (df)#	p-value
Age			1.971 (3)	0.579
20-30 years old	29 (22.1)	21.0 (7)		
31-40 years old	75 (57.3)	23.0 (5)		
41-50 years old	25 (19.1)	22.0 (4)		
> 50 years old	2 (1.5)	21.5		
Parents			-1.786	0.074
Father	25 (19.1)	20.0 (5)		
Mother	106 (80.9)	22.5 (5)		
Marital status			0.994 (3)	0.803
Married	123 (93.9)	22.0 (5)		
Divorced	2 (1.5)	22.0		
Widow/ Widower	2 (1.5)	21.5		
Single parent	4 (3.1)	20.0 (3)		
Races			6.727 (3)	0.081
Malay	59 (45.0)	22.0 (5)		
Chinese	14 (10.7)	24.0 (4)		
Sarawak Dayak	52 (39.7)	23.0 (5)		
Others	6 (4.6)	24.0 (10)		
Places of living			-2.179	0.029
Rural	23 (17.6)	21.0 (5)		
Urban	108 (82.4)	23.0 (5)		
Education level			15.591 (3)	0.001
No formal education	2 (1.5)	19.0		
Primary school	8 (6.1)	18.0 (4)		
Secondary school	85 (64.9)	22.0 (5)		
Tertiary school	36 (27.5)	23.0 (6)		
Employment status			-0.007	0.994
Employed	81 (61.8)	22.0 (5)		
Unemployed	50 (38.2)	22.0 (5)		
Family income			0.956 (3)	0.812
Less than RM 2000	61 (46.6)	22.0 (5)		
RM 2000 – RM 5000	49 (37.4)	22.0 (6)		
RM 5000 – RM 8000	13 (9.9)	23.0 (5)		
More than RM 8000	8 (6.1)	23.0 (5)		
Family history of asthma			-1.879	0.060
Yes	63 (48.1)	22.0 (5)		
No	68 (51.9)	22.5 (5)		

*Mann-Whitney U, #Kruskal-Wallis, $p < 0.05$
Multivariable analysis (i.e.: ANCOVA) was not conducted due to violation some of the assumptions.
IQR - Interquartile range

Table VI. Correlations between mean Parental Perceptions of Childhood Asthma Scores with mean Asthma Knowledge Scores

Parental Asthma Perceptions	Total Asthma Knowledge Scores	
	Correlation (r)	P-value*
Consequences	0.081	0.358
Timeline (acute/chronic)	0.184	0.035
Parental Control	0.066	0.455
Treatment Control	-0.005	0.959
Symptoms	0.058	0.507
Concern	-0.048	0.589
Illness Coherence	0.058	0.509
Emotional	0.093	0.292

*Spearman Correlation, $p < 0.05$

Table VII. Correlations between mean Parental Perceptions of Childhood Asthma Scores with C-ACT Scores

Parental Asthma Perceptions	C-ACT Scores	
	Correlation (r)	P-value*
Consequences	-0.063	0.472
Timeline (acute/chronic)	-0.285	0.001
Parental Control	0.186	0.033
Treatment Control	-0.044	0.618
Symptoms	-0.383	<0.001
Concern	-0.129	0.143
Illness Coherence	-0.036	0.682
Emotional	-0.077	0.383

*Spearman Correlation, $p < 0.05$

Table VIII. Correlations of Total Asthma Knowledge Scores with Parents' and Clinical Variables

Variables	Total Asthma Knowledge Scores	
	Correlation (r)	P-value*
Marital status	-0.120	0.172
Races	0.169	0.054
Living place	0.074	0.401
Parent's education level	0.338	<0.001
Parent's employment status	-0.030	0.730
Family income	0.394	<0.001
Family history of asthma	-0.073	0.409
Children age diagnosed with asthma	0.045	0.607
No. of hospitalisation due to asthma exacerbation in last year	-0.025	0.778
C-ACT total scores	0.024	0.783

*Spearman Correlation, $p < 0.05$

DISCUSSION

The Parental Asthma Perceptions Questionnaire offers a rapid and fairly effective evaluation of parents' views on their children's asthma. Thus, it can be valuable in clinical settings as an initial discussion point during counselling sessions to address parental concerns regarding their children's asthma, feelings of being overwhelmed, and beliefs about asthma treatment. Within parental asthma perceptions, the highest score was in "treatment control," while the lowest was in "timeline." This suggests that most parents perceived asthma treatment from the hospital as effective in managing their children's asthma. Conversely, responses to "timeline" suggest that many parents believed their children would recover quickly from asthma, perceiving it as a short-term disease rather than a chronic respiratory condition that might persist throughout their lives. This aligns with previous studies where parents viewed asthma as a series of acute episodes [25-27]. One possible explanation for this perception is a lack of asthma knowledge among parents, potentially influenced by their educational backgrounds. However, the "illness coherence" score in the illness representation dimension was moderately high (8 out of 10) in this study. This suggests that parents of asthmatic children feel they had a good understanding of the disease. Interestingly, this contrasts with their belief in asthma's acute nature. They believed their understanding of asthma aided in managing their child's asthma at home, likely contributing to their high score in the "parental control" aspect of illness representation.

Asthma education plays a crucial role in managing asthma. Studies have shown that effective education programmes can significantly reduce asthma morbidity, hospitalisations, and emergency room visits due to asthma exacerbations [28-31]. Parents, being the primary link between doctors and asthmatic children, need to grasp basic asthma concepts. However, in this study, the parents had only moderate knowledge about asthma, especially regarding the roles of asthma medications. For instance, approximately 90% of the respondents were unaware of the specific functions of controller and rescue inhalers in asthma management. This lack of clarity mirrors findings from other studies where confusion existed among parents about these medication roles [26,32-33].

Moreover, parental concerns about the side effects of asthma medications, particularly controller inhalers used daily, are well-documented [34-38]. Surprisingly, in this study, most parents could not identify these side effects. This lack of awareness aligns with previous research where a high percentage of parents were unaware of asthma medication's adverse effects [38]. Only a small fraction of parents correctly answered a question about the comparative side effects of salbutamol inhalers versus oral salbutamol. Many parents in this study claimed they had not been adequately informed about the adverse effects of different routes of asthma drug administration during medical consultations or counselling sessions. This misinformation could lead to non-adherence to inhaler treatments, especially among parents who are overly concerned about the side effects of inhaled therapy compared to oral asthma medications. These findings are consistent with

a study conducted in Kuala Lumpur, which indicated that parents concerned about inhaled therapies were more likely to perceive the oral route as superior and preferable for treatment [36]. Addressing these parental misconceptions through proper asthma education is vital for achieving better asthma control.

The vast majority of our respondents (97%) knew that exposing asthmatic children to cigarette smoke at home worsened their asthma. This finding aligns with three other studies supporting our results [39-41]. Many studies have explored the harmful effects of environmental cigarette smoke on asthma control in children, with the negative effects of tobacco smoke exposure highlighted by extensive media campaigns in Malaysia [42-43]. Additionally, most respondents (94.7%) agreed that inhaling paint fumes, gasoline, smoke, or haze can trigger asthma attacks, indicating a good understanding of asthma's causes.

Moreover, about three-quarters of respondents agreed that asthma can be inherited and linked to lung inflammation. Similar perceptions were found in studies from the United States and India, where asthma was often seen as hereditary, while a study from Pakistan portrayed it as contagious [37,44-45]. Differences in asthma perceptions across populations may stem from varying levels of education, quality of healthcare information, and healthcare system structures. To ensure optimal treatment for childhood asthma, it is crucial to educate parents that asthma is not solely hereditary; environmental factors also play a significant role in asthma susceptibility and triggering attacks.

This study indicates that parents' demographics like gender, marital status, race, location, job status, and family asthma history did not affect their awareness of childhood asthma. However, notable differences in asthma knowledge scores were observed based on parents' education levels, family income, and ages. Consistent with prior research, the results suggest that parents with higher education had a deeper understanding of asthma compared to those with lower education [17,25,30]. Educated parents appeared to leverage their educational background to grasp and assimilate asthma knowledge, understanding the core aspects of the condition. Conversely, parents with lower socioeconomic status exhibited lower asthma knowledge scores, possibly due to their lower educational attainment. This was evident as most parents with low income had only completed secondary education, potentially explaining the lower asthma knowledge scores among this demographic.

The study highlights significant variations in C-ACT scores based on parents' living environment and education levels. These findings align with a study from Canada, which found that children's asthma control in rural areas was inferior to that in urban areas [46]. One plausible explanation is that urban parents have easier access to medical facilities like government hospitals or private clinics, enabling better asthma care for their children compared to those in rural areas. Furthermore, children of parents with higher education levels tended to have higher C-ACT scores. This corresponds with a study by Strömberg Celind F et al., which associated parents' higher education levels with improved asthma control in children [47].

The study's results indicated a significant albeit weak positive relationship between overall asthma knowledge scores and parental perceptions of the illness duration ($r = 0.184$, $p = 0.035$). This implies that parents with greater asthma knowledge perceived their child's asthma to be of longer duration. This association can be attributed to parents who have a better understanding of asthma and recognize it as a chronic, incurable respiratory condition. They viewed childhood asthma as likely to be permanent rather than temporary in their children's lifetime. This finding aligns with prior research [48-49]. Conversely, other parental perceptions about childhood asthma did not show a significant correlation with asthma knowledge scores in this study.

Further analysis reveals a significant inverse correlation between C-ACT scores and parental perceptions of asthma duration ($r = -0.285$, $p = 0.001$) and symptoms ($r = -0.383$, $p < 0.001$). This indicates that parents with higher C-ACT scores for their asthmatic children believed that their children would experience a shorter duration of asthma and fewer symptoms at home. Most parents believed that asthma duration could be reduced if their children's asthma was completely under control. Likewise, parents reported fewer asthma symptoms at home when their children's asthma was well-controlled. Conversely, there was a notable positive correlation between C-ACT scores and parental perception of asthma control, where higher C-ACT scores were directly linked to parents' belief in their ability to help their children manage their asthma at home. This can be explained by the heightened awareness of parents who understand the importance of avoiding triggers in managing childhood asthma, leading to better disease control and higher C-ACT scores [49].

Several studies indicate a correlation between parents' asthma knowledge and their educational background. In line with these findings, our study reveals a significant association between parents' education levels and their overall asthma knowledge scores ($r = 0.338$, $p < 0.001$) [17,25,30], suggesting that higher education was associated with better asthma knowledge. Nonetheless, no significant relationship was found between parents' asthma knowledge and the duration of their child's asthma diagnosis ($r = 0.045$, $p = 0.607$). This contrasts with a previous study suggesting that longer experience with a child's asthma could lead to improved asthma knowledge, highlighting the importance of experience and communication with healthcare providers [25].

Interestingly, our study did not find a significant association between parents' asthma knowledge and asthma control levels ($r = 0.024$, $p = 0.783$). This implies that higher knowledge scores among parents did not necessarily translate to better control of asthma symptoms in their children. This aligns with research by Silva CM et al., which also found no association between parents' asthma knowledge and children's asthma outcomes, such as nocturnal symptoms, asthma exacerbations, and missed school days [25]. This discrepancy may be attributed to parents with poor asthma knowledge who tended to underreport symptoms, particularly nocturnal symptoms, as they failed to recognise them as asthma symptoms during assessments. Consequently, higher C-ACT scores might be achieved even when a child's asthma was poorly controlled.

Limitations of the Study

Despite this study representing an innovative attempt to explore how parents' perceptions and knowledge of asthma impact childhood asthma control levels, several limitations should be acknowledged. As this study was conducted at a single-centre tertiary hospital, its findings may not be generalisable to all Malaysian parents' asthma knowledge and perceptions. However, it could serve as a reference or basis for comparison with existing studies on parental asthma knowledge. Furthermore, this study did not include an objective measure, such as pulmonary function or peak expiratory flow rate, even though the evaluation of clinical control by the child's doctors was included. As this study utilised a self-administered questionnaire, the possibility of recall bias cannot be excluded. Additionally, data provided by fathers, who are typically not the primary caregivers in asthma management, may be less reliable.

CONCLUSION

The study reveals that socio-demographic factors influenced asthma knowledge and control among parents. Parents aged 41-50, with tertiary education and higher income, tended to have better asthma knowledge while urban-dwelling and more educated parents showed improved asthma control. Parental perception of the asthma timeline was significantly associated with both asthma knowledge and control. Despite a positive correlation between asthma knowledge scores and the education level of parents, their asthma knowledge and perceptions did not significantly influence the control of their children's asthma. Other factors should be further investigated.

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CONFLICT OF INTEREST

No conflict of interest declared.

REFERENCE

[1] Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention, 2018. Available from: http://www.ginasthma.org/guidelines-gina-report-global-strategyfor-asthma.html

[2] Institute for Public Health (IPH). The Third National Health and Morbidity Survey 2006 Vol. II. Kuala Lumpur: IPH; 2008.

[3] Rabe KF, Adachi M, Lai CW, Soriano JB, Vermeire PA, Weiss KB, Weiss ST. Worldwide severity and control of asthma in children and adults: the global asthma insights and reality surveys. J Allergy Clin Immunol 2004;114:40–47. https://doi.org/10.1016/j.jaci.2004.04.042

[4] Trollvik A, Severinsson E. Influence of an asthma education program on parents with children suffering from asthma. Nurs Health Sci 2005;7:157–163. https://doi.org/10.1111/j.1442-2018.2005.00235.x

[5] Bacharier LB, Boner A, Carlsen KH, Eigenmann PA, Frischer T, Go¨tz M, Helms PJ, et al. Diagnosis and treatment of asthma in childhood: a PRACTALL consensus report. Allergy 2008;63:5–34. https://doi.org/10.1111/j.1398-9995.2007.01586.x

[6] Meng A, McConnell S. Decision-making in children with asthma and their parents. J Am Acad Nurse Pract 2002;14:363–371. https://doi.org/10.1111/j.1745-7599.2002.tb00137.x

[7] Kaugars AS, Klinnert MD, Bender BG. Family influences on pediatric asthma. J Pediatr Psychol 2004;29:475–491. https://doi.org/10.1093/jpepsy/jsh051

[8] Fiese BH, Wamboldt FS. Tales of pediatric asthma management: family-based strategies related to medical adherence and health care utilization. J Pediatr 2003;143:457–462. https://doi.org/10.1067/s0022-3476(03)00448-7

[9] Klinnert M, McQuaid E, Gavin L. Assessing the family asthma management system. J Asthma 1997;34:77–88. https://doi.org/10.3109/02770909709071206

[10] Faber HJ, Capra AM, Finkelstein JA, Lozano P, Quesenberry CP, Jensvold NG, Chi FW, et al. Misunderstanding of asthma controller medications: association with nonadherence. J Asthma 2003;40: 17–25. https://doi.org/10.1081/jas-120017203

[11] Yoos HL, Kitzman H, McMullen A, Sidora K. Symptom perception in childhood asthma: how accurate are children and their parents? J Asthma 2003;40:27–39. https://doi.org/10.1081/jas-120017204

[12] Stout JW, Visness CM, Enright P, Lamm C, Shapiro G, Gan VN, Adams III GK, et al. Classification of asthma severity in children: the contribution of pulmonary function testing. Arch Pediatr Adolesc Med 2006;160:844–850. https://doi.org/10.1001/archpedi.160.8.844

[13] Bahari MB, Nik Mat NM. Parental knowledge of childhood asthma in an outpatient setting. Malays. J. Pharm. Sci 2005; Vol.3, No.1,1-10. http://web.usm.my/mjps/

[14] Fadzil A, Norzila MZ. Parental asthma knowledge. Med. J. Malaysia 2002; 57:474-481. https://api.semanticscholar.org/CorpusID:10873022

[15] Zhao J, Shen K, Xiang L, et al. The knowledge, attitudes and practices of parents of children with asthma in 29 cities of China: a multi-center study. BMC Pediatr 2013;13(1):20。 https://doi.org/10.1186/1471-2431-13-20

[16] Naing L, Winn T, Rusli B. Determination of sample size. Malays J Med Sci 2003;10(2):84-6.

[17] Ho J, Bender BG, Gavin LA, O'Connor SL, Wamboldt MZ, Wamboldt FS. Relations among asthma knowledge, treatment adherence, and outcome. J Allergy Clin Immunol 2003;111: 498–502. https://doi.org/10.1067/mai.2003.160

[18] Fitzclarence CA, Henry RL. Validation of an asthma knowledge questionnaire. J Paediatr Child Health 1990;26:200–204. https://doi.org/10.1111/j.1440-1754.1990.tb02429.x

[19] Bahari MB, Nur N Md, Ab Rahman Ab Fatah. A knowledge of asthma in school children: A survey among primary school teachers. Singap. Med. J 2003; 44:131–135.
[20] Rodriguez-Martinez CE, Sossa MP. Validation of an asthma knowledge questionnaire for use in parents or guardians of children with asthma. Arch Bronconeumol 2005;41(8):419–24. https://doi.org/10.1016/s1579-2129(06)60256-5
[21] Broadbent E, Petrie KJ, Main J, Weinman J. The brief illness perception questionnaire. J Psychosom Res 2006;60(6):631–637. https://doi.org/10.1016/j.jpsychores.2005.10.020
[22] Chew BH, Vos RC, Heijmans M, Shariff-Ghazali S, Fernandez A, Rutten Guy E.H.M. Validity and reliability of a Malay version of the brief illness perception questionnaire for patients with type 2 diabetes mellitus. BMC Med. Res. Methodol 2017; 17:118. https://doi.org/10.1186/s12874-017-0394-5
[23] Liu AH, Zeiger RS, Welch M, et al. Development and cross-sectional validation of the Childhood Asthma Control Test. J Allergy Clin Immunol 2007;119:817–825. https://doi.org/10.1016/j.jaci.2006.12.662
[24] Chen HH, Wang JY, Jan RL, et al. Reliability and validity of childhood asthma control test in a population of Chinese asthmatic children. Qual Life Res 2008;17: 585. https://doi.org/10.1007/s11136-008-9335-4
[25] Silva CM, Barros L. Asthma knowledge, subjective assessment of severity and symptom perception in parents of children with asthma. J Asthma 2013; 50(9): 1002–1009. https://doi.org/10.3109/02770903.2013.822082
[26] Arcoleo K, Zayas LE, Hawthorne A, Begay R. Illness representations and cultural practices play a role in patient-centered care in childhood asthma: experiences of Mexican mothers. J Asthma 2015;52:699–706. https://doi.org/10.3109/02770903.2014.1001905
[27] Yoos HL, Kitzman H, Henderson C, McMullen A, Sidora-Arcoleo K, Halterman JS, Anson E. The impact of the parental illness representation on disease management in childhood asthma. Nurs Res 2007;56:167–174. https://doi.org/10.1097/01.nnr.0000270023.44618.a7
[28] Bravata DM, Gienger AL, Holty JC, Sundaram V, Khazeni N, Wise PH, McDonald KM, et al. Quality improvement strategies for children with asthma. Arch Pediatr Adolesc Med 2009;163: 572–581. https://doi.org/10.1001/archpediatrics.2009.63
[29] Butz A, Pham L, Lewis L, Lewis C, Hill K, Walker J, Winkelstein M. Rural children with asthma: impact of a parent and child asthma education program. J Asthma 2005;42:813–821. https://doi.org/10.1080/02770900500369850
[30] Liu C, Feekery C. Can asthma education improve clinical outcomes? An evaluation of a pediatric asthma education program. J Asthma 2001;38:269–278. https://doi.org/10.1081/jas-100000114
[31] Coffman JM, Cabana MD, Halpin HA, Yelin EH. Effects of asthma education on children's use of acute care services: a meta-analysis. Pediatrics 2008;121:575–586. https://doi.org/10.1542/peds.2007-0113
[32] Deis JN, Spiro DM, Jenkins CA, Buckles TL, Arnold DH. Parental knowledge and use of preventive asthma care measures in two pediatric emergency departments. J Asthma 2010;47: 551–556. https://doi.org/10.3109/02770900903560225
[33] Grover C, Goel N, Chugh K, Gaur SN, Armour C, van Asperen PP, Moles RJ, et al. Medication use in Indian children with asthma: the user's perspective. Respirology (Carlton, Vic) 2013;18:807–813. https://doi.org/10.1111/resp.12081
[34] Abu-Shaheen AK, Nofal A, Heena H. Parental Perceptions and Practices toward Childhood Asthma. BioMed Research International 2016;1–7. https://doi.org/10.1155/2016/6364194
[35] Zaraket R, Al-Tannir MA, Abdulhak AAB, Shatila A, Lababidi H. Parental perceptions and beliefs about childhood asthma: a cross-sectional study. Croatian Medical Journal 2011;52(5), 637–643. https://doi.org/10.3325/cmj.2011.52.637
[36] Chan PW, DeBruyne JA. Parental concern towards the use of inhaled therapy in children with chronic asthma. Pediatr Int 2000;42:547-51. https://doi.org/10.1046/j.1442-200x.2000.01278.x
[37] Van Sickle D, Wright AL. Navajo perceptions of asthma and asthma medications: clinical implications. Pediatrics 2001;108:E11. https://doi.org/10.1542/peds.108.1.e11
[38] Lal A, Kumar L, Malhotra S. Knowledge of asthma among parents of asthmatic children. Indian Pediatr 1995;32:649–55.
[39] AlOtaibi E, AlAteeq M. Knowledge and practice of parents and guardians about childhood asthma at King Abdulaziz Medical City for National Guard, Riyadh, Saudi Arabia. Risk Management and Healthcare Policy 2018; 11:67–75. https://doi.org/10.2147/rmhp.s143829
[40] BinSaeed AA. Caregiver knowledge and its relationship to asthma control among children in Saudi Arabia. J Asthma 2014;51(8):870–875. https://doi.org/10.3109/02770903.2014.906608
[41] Mahabee-Gittens M. Smoking in parents of children with asthma and bronchiolitis in a pediatric emergency department. Pediatr Emerg Care 2002;18(1):4–7. https://doi.org/10.1097/00006565-200202000-00002
[42] Gerald LB, Gerald JK, Gibson L, Patel K, Zhang S, McClure LA. Changes in environmental tobacco smoke exposure and asthma morbidity among urban school children. Chest 2009;135(4):911–916. https://doi.org/10.1378/chest.08-1869
[43] Soussan D, Liard R, Zureik M, Touron D, Rogeaux Y, Neukirch F. Treatment compliance, passive smoking, and asthma control: a three year cohort study. Arch Dis Child 2003;88(3):229–233. https://doi.org/10.1136/adc.88.3.229
[44] Shivbalan S, Balasubramanian S, Anandnathan K. What do parents of asthmatic children know about asthma?: An Indian perspective. Indian J Chest Dis Allied Sci 2005;47:81-7. https://pubmed.ncbi.nlm.nih.gov/15832951/
[45] Hazir T, Das C, Piracha F, Waheed B, Azam M. Carers' perception of childhood asthma and its management in a selected Pakistani community. Arch Dis Child 2002;87:287-90. https://doi.org/10.1136/adc.87.4.287
[46] Lawson JA, Rennie DC, Cockcroft DW, Dyck R, Afanasieva A, Oluwole O, Afsana J. Childhood asthma, asthma severity indicators, and related conditions along an urban-rural gradient: a cross-sectional study. BMC Pulmonary Medicine 2017;17(1). https://doi.org/10.1186/s12890-016-0355-5
[47] Strömberg Celind F, Wennergren G, Vasileiadou S, Alm B, Åberg N, Goksör E. Higher parental education was associated with better asthma control. Acta Paediatr 2019;108(5):920-926. https://doi.org/10.1111/apa.14610
[48] Karabulutlu EY, Okanlı A. Assessment of illness perception in haemodialysis patients. Anatolian Journal of Nursing and Health Sciences 2011;14:4.
[49] Bahçecioğlu, Gülcan, Cevik Akyl, Rahsan. Determination of effect on asthma control of illness perception of asthma patients. Acta Medica Mediterranea 2014;30: 591-600.

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Original Research Article

Fabrication, Physicochemical and Pharmaceutical Characterization of Losartan Potassium–Loaded Buccal Films

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ABSTRACT

Introduction: Buccal films for anti-hypertensive drugs like losartan potassium can avoid hepatic first-pass metabolism, improve bioavailability, and enhance patient compliance. **Objective:** The purpose of this study was to develop and characterize buccal films of losartan potassium, to achieve sustained and complete release and permeation of the drug over a reasonable period, without the risk of the film being dislodged from buccal mucosa during use. **Method:** Buccal films with different ratios of hydrophilic (HPMC K15M), hydrophobic polymers (Eudragit RL 100) (1:1, 2:1, and 3:1), along with a fixed percentage of drug loading and mucoadhesive polymer Carbopol 934P, were developed using the solvent casting technique. The films were subjected to *in -vitro* analyses and tests to assess their physicochemical, mechanical, and pharmaceutical properties. **Results:** The films were found to be satisfactory regarding handling characteristics, mechanical properties, swelling index, mucoadhesivity, *in -vitro* release, and permeation. *In vitro* drug release and permeation studies (across dialysis membrane) in simulated saliva (pH 6.8) using a Franz diffusion cell revealed that films containing HPMC K15M and Eudragit RL100 in a ratio of 3:1 could sustain the release of losartan potassium for 6 hrs, achieving a release of 95.39±0.37%, as well as a permeation of 98.38±2.08% drug occurred across synthetic membrane in 6 hrs. Interpretation of kinetic modeling of release, permeation, and diffusional transport mechanism data indicates Higuchi kinetics, matrix formation with non-Fickian transport, and a constant rate of permeation. The permeability coefficient, steady-state flux values, and kinetics of release and permeation showed that the film is the most suitable for further development and clinical application. **Conclusion:** HPMC K 15M and Eudragit RL 100 in a ratio of 3 :1 could form a swellable matrix from which maximum release of losartan potassium occurred within 6 hrs, and with a constant rate of permeation across the synthetic membrane, attaining completion in 6 hrs. Thus, this composition is likely to produce similar results *in vivo* and has a promising prospect for commercialization.

INTRODUCTION

The World Health Organization (WHO) targets the control of blood pressure with affordable and generic anti-hypertensive agents. However, conventional formulations often fail to manage erratic fluctuations in blood pressure in compromised patients, which drives research into the development of more efficient drug delivery systems using existing molecules through economically viable and technologically feasible processes [1,2].

Buccal films may serve as better alternatives to oral or parenteral administration of anti-hypertensive drugs in geriatric patients, those who cannot swallow oral medications, patients with vomiting tendencies, or patients experiencing severe pain due to serious health concerns [3]. They offer significant benefits owing to their specific physicochemical and pharmacokinetic attributes, allowing drugs to enter systemic circulation directly. This results in a comparatively rapid onset of action that can be sustained for the intended duration of therapy, without being subjected to hepatic first-pass metabolism. [4,5]. During the application of buccal films, the film should be positioned under the tongue or behind the lower lip with a dry finger and allowed to remain there until its action is complete. The film adheres to the tissue due to bio-adhesive polymers [6, 7, 8].

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Losartan potassium (MW:461), an angiotensin II receptor (type AT1) antagonist, is efficiently absorbed after oral administration but is extensively metabolized during the hepatic first-pass, resulting in only 33% systemic bioavailability [9]. Allergic reactions and side effects associated with the oral administration of losartan potassium can include swelling of the face, oral cavity, and throat, which may cause difficulty in swallowing. Moreover, common serious side effects include dizziness and sudden hypotension, which are difficult to reverse if the medication is administered orally [10]. However, if administered as a buccal film, the film can be removed from the buccal cavity as soon as the patient feels uncomfortable or experiences a sudden drop in blood pressure. Buccal films of losartan potassium are thus expected to mitigate the serious adverse effects and allergic reactions mentioned above. They can be viable alternatives to tablets in geriatric, unconscious patients, and those with nausea tendencies. The molecule's low molecular weight and lipophilicity favour the fabrication of buccal films [11,12]. Several studies have reported that molecules with molecular weights higher than 20 kDa fail to permeate efficiently through the buccal mucosal epithelium. For polar molecules, there is a correlation between the permeability coefficients of drugs and their molecular weights. The penetration of high molecular weight hydrophilic molecules is hindered due to the membrane-coating granules liberating lipophilic molecules [13, 14, 15, 16, 17].

A literature survey indicates few studies on buccal films of losartan potassium for fast/rapid action or controlled release [18,19, 20, 21, 22, 23]. However, several studies on the development and characterization of transdermal patches of losartan potassium have been reported [24, 25, 26]. In most cases, maximum drug release from buccal films was found to be 93-98% within 4-8 hrs when studied *in vitro* [20, 21]. *Ex vivo* permeation studies using animal buccal mucosa showed permeation of a maximum of 80% of the drug in 6-8 hrs [20, 21]. Since the gap between two consecutive food intakes is typically 4 hrs, it is desirable to avoid the risk of dislodgement of the buccal films. Buccal films with drug release and permeation completed within 4 hrs should be the most preferable. In none of the reported studies did the buccal films could release more than 90% of payload within 4 hrs. Only 80% of the released drug could permeate in 6-8 hrs, leading to drug wastage, therapeutic inefficacy, and an economic burden on patients.

In an attempt to develop buccal films that can release their maximum load of losartan potassium within 4 hrs, the present investigation focuses on the development and characterization of losartan potassium buccal films to leverage the potential benefits and alleviate the limitations of oral, and parenteral routes, thus filling the lacunae in existing studies.

METHOD

Materials

Losartan potassium, Carbopol 934P, and propylene glycol were procured from Yarrow Chem Products and Loba Chemie Pvt. Ltd., Mumbai, India, respectively. Hydroxypropylmethyl cellulose (HPMC) K15M, and Eudragit RL 100 were procured from Colorcon, USA, and Evonik, Germany, respectively. Ethanol (95%) was purchased from Changshu Hongsheng Fine Chemical Co. Ltd., China. All chemicals and reagents used in the study were of the highest purity.

Preparation of losartan potassium-loaded buccal film

HPMC of varying grades and different commercial varieties of Eudragit were employed in combination with other polymers and plasticizers by solvent casting [27, 28, 29]. Carbopol 934P was employed as a buccoadhesive polymer. Preformulation drug-free trial batches were developed using HPMC K 15M (5% w/v ethanolic dispersion) and Eudragit RL 100 in the ratios of 1:1, 1:2, 2:1, 1:3, 3:1, and Carbopol 934P (1.67% w/w). The polymer ratios were selected based on outcomes from previous investigations on buccal or transdermal patches of drugs like rivastigmine, flurbiprofen, or ocular inserts of azithromycin [27, 28, 29]. In these studies, the HPMC-Eudragit RL 100 blend was used as the rate-controlling polymers. The HPMC concentration was fixed at 5% w/v to facilitate homogeneous dispersion, pourability, spreading, and efficient drying of the films. The use of dibutyl phthalate as a plasticizer at 30% and 22.5%w/v of the polymer weight resulted in highly oily films [30, 31, 32] and was thus substituted with propylene glycol (1.5%w/v) [18, 23, 33, 34]. HPMC K 15M and Eudragit RL 100 weighed, and the drug was added and dispersed in ethanol (95%) with stirring. The HPMC-Eudragit-drug dispersion was added to Carbopol dispersion, followed by addition of plasticizer, stirred magnetically at 25°C to ensure complete solvent removal. The viscous dispersion was then poured into the mould and set aside for drying overnight at 25°C. The dry films were peeled off and stored in a desiccator for future evaluation [27, 35, 36]. The composition of the losartan potassium-loaded buccal film is given in Table I.

Differential Scanning Calorimetric analysis (DSC)

DSC was employed to record the thermograms of pure losartan potassium, individual polymers, and physical mixture of losartan potassium-HPMC K15M/Eudragit RL 100/Carbopol 934 P) (heating rate: 40° C/min; temperature range:30 - 300 °C; nitrogen flow rate: 20 ml/min) using Perkin Elmer DSC 4000 (USA) [37].

Organoleptic and visual characteristics of buccal films

The buccal films were manually observed for organoleptic characteristics and visual appearance, including colour, transparency, odour, smoothness, stickiness, presence of air bubbles, and wrinkles at the edges [38].

Physicochemical properties of buccal films

A digital micrometer screw gauge, Vernier calipers, and digital weighing balance (Mettler Toledo, India; Model: ME204) were utilized to determine the film thickness, diameter, and weight from each batch (n=3). An average of the three values for each composition was recorded [38, 39].

To determine the surface pH, buccal films (n=3) of each composition were soaked in simulated saliva (1 ml,pH 6.8) for 15 minutes at 25 °C to facilitate swelling. The electrode was then placed on the buccal film surface and allowed to equilibrate for 1 minute, after which the surface pH was determined using a pH meter (Systronics/Indian Instrument, India; Model: LI 120) [38, 39].

For the drug content assay, a methanolic solution of the buccal film was prepared, filtered through Whatman filter paper (grade 4), diluted appropriately, and absorbances were estimated spectrophotometrically using a UV-vis spectrophotometer (Shimadzu, Japan; Model: UV-19001) at 207 nm. The drug loading efficiency (%) was calculated using Equation I. Studies were done in triplicate [40, 41].

Equation I:

$$Drug\ loading\ efficiency\ (\%) = \frac{Amount\ of\ drug\ liberated\ into\ methanol}{Amount\ of\ drug\ theoretically\ added} \times 100$$

Mechanical properties of buccal films

Folding endurance was evaluated by repeatedly folding a single film along the same line at 180º until it broke [42]. Other parameters assess for the film's mechanical strength included tensile strength, percentage elongation at break, and peel strength [Equations II-IV] [42, 43]. Studies were done in triplicate for each formulation.

Equation II:

$$Tensile\ strength = \frac{Force\ at\ break}{Initial\ cross-sectional\ area\ of\ the\ film\ (sq.mm.)}$$

Equation III:

$$\%\ elongation\ at\ break = \frac{Change\ in\ length\ (mm)}{Initial\ length\ (mm)} \times 100$$

Equation IV:

$$Peel\ strength\ (kg/mm) = \frac{Force\ required\ to\ peel\ (kg)}{Width\ of\ the\ film\ (mm)}$$

Pharmaceutical characterization of buccal films

Swelling study

The buccal film (W_1 gm) was kept in the simulated saliva (pH 6.8). The hydrated film was weighed (W_2 gm) at predetermined intervals until a constant value was attained [37]. The percentage swelling index was computed using Equation V.

Equation V:

$$\%\ Swelling\ index = \frac{W2 - W1}{W1} \times 100$$

Determination of ex vivo mucoadhesive property

The mucoadhesive property (strength) of the buccal films was estimated using a Texture Analyser (TA. XT Plus, Stable Micro Systems, Surrey, UK), equipped with a 5-Kg load cell and fitted with a mucoadhesive test rig. Porcine buccal mucosa was employed, and work-of-adhesion (WOA) (mJ/cm_2) was recorded. For each buccal film, experiments were repeated thrice. Measurements were done at 25°C and a relative humidity of 75% [44, 45].

Characterization of in vitro release behaviour of losartan potassium-loaded buccal films

The release profile of losartan potassium from buccal films was studied in a Franz diffusion cell in simulated saliva (pH 6.8). A buccal film (1x1 cm_2) (containing 0.42 mg of drug/cm_2) was used. The temperature was controlled at 37±0.5° C, and the stirring rate was set at 100 rpm for 8 hrs. Sink conditions were maintained throughout this period. Aliquots of 5 ml were withdrawn, replenished with fresh simulated saliva, filtered through Whatman filter paper, and assayed spectrophotometrically at 224nm [46]. Studies were done in triplicate. Cumulative percentage release (CPR) was calculated from observed absorbance values and plotted against. time (minutes).

Characterization of in vitro permeation behaviour of losartan potassium-loaded buccal films

In the permeation studies, a synthetic membrane (Dialysis membrane HIMEDIA, MWCO: 12000-14000 Daltons) was used in the Franz diffusion cell. Other experimental conditions and analyses were done identically to the *in vitro* drug release

studies. Cumulative percentage permeation (CPP) was calculated similarly.

Analysis of release and permeation behaviours of buccal films containing losartan potassium

To identify the processes governing the release of the drug from the buccal film, the data were fitted into zero-order, first-order, Higuchi, and Korsmeyer-Peppas equations using Microsoft Excel 2019 [42]. The kinetics of drug permeation across buccal mucosa was estimated by fitting the permeation data across the synthetic dialysis membrane to the equations for zero-order and first-order kinetics. The kinetic rate constant values were tabulated. The Korsmeyer-Peppas equation was used to obtain the value of the diffusion exponent ('n'), which indicated Fickian or non-Fickian diffusion [47].

For model-independent characterization of release and permeation profiles, the time taken for 50% of the drug to be released and permeated (t_{50}) was calculated and compared. For permeation data, drug flux, $J(SS_{flux})$ (mg/cm^2.min) at steady-state was estimated from Equation VI, and the permeability coefficient K_p was obtained by dividing the flux by the drug content [48].

Equation VI:

$$SSflux = dQ/dt \; x \; 1/A$$

(where dQ/dt is the slope of the truncated linear portion of the curve, i.e., cumulative amount of permeated drug per unit time (mg/minute), and A is the area available for diffusion (cm^2).

Statistical analysis

Experimental data were processed and analyzed using GraphPad Instat 3 statistical software (GraphPad, San Diego, CA, USA). Data were expressed as means ± SD (standard deviation) of triplicate repetitions. For each study and result obtained, $P<0.05$ denoted statistically significant values.

RESULTS

Drug-polymer compatibility study

In preliminary scanning of drug-polymer compatibility by FTIR spectrophotometry, no interaction or incompatibility was detected (data not shown) [49, 50, 51]. The DSC thermogram of pure losartan potassium showed an onset and end of melting at 272.8°C and 291 °C, with another less prominent endothermic peak. The endothermic peaks of HPMC K 15M, Eudragit RL 100, and Carbopol 934P matched with the reported values [50, 51, 52] (Figure I). In the physical mixture, an endothermic peak at 265.41°C was visible, closely matching that of pure losartan potassium [37].

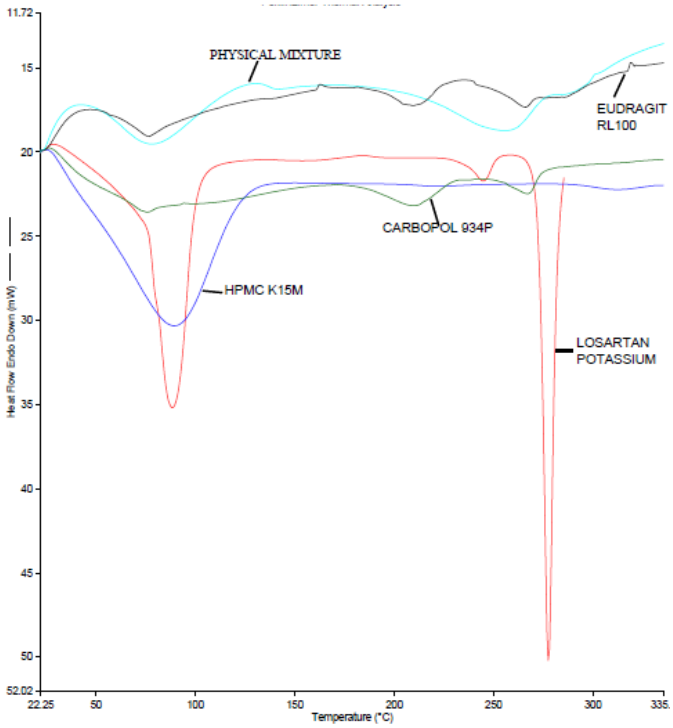

Figure I. Drug-polymer compatibility study: Overlaid DSC thermograms of losartan potassium, HPMC K15M, Eudragit RL100, Carbopol 934P and their physical mixture in the ratio of 1:1:1:1.

Pre-formulation study outcomes

During preformulation studies, only the buccal films with HPMC K15M and Eudragit RL 100 in the ratios of 1:1, 2:1, and 3:1, containing 1.67% w/v Carbopol 934P and 1.5% w/v of propylene glycol, produced peelable films with satisfactory mechanical properties and aesthetic appeal. Thus, these compositions were considered optimized formulations for the loading of losartan potassium at 1.0% w/w of the total polymer weight. The proposed ratios of HPMC K 15M and Eudragit RL 100 are likely to achieve zero-order constant release or form a matrix-type film from which drug release may occur by Fickian or non-Fickian diffusion [27, 28, 29].

Table I. Composition of losartan potassium-loaded buccal films.

Composition	Formulation		
	F1	F2	F3
Losartan potassium (%w/w)	1.0	1.0	1.0
HPMC K15M (% w/v)	5.0	6.6	7.5
Eudragit RL100 (% w/v)	5.0	3.3	2.5
Carbopol 934P (% w/v)	1.67	1.67	1.67
Propylene glycol (% w/v)	1.5	1.5	1.5
Ethanol (ml)	15	15	15

Organoleptic, physicochemical, mechanical, and pharmaceutical characteristics of buccal films containing losartan potassium

The organoleptic, visual characteristics, physicochemical, mechanical, and pharmaceutical characteristics of buccal films containing losartan potassium are tabulated in Table II.

Table II. *In vitro* organoleptic, physicochemical and mechanical characterisation of losartan potassium buccal films.

Properties	F1	F2	F3
Color	White	White	White
Transparency	Translucent	Translucent	Translucent
Stickiness	Non-sticky	Non-sticky	Non-sticky
Wrinkles	Wrinkle free	Wrinkle free	Wrinkle free
Smoothness	Smooth	Smooth	Smooth
Odor	No Odor	No Odor	No Odor
Mean thickness (mm)	0.7±0.01	0.8±0.01	0.6±0.02
Diameter (cm)	5.97±0.1	6.00±0.2	6.00±0.1
Weight variation (mg)*	30.26±2.38	33.39±2.11	37.54±1.45
Surface pH at 25 ºC*	6.65±0.03	6.72±0.02	6.68±0.04
Drug loading efficiency (%)*	95.75±0.56	93.56±1.61	98.23±0.89
Folding endurance	>150	>150	>150
Tensile strength (Kg/mm^2)*	2.12±0.021	1.93±0.047	1.71±0.035
Elongation at break (%)*	80.21±2.35	71.48±2.26	62.36±1.73
Peel strength (Kg/mm)*	1.99±0.06	1.86±0.08	1.69±0.07
Swelling index(%)*	74.09 ±8.43	87.09 ±2.68	111.14± 9.81
Work of adhesion* (mJ/cm^2)	62.46 ±4.38	64.96± 5.08	61.73±5.26

***(Data represented as mean ± standard deviation; n=3. For all the studies, p <0.05)**

In vitro release and permeation profiles of losartan potassium

The highest release of 95.39±0.37% losartan potassium was observed with F3 in 6 hrs. F2 released 93.32 ±4.43% % in 7 hrs, while F1 released 66.71±2.23% in 8 hrs ($p< 0.05$) (Figure II(a)). *In vitro* permeation through the artificial dialysis membrane followed patterns identical to the drug release data, with the highest permeation of 98.38±2.08% occurring in 6 hrs from F3 and the least permeation of 59.08±0.47% from F1 in 8 hrs. From F2, 95.39±3.96% of drug permeated in 7.5 hrs ($p< 0.05$). A graphical representation of permeation profiles can be seen in Figure II(b).

Kinetic modeling of drug release and permeation data

The buccal films followed Higuchi kinetics, indicating matrix formation by HPMC K 15M, Eudragit RL 100, and Carbopol 934P. The highest value of the Higuchi rate constant of 4.5945 %.min$^{-0.5}$ was obtained for F3, while the least of 3.0569 %.min$^{-0.5}$ was observed F2 (Table III).

Model-independent analysis of drug release data revealed that F3 had the least t_{50} value of <150 minutes, while F1 had the maximum t_{50} value of >220 minutes (Table III).

Permeation followed zero-order kinetics. The steady-state flux of F3 was 0.1623 mg/cm^2/min, with a Kp value of 0.1745 mg/cm^2 (Table III).

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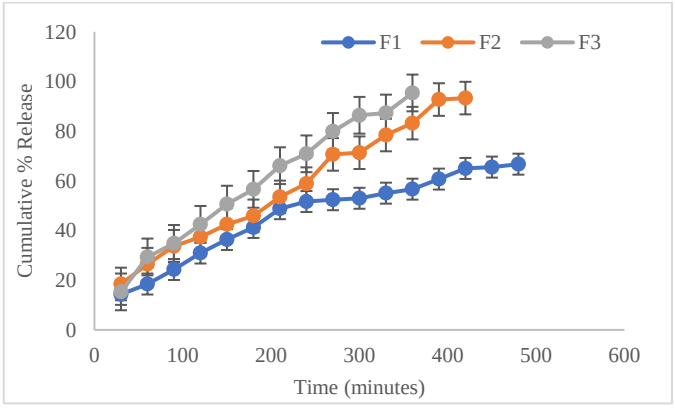

Figure II(a). *In* vitro release profiles of losartan potassium from HPMC K15M-Eudragit RL 100-Carbopol 934P buccal films in simulated saliva (pH 6.8).

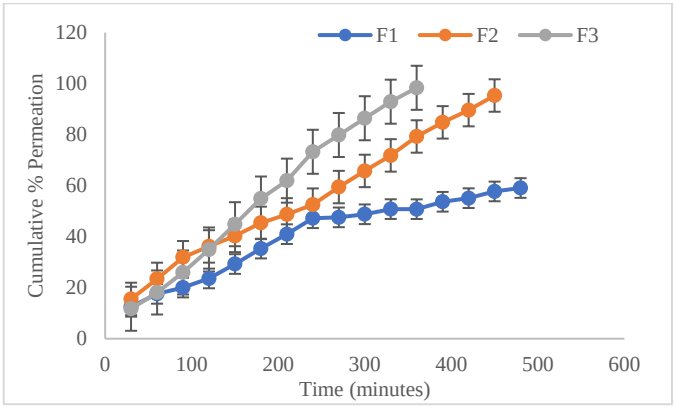

Figure II(b). *In* vitro permeation profiles of losartan potassium from HPMC K15M-Eudragit RL 100-Carbopol 934P buccal films in simulated saliva (pH 6.8).

Table III. Model dependent and independent value from release and permeation data.

Release Data	Formulation		
	F1	F2	F3
Higuchi rate constant (mg.min$_{-0.5}$)	3.0569	3.9585	4.5945
Diffusional exponent (n)	0.526	0.520	0.620
t_{50} (minutes)	222	196	147
Permeation Data	**Values Of Model-Dependent and Independent Parameters**		
Zero order rate constant (mg.min^{-1})	0.1697	0.2294	0.2885
t_{50} (min)	316	220	165
Jss (mg/cm^2. minutes)	0.1114	0.1246	0.1623
Kp	0.1197	0.1339	0.1745

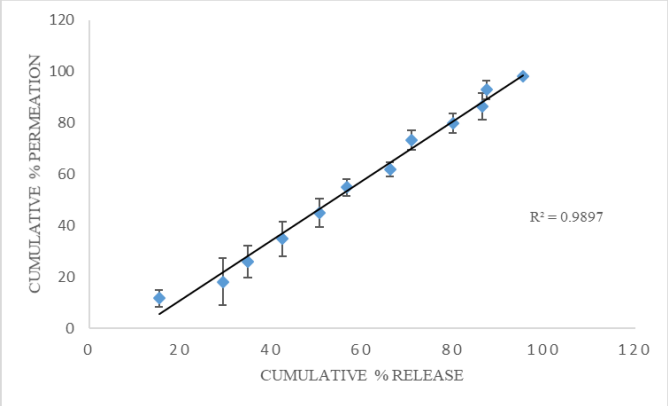

Figure III. Correlation between in vitro drug release and permeation profiles of losartan potassium-loaded buccal films with HPMC K 15M and Eudragit RL 100 in the ratio of 3:1.

A good correlation was found between *in vitro* release and permeation profiles (r^2 = 0.9897) for F3, and for the other two formulations, the r^2 was above 0.98 (Figure III).

DISCUSSION

The physical mixture of losartan potassium with HPMCK15M, Eudragit RL100, and Carbopol 934P did not reveal any incompatibility. The thickness and diameter of the buccal films were found to be acceptable for easy handling before and during administration. The surface pH (at 25 ºC) values matched the reported values of 6.28±0.25 to 6.98 ± 0.01 [53, 54, 55] and were thus physiologically compatible, posing no risk of irritation, discomfort, or inflammation of the buccal mucosa [16]. In healthy humans, the pH of the saliva lies between 6.3 and 7.3 [36,54].

Drug loading efficiency was identical to the values for ramipril buccal patches [39, 42]. The low standard deviations in drug loading efficiency values indicates a homogeneous distribution of the drug in the formulations [56].

Analysis of the buccal films' mechanical characteristics revealed tensile strength, percentage elongation at break, and peel strength depended on the amount of Eudragit RL 100. The percentage elongation at break values of the films varied between 62-80%. In a study on terbinafine hydrochloride buccal films of HPMC-PVP K30, the percentage elongation at break values was found to depend on changes in the percentages of HPMC or PVP [57]. Since the percentage of HPMC in the films was fixed in the present investigation, slight variations in the parameter might be attributed to variation in the percentage of Eudragit RL 100. The greater the amount of Eudragit in the films, the better the mechanical strength and stability of the film. Eudragit RL 100–based bioadhesive buccal patches of tizanidine demonstrated a folding endurance value of 91, while in the present case, the value (>150) is much higher, indicating the positive impact of HPMC on the film flexibility [58, 59]. Folding endurance (>150) was found to be acceptable imparting a satisfactory degree of flexibility to the film. This is extremely preferable, as it would prevent easy dislodging of the films from the site of application or rupture of film during positioning in the buccal cavity [58]. Tensile strength values were slightly higher than those for buccal films of losartan potassium made from hydrophilic polymers [42]. In the literature, wide variation in the mechanical parameters could be attributed to differences in the film composition. Reported values of peel strength were found to be much lower in transdermal patches made of polyvinylpyrrolidone-ethylcellulose-HPMC-chitosan than the observed values [24].

For a buccal film to work efficiently, the film must be hydrated and swell to adhere to the buccal mucosa. The swelling of films was affected by the proportion of hydrophilic HPMC and hydrophobic Eudragit and was reduced by Eudragit-RL100 [59]. Similar observations were made in the present study. The swelling index values for the films of three different compositions indicates a decrease with an increase in the amount of hydrophobic Eudragit from F3 to F1. In the literature, the swelling index values of mucoadhesive films with HPMC-chitosan-Carbopol 934P, HPMC K15M-Carbopol-PEG 6000, and HPMC-sodium alginate-Carbopol 934P were found to lie between 10-33 [60, 61, 62, 63, 64, 65]. However, the HPMC K15M-Eudragit RL 100 films exhibited much higher swelling index values. The rapid imbibition of aqueous medium by HPMC is likely to make the film porous, facilitating the influx of bulk medium and ultimately accelerating the dissolution of losartan potassium molecules followed by their diffusion out of the film [59]. Therefore, F3, with a significantly higher swelling index, should adhere strongly to the mucosal surface and exhibit the desired release profile. Statistically insignificant differences in the work of adhesion values might have resulted from the same percentage of Carbopol 934P in the films. The mucoadhesive strength has been reported as 3760-5617dynes/cm^2 or 9-12g [59, 62, 63, 64]. However, the values for the films under investigation were low, although the swelling index was better.

As expected, F3, with minimum Eudragit and maximum HPMC, offered the least hindrance to the absorption of simulated saliva and exhibited maximum *in vitro* drug release. The incorporation of hydrophobic Eudragit in the composition retarded the release of glipizide from bio-adhesive films [59]. Meher *et. al.* (2013) reported 71-75% release of carvedilol in 12 hrs from HPMC K15M: Eudragit RSPO: Carbopol 934P: methylcellulose films [36]. Films made with different proportions of HPMC K 15M and Eudragit RL 100/Carbopol 934P released 72-96% anti-hypertensive drugs in 3-24 hrs [21, 38, 39, 40, 66, 67]. In the case of losartan potassium, more than 90% release was observed from buccal films of HPMC K15M-Eudragit RL 100 and Eudragit E 100-PVP K30 [21, 22]. No loss in the structural integrity of the buccal films could be

detected during the *in vitro* dissolution test, indicating swelling- and diffusion-controlled drug release [56]. *Ex vivo* permeation studies of losartan potassium and other anti-hypertensives from buccal films of hydrophilic polymers revealed 76-99% in 6-24 hrs [20, 34, 38, 39, 67, 68, 69]. In the present study, faster permeation might have been due to the use of artificial dialysis membrane instead of animal buccal mucosa.

The polymeric combination resulted in a matrix type of buccal film, as evident from compliance with Higuchi kinetics. Kinetic modeling of drug release data from films made of Eudragit E 100-PVP K 30 and HPMC-PVP-Carbopol 940 suggested matrix formation [21, 70].

Drug release occurred by Fickian diffusion from F1 and F2 and by non-Fickian or anomalous diffusion from F3 (Table III). Non-Fickian diffusion suggests the involvement of polymer swelling and chain relaxation due to swellable HPMC. Both Fickian and non-Fickian diffusion have been reported to occur from films made of HPMC-Eudragit [27, 28, 29]. Zero-order kinetics of drug permeation across dialysis membrane indicates a constant rate of permeation, an ideal and desirable behavior for buccal films. Higher values of steady-state flux indicate permeation of a greater amount of the drug at a faster rate through the same unit area of films with comparable properties. Since the goal of the present investigation is to fabricate buccal films through which drug release occurs in a controlled manner and released drug permeates through the buccal mucosa at a constant rate, the selection of optimum film depends significantly on magnitudes of steady-state flux and apparent permeability coefficient. With piroxicam cocrystal-loaded buccal films, the flux values were relatively lower than in the present case with F3, and with atenolol films, the reported value of steady-state flux was quite higher, which might be due to the presence of sodium alginate instead of any hydrophobic polymeric film former [62, 71, 72].

Future prospects

Further formulation development is necessary to improve mucoadhesive strength, controlled and complete release, and permeation of losartan potassium at a constant rate within 4 hrs. Since the time gap between two consecutive food intakes is usually 4 hrs, this is considered an important criterion. Before conducting *in vivo* studies in suitable animal models, *ex vivo* permeation studies and *in vitro* stability studies should be planned. Lastly, studies to assess the irritation and toxicity potential of the film on the buccal mucosa need to be conducted.

CONCLUSION

Fabrication of buccal films with varying ratios of HPMC K15M and Eudragit RL 100, while loading of fixed percentages of losartan potassium and Carbopol 934P, indicates a significant effect of the relative amounts of hydrophilic and hydrophobic polymers on *in vitro* drug release, permeation profiles, and drug diffusion mechanism. In summary, it can be concluded that the optimum ratio of HPMC K15M-Eudragit RL 100 (3:1) can lead to buccal films with satisfactory organoleptic, physicochemical, and mechanical properties, achieving sustained release and permeation of losartan potassium for the management of aberrant and fluctuating problems hypertension. This formulation could be particularly beneficial for ambulatory patients, bedridden patients, or those with serious health issues that preclude the administration of frequent oral doses or injections.

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CONFLICT OF INTEREST

No conflict of interest declared.

REFERENCE

[1] Geevar Z, Krishnan M N, Venugopal K, Sanjay G, Harikrishnan S, Mohanan PP, *et al*. Prevalence, awareness, treatment, and control of hypertension in young adults (20–39 Years) in Kerala, South India. Front Cardiovasc Med 2022; 9:1-11. https://doi.org/10.3389/fcvm.2022.765442

[2] Ezzati M, NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. Lancet 2021; 398:957-80. https://doi.org/10.1016/s0140-6736(21)01330-1

[3] Shipp L, Liu F, Varsani L K, Okwuosa T C. Buccal films: A review of therapeutic opportunities, formulations & relevant evaluation approaches. J Contr Release 2022; 352:1071-92. https://doi.org/10.1016/j.jconrel.2022.10.058

[4] Yelave A, Bhagwat G. Mucoadhesive buccal films: A novel approach for the delivery of anti-hypertensive drugs. Asian J Pharm Clin Res 2021;14(4):12-21. http://dx.doi.org/10.22159/ajpcr.2021.v14i4.40654

[5] Gite S S, Shinkar D M, Saudagar R B. Mucoadhesive buccal drug delivery: An overview. J Adv Pharm Educ Res 2013;3(4):319-32.

[6] RxList®, drugs a-z list belbuca (buprenorphine buccal film) drug; [cited November 19, 2024]. Available from https://www.rxlist.com/belbuca-drug.htm

[7] Cleveland Clinic, Health Library/Drugs, Devices & Supplements/Buprenorphine Buccal Film; [cited November 19, 2024]. Available from https://my.clevelandclinic.org/health/drugs/19285-buprenorphine-buccal-film

[8] BioXcel Therapeutics, Inc. How to Take IGALMI™ (dexmedetomidine); [cited November 19, 2024]. Available from https://www.igalmi.com/bipolar-disorder/how-to-take-igalmi

[9] National Library of Medicine, National Center for Biotechnology of Information; [cited November 19, 2024]. Available from https://pubchem.ncbi.nlm.nih.gov/compound/Losartan-Potassium

[10] WebMD LLC, Drugs & Medications Losartan (Cozaar); [cited November 19, 2024]. Available from https://www.webmd.com/drugs/2/drug-6616/losartan-oral/details

[11] Dave V, Sohgaura A, Tak K, Reddy KR, Thylur RP, Ramachandraiah K, et al. Ethosomal polymeric patch containing losartan potassium for the treatment of hypertension: In-vitro and in-vivo Evaluation. Biomed Phys Eng Expr 2019; 5:1-14. http://dx.doi.org/10.1088/2057-1976/ab4fa4

[12] Gorle A, Patil P, Bhaskar R, Ola M. Development and evaluation of buccal film containing antihypertensive agent. The Pharma Innovation J 2015;4(1):53-60.

[13] Nappinnai M, Chandanbala R, Balaijirajan R. Formulation and evaluation of nitrendipine buccal films. Ind J Pharm Sci 2008; 70 :631-35. https://doi.org/10.4103/0250-474X.45402

[14] Hanif M, Zaman M, Chaurasiya V. (2014). Polymers used in buccal film: A review. Designed Monomers Polymers 2014; 18:105–11. https://doi.org/10.1080/15685551.2014.971389

[15] Wanasathop A, Patel PB, Choi HA, Li SK. Permeability of buccal mucosa. Pharmaceutics 2021; 13:1814. https://doi.org/10.3390/pharmaceutics13111814

[16] Hans E. Junginger, Janet A. Hoogstraate, J.Coos Verhoef. Recent advances in buccal drug delivery and absorption — *in vitro* and *in vivo* studies. J Contr Rel 1999; 62:149-59. https://doi.org/10.1016/s0168-3659(99)00032-2

[17] Sadique S, Sri S R. Preparation and evaluation of fast dissolving oral film of losartan potassium. Res J Pharm Dosage Forms Tech 2020;12(1):13-16. https://doi.org/10.5958/0975-4377.2020.00003.8

[18] Raza S N, Kar A H, Wani T U, Khan N A. Formulation and evaluation of mouth dissolving films of losartan potassium using 3^2 factorial design. Int J Pharm Sci Res 2018;10(3):1402-11. http://dx.doi.org/10.13040/IJPSR.0975-8232.10(3).1402-11

[19] Singh A, Srivastava A, Saxena P, Jough S S, Tiwari P, Srivastava. Delivery of drug via buccal drug delivery system in the form of patch for the anti-hypertension disease. Int J Pharm Biol Sci 2018 8(1):327-34.

[20] Shivhare U D, Bodkhe PD, Bhusari K P, Mathur V B. Formulation and evaluation of buccoadhesive films of losartan potassium. Der Pharmacie Lettre 2010; 2: 251-60. https://doi.org/10.37022/jiaps.v8i3-S.528

[21] Basha D C, Sudha B N. A brief chronological overview of buccal film formulations. Chettinad Health City Med J. 2022; 11:53-60. http://dx.doi.org/10.24321/2278.2044.202241

[22] Ikram MD, Gilhotra N, Gilhotra RM. Formulation and optimization of mucoadhesive buccal patches of losartan potassium by using response surface methodology. Adv Biomed Res 2015; 4:239-52. https://doi.org/10.4103/2277-9175.168606

[23] Ericka A A, Pablo S C, Roberto D T, Jose Juan EC. Design and evaluation of losartan transdermal patch by using solid microneedles as a physical permeation enhancer. Iran J Pharm Res 2020;19 :138-52. https://doi.org/10.22037/ijpr.2019.1100912

[24] Fatima A A, Chukwuka U K. Development and *in-vitro* evaluation of matrix-type transdermal patches of losartan potassium. Univers J Pharm Res 2017;2 :39-43. http://dx.doi.org/10.22270/ujpr.v2i2.R5

[25] Pisipati A, Venkata Satya S C. Formulation and characterization of antihypertensive transdermal delivery system. J Pharm Res 2013; 6:551-54.

[26] Mohapatra P K, Boddu P K, Patel P S, Verma H C, Sahoo S. Development and evaluation of trans buccal patches based on natural and synthetic polymers loaded with rivastigmine using solvent casting technique. Res J Pharm Technol. 2021;14(10):5133-40. https://doi.org/10.52711/0974360X.2021.00894

[27] Joshi R, Garud N. Development, optimization and characterization of flurbiprofen matrix transdermal drug delivery system using Box–Behnken statistical design. Future J Pharm Sci 2021; 7:57. http://dx.doi.org/10.1186/s43094-021-00199-2

[28] Patra N, Priya R, Swain S, Jena G K,Panigrahi K C, Ghose D. Pharmaceutical significance of Eudragit: A review. Future J Pharm Sci 2017; 3:33-45. https://doi.org/10.1016/j.fjps.2017.02.001

[29] Bharath K V, Ashok K A, Sudheer B, Suresh K K, Srinivasa R V, Kirtinidhi K, *et. al.* Formulation design, *in-vitro* evaluation and stability studies on mucoadhesive buccal films of anti-anginal calcium channel blocker. J Appl Pharm Sci 2011;1(6):136-42.

[30] Sneidova E, Dittrich M. Snejdrova E, Dittrich M. Pharmaceutical applications of plasticized polymers. In. Md Luqman, editor. Recent advances in plasticizers, InTech, 2012. p 69-90. http://dx.doi.org/10.5772/36543

[31] Al-Dhubiab B E. *In-vitro* and *in-vivo* evaluation of nano-based films for buccal delivery of zolpidem. Braz Oral Res. 2016;30(1): e126. https://doi.org/10.1590/1807-3107bor-2016.vol30.0126

[32] Swathi N, Jayaprakash D. Formulation Development and evaluation of captopril mouth dissolving films. Int J Chemtech Res2019;12(3):17-27. http://dx.doi.org/10.20902/IJCTR.2019.120303

[33] Malipeddi V R, Awasthi R, Ghisleni D D M, Braga M D S, Kikuchi I S, Andreoli Pinto T D J, *et al*. Preparation and characterization of metoprolol tartrate containing matrix type transdermal drug delivery system. Drug Deliv Transl Res 2016; 9:1-9. https://doi.org/10.1007/s13346-016-0334-7

[34] Mane M, Patole N, Jadhav T. Studies on formulation and evaluation of buccal patch for delivery of an anti-hypertensive drug. Int J Innov Sci Res Tech 2022;7(11):536-43. https://doi.org/10.5281/zenodo.7374802

[35] Meher J G, Tarai M, Yadav N P, Patnaik A, Mishra P, Yadav K S. Development and characterization of cellulose–polymethacrylate mucoadhesive film for buccal delivery of carvedilol. Carbohydr Polym 2013; 96:172– 80. https://doi.org/10.1016/j.carbpol.2013.03.076

[36] Saifali T, Rehan D, Khan G J *et al.* Formulation and evaluation of floating matrix tablet of captopril and losartan potassium in treatment and management of hypertension. Int J Adv Res Innov Idea Edu 2022 8(4):20-28.

[37] Haju S, Yadav S. Formulation and evaluation of cilnidipine mucoadhesive buccal film by solvent casting technique for the treatment of hypertension. Int J Pharm Pharm Sci 2021;13(9):34-43. http://dx.doi.org/10.22159/ijpps.2021v13i9.42641

[38] Anil A, Sudheer P. Design and evaluation of mucoadhesive buccal patch of ramipril. Int J Pharm Sci Rev Res 2018; 50 :121-29.

[39] Bada P K, Sahu P K, Abhinov T. Simple spectrophotometric methods for simultaneous determination of losartan potassium and atorvastatin calcium in combined dosage forms. J Chem Pharm Sci 2011 4(3):127-31.

[40] Koland M, Charyulu N R. Design and *in-vivo* evaluation of buccoadhesive hydrophilic polymer matrix films of losartan potassium. IndJ Pharm Edu Res 2016;50(2):115-24. http://dx.doi.org/10.5530/ijper.50.2.26

[41] Mukhopadhyay R, Gain S, Verma S, *et al.* Polymers in designing the mucoadhesive films: A comprehensive review. Int J Green Pharm 2018; 12(2):1-15. https://doi.org/10.22377/ijgp.v12i02.1783

[42] Eleftheriadis G, Monou P, Bouropoulos N, *et al.*, Fabrication of mucoadhesive buccal films for local administration of ketoprofen and lidocaine hydrochloride by combining fused deposition modeling and inkjet printing. J Pharm Sci. 2020;109:2757-66. https://doi.org/10.1016/j.xphs.2020.05.022

[43] Khan N, Darwis Y, Khiang P K. Preliminary investigation of in-vitro bioadhesive properties of selected natural gums. Archives Pharm Pract. 2015;6(1):3-11. http://dx.doi.org/10.4103/2045-080X.151280

[44] Kumar Y G, Sreekanth J, Satyavati D, *et al*. Formulation design and invitro evaluation of sustained release matrix tablets of losartan potassium using HPMC polymers. Int J Pharm Tech Res 2013;5(3):1332-44.

[45] Daru H, Daru Z. Thiolation of arabinoxylan and its application in the fabrication of controlled release mucoadhesive oral films. J Pharm Sci 2017;25(6):1-13. https://doi.org/10.1186/s40199-017-0172-2

[46] Mohamed M I, Haider M, Muaadh A Mohamed Ali. Buccal mucoadhesive films containing antihypertensive drug: *In-vitro/in-vivo* evaluation. J Chem Pharm Res 2011;3(6):665-86.

[47] Shimadzu, FTIR Talk Letter, volume 2; [cited November 20, 2024]. Available from https://www.shimadzu.com

[48] Bhusara H S, Patel A T, Patel M D. Development of gastroretentive floating tablets of losartan potassium by sublimation method. Int J Pharm Chem Anal 2021; 8:66-74. http://dx.doi.org/10.18231/j.ijpca.2021.014

[49] Mahmood A, Mahmood A, Ibrahim M A, *et al*. Development and evaluation of sodium alginate/Carbopol 934P-co-poly (methacrylate) hydrogels for localized drug delivery. Polymers (Basel). 2023;15(2):311. https://doi.org/10.3390/polym15020311

[50] Salatin S, Barar J, Barzegar-Jala li M, *et al*. Formulation and evaluation of Eudragit RL-100 nanoparticles loaded in-situ forming gel for intranasal delivery of rivastigmine. Adv Pharm Bull. 2020; 1:20-29. https://doi.org/10.15171/apb.2020.003

[51] El-Masry S M, Helmy S A. Hydrogel-based matrices for controlled drug delivery of etamsylate: Prediction of in-vivo plasma profiles.Saudi Pharm J 2020. Article in Press. https://doi.org/10.1016/j.jsps.2020.10.016

[52] Gannu R, Vamshi Vishnu Y, Kishan V, Madhusudan Rao Y. Development of nitrendipine transdermal patches: in-vitro and ex-vivo characterization. Curr Drug Deliv 2007 4:69-76. https://doi.org/10.2174/156720107779314767

[53] Salehi S, Boddohi S. New formulation and approach for mucoadhesive buccal film of rizatriptan benzoate. Prog Biomater. 2017; 6:175-87. https://doi.org/10.1007/s40204-017-0077-7.

[54] Abdella S, Afinjuomo F, Song Y, *et al.* Mucoadhesive buccal film of estradiol for hormonal replacement therapy: Development and i*n-vivo* performance prediction. *Pharmaceutics* 2022; *14:542*. https://doi.org/10.3390/pharmaceutics14030542

[55] Pereira F F, Campos A F, daCruz F, et al. Manufacture and characterization of mucoadhesive buccal films based on pectin and gellan gum containing triamcinolone acetonide, Int J Polym Sci 2018;2403802, 10 pages. https://doi.org/10.1155/2018/2403802

[56] Arpa M D, Ünükür M Z, Erim Ü C. Formulation, characterization and *in vitro* release studies of terbinafine hydrochloride loaded buccal films. J Res Pharm. 2021; 25: 667-80. http://dx.doi.org/10.29228/jrp.58

[57] Pendekal M S, Tegginamat P K, Formulation and evaluation of a bioadhesive patch for buccal delivery of tizanidine, Acta Pharm Sinica B, 2012;2(3) :318-24. https://doi.org/10.1016/j.apsb.2011.12.012

[58] Semalty M, Semalty A, Kumar G. Formulation and characterization of mucoadhesive buccal films of glipizide. Ind J Pharm Sci. 2008; 70:43-48. https://doi.org/10.4103/0250-474X.40330

[59] Lodhi M, Dubey A, Narayan R, *et al*. Formulation and evaluation of buccal film of Ivabradine hydrochloride for the treatment of stable angina pectoris. Int J Pharm Investig. 2013;3(1):47-53. https://doi.org/10.4103/2230-973X.108963

[60] Nair A B, Al-Dhubiab B E, Shah J, *et. al.* Mucoadhesive buccal film of almotriptan improved therapeutic delivery in rabbit model. Saudi Pharm J. 2020; 28(2):201-209. https://doi.org/10.1016/j.jsps.2019.11.022

[61] Ammanage A, Rodriques P, Kempwade A. Formulation and evaluation of buccal films of piroxicam co-crystals. Future J Pharm Sci 2020; 6:1-16. https://doi.org/10.1186/s43094-020-00033-1

[62] Begum, Yasmin M, Alqahtani, Ali, Ghazwani, Mohammed, *et. al.* Preparation of Carbopol 934 based ketorolac tromethamine buccal mucoadhesive film: *In-vitro*, *ex-vivo*, and *in-vivo* assessments. Int J Polymer Sci 2021; 4786488:1-11. https://doi.org/10.1155/2021/4786488

[63] Tan Y T, Peh KK, Al-Hanba O. Investigation of interpolymer complexation between Carbopol and various grades of polyvinylpyrrolidone and effects on adhesion strength and swelling properties. J Pharm Pharm Sci. 2001;4(1):7-14.

[64] Samanthulai K, Mahendra Kumar C B, Bairi A, Satla S. Development, in-vitro and ex-vivo evaluation of muco-adhesive buccal tablets of hydralazine hydrochloride. Braz J Pharm Sci. 2022;58:e18635. http://dx.doi.org/10.1590/s2175-97902020000318635

[65] Verma S, Malik V, Ashima. Formulation, evaluation and optimization of transdermal patches of losartan potassium. World J Pharm Sci 2016;4(5):277-84.

[66] Benedict A, Paul I R, Mathews M M, *et al*. Formulation and evaluation of buccal film of an antihypertensive drug. J Innov Appl Pharm Sci. 2013;8[3-S]:75-80. http://dx.doi.org/10.37022/jiaps.v8i3-S.528

[67] Yelave A, Bhagwat G S, Siddique A R. Incorporation of antihypertensive Class iv drug in novel buccal film formulation. Asian J Pharm Res. 2024;14(1):15-4.

[68] https://doi.org/10.52711/2231-5691.2024.00003

[69] Narayan S, Adhikari R, Panda S. Development evaluation and characterization of losartan potassium buccal patches using hydrophilic polymers. Int J Pharm Sci Res 2018;9(12): 5474-84. https://doi.org/10.13040/IJPSR.0975-8232.9(12).5474-84

[70] Muzib Y I, Kumari K S. Mucoadhesive buccal films of glibenclamide: Development and evaluation. Int J Pharm Investig 2011; 1(1):42-7. https://doi.org/10.4103/2230-973X.76728

[71] Md Ali M A, Md Sabati A, Ali A. Formulation and evaluation of baclofen mucoadhesive buccal films. FABAD J Pharm Sci. 2017;42(3);179-90.

[72] Adhikari S N R, Nayak B S, Nayak A K, Mohanty B. Formulation and evaluation of buccal patches for delivery of atenolol. AAPS Pharm Sci Tech 2010;11(3):1038-40. https://doi.org/10.1208/s12249-010-9459-z

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Original Research Article

Public's Willingness to Pay for COVID-19 Self-Test Kits in Malaysia: A Web-Based Survey

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ABSTRACT

Introduction: The COVID-19 Antigen Rapid Test Kit (self-test) has been a critical tool in Malaysia's public health response, approved by the Ministry of Health (MOH) for detecting COVID-19 antigens using saliva or nasal swabs. This study evaluates the public's willingness to pay (WTP) for these self-test kits and identifies the factors influencing this willingness. **Method:** A cross-sectional, web-based survey was conducted among members of the public in Malaysia from March to December 2022. The self-administered questionnaire assessed respondents' exposure to COVID-19, vaccination status, awareness of self-test kits, and WTP. The contingent valuation method was applied, with price points ranging from RM 3.00 to RM 20.00. **Results:** Among the 268 respondents, 96.6% had previously purchased a COVID-19 self-test kit, and 91.0% were aware of both nasal and saliva-based kits. A majority (73.5%) expressed a willingness to pay for these kits, with a mean maximum price of RM 9.16 and a median of RM 6.00. Significant predictors of higher WTP included female gender (P = 0.013) and student status (P = 0.013). The primary reasons for refusal to pay were cost and affordability (62.7%). **Conclusion:** This study demonstrates a strong willingness among the Malaysian public to pay for COVID-19 self-test kits. These findings provide critical insights for policymakers and health authorities in setting prices and considering subsidies to enhance public health preparedness for future pandemics.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by a newly discovered coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), which was initially discovered in Wuhan, China, in December 2019 [1]. Data from 2019 has estimated about 5.09 million people died from COVID-19 worldwide, with Malaysia contributing 1.71% of all deaths [2]. According to the most recent data records from the KKMNOW (Ministry of Health's One-stop Centre for Malaysia's Health Data) website on 22nd April 2024, Malaysia has recorded a total of 37,349 deaths [3].

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One of the important public health measures against COVID-19 advocated by the World Health Organisation (WHO) is to ensure the availability of COVID-19 Rapid Diagnostic Tests (RDT) in the community [4]. In accordance with Malaysia's, Prevention and Control of Infectious Diseases Act 1988 (Act 342), testing plays a crucial role in the early identification of cases and close contacts to manage the cases and implement preventative and control measures. The COVID-19 Antigen Rapid Test Kit (self-test) is an RDT device approved by Ministry of Health Malaysia (MOH) and Medical Device Authority (MDA) for the detection of antigens causing COVID-19 by using saliva or nasal swab.

Rapid test-kit antigen (RTK-Ag) detects SARS-CoV-2 viral proteins directly and offers the advantage of providing fast results, being affordable, and being suitable for point-of-care testing [5]. It has been used in Malaysia since May 6, 2020, as an alternative to reverse-transcription polymerase chain reaction (RT-PCR) testing, providing results in a shorter period and offering services when RT-PCR testing is not readily available. The RDT kits are widely available and can be purchased at community pharmacies and private health facilities, or supplied by MOH facilities as required [6].

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In a bid to encourage regular self-testing, the government has gradually reduced the prices of the RTD kits to increase their affordability for the public. Despite their widespread availability and the potential to change the scenario of COVID-19 diagnosis and management, in-depth explorations of the public's willingness to pay for the COVID-19 RDT kits are still important to guide price setting, price differentiation, price subsidization, and other program design features that enhance affordability, equity, and uptake.

This study was designed to assess the extent of willingness to pay, awareness, and perceptions among the public on the COVID-19 self-test kits, as well as to examine the level and determinants behind their willingness of pay for the self-testing kits.

METHOD

This was a cross-sectional descriptive survey involving the public, conducted from March to December 2022. Malaysian citizens aged 18 years old and above, without cognitive disabilities who understand Malay and English language were included. Those refused to provide consent excluded from the study. To determine the sample size, as there was no consensus on the optimal sample size for Willingness-To-Pay (WTP) studies [7], a minimum target of 250 responses was set.

The data collection tool comprised of sections on history of exposure to COVID-19 infection (1 question), COVID-19 vaccination status (3 questions), awareness of the COVID-19 self-test kits (3 questions), attitude towards COVID-19 self-test kits (1 question), willingness to pay for the COVID-19 test kits (14 questions), and demographic data of the respondents (7 questions). The questions were developed in consultation with senior pharmacists, with specific WTP questions on WTP modelled after a similar study conducted in Kenya [8].

Questions regarding COVID-19 vaccination status included the number of doses received and their types. The awareness section assessed knowledge about the existence of COVID-19 self-test kits, types available and whether respondents had purchased COVID-19 test kits prior to the study. The attitude sectionincluded 10 multiple-choice questions with "Yes" or "No" options, asking respondents about their willingness to conduct COVID-19 self-tests under various scenarios, such as before and after interstate or international travel, before attending courses or meetings, or when symptomatic or a close contact of a confirmed case.

The assessment of WTP was divided into two main aspects. First, we evaluated perspectives on who should cover the costs of COVID-19 self-test kits – either individuals, employers, the government, or healthcare insurance providers- either partially or in fully. Respondents were also asked if they were willing to pay for their own COVID-19 self-test kits before evaluating their willingness to pay at different prices. A dichotomous-choice (Yes or No) contingent valuation method was applied to gauge WTP at prices, ranging from RM 3.00 to RM 20.00 per set of COVID-19 test kit, with increments of RM 2.00 to RM 3.00 price between each bid. Additionally, respondents indicated the maximum price they were willing to pay for a COVID-19 self-test kit. If the respondents were not willing to pay for a COVID-19 self-test kit, they were required to inform the underlying reasons.

Demographic data collected in included ethnicity, age, gender, current state of residence, location category of residence (urban, suburban or rural), highest education level (primary, secondary, college/university or no formal education), occupation (government, private/self-employment, student, retiree or unemployed), living status (alone, with family or with non-family members), and monthly household income.

The pilot study revealed redundancy in two questions, which were combined: "No history of COVID-19 contact whatsoever" and "History of being a person under investigation (PUI) or person under surveillance (PUS)". The finalised questionnaire was produced electronically via Google Forms, and disseminated through social media platforms, namely Facebook, Instagram, Twitter and WhatsApp messenger, to promote public participation.

IBM SPSS Statistics Version 20.0 was used to analyse the study findings. Descriptive statistics were used to describe demographic data of the respondents, including the use of Chi-Square or Fischer-Exact Tests for categorical data comparison. Numerical data, presented as means with standard deviations were analysed via T-Test or Mann-Whitney Tests. Pearson's and Spearman's Correlation Co-efficient tests were used to evaluate the association between different variables.

This study was registered with the National Medical Research Register (NMRR ID-22-00132-GWX). Ethical approval was obtained from the Medical Research Ethics Committee (MREC) in the Ministry of Health Malaysia before commencement of the study.

RESULTS

Demographic characteristics

A total of 280 responses were initially received from the survey. However, upon further screening, 12 respondents did not fulfil the inclusion criteria of the study, including nationality and age limits, and was hence excluded from our analysis. This resulted in a final total of 268 respondents (no duplicate or missing data were found among the finalised sample). The demographic

Table I. Demographic Characteristics (n=268)

Demographic Characteristic	Demographic Characteristic	n (%)
Age group	18-25	57 (21.3)
	26-35	60 (22.4)
	36-45	71 (26.5)
	46-55	70 (26.1)
	56-65	8 (3.0)
	65 and above	2 (0.7)
Gender	Male	66 (24.6)
	Female	202 (75.4)
Race	Malay	237 (88.4)
	Chinese	20 (7.5)
	Indian	9 (3.4)
	Minangkabau	1 (0.4)
	Suluk	1 (0.4)
Residence	Current State of Kedah	124 (46.3)
	Selangor	32 (11.9)
	Perak	28 (10.4)
	Wilayah Persekutuan Kuala Lumpur	17 (6.3)
	Pahang	14 (5.2)
	Pulau Pinang	12 (4.5)
	Johor	11 (4.1)
	Kelantan	11 (4.1)
	Terengganu	6 (2.2)
	Negeri Sembilan	4 (1.5)
	Sabah	4 (1.5)
	Melaka	2 (0.7)
	Sarawak	2 (0.7)
	Wilayah Persekutuan Labuan	1 (0.4)
Location of Residence	Urban	149 (55.6)
	Suburban	60 (22.4)
	Rural	59 (22.0)
Education Level	College/University	236 (88.1)
	Secondary School	31 (11.6)
	No Formal Education	1 (0.4)
Occupation	Government	139 (51.9)
	Private/Self	78 (29.1)
Employment	Retired	8 (3.0)
	Student	23 (8.6)
	Unemployed	20 (7.5)
Living Status	Alone	26 (9.7)
	With Family	225 (84.0)
	With Non-Family	17 (6.3)
Monthly Household Income	Less than RM1,000	10 (3.7)
	RM1,001-RM2,000	28 (10.4)
	RM2,001-RM3,000	34 (12.7)
	RM3,001-RM4,000	46 (17.2)
	RM4,001-RM5,000	29 (10.8)
	More than RM5,000	121 (45.1)

characteristics of the respondents are illustrated in Table I. The majority of the respondents were female (n=202, 75.4%), aged between 36-45 years (n=71, 26.5%), Malay (n = 237, 88.4%), residing in Kedah state (n=124. 46.3%), living in urban area (n=149, 55.6%), having completed tertiary education (n=236, 88.1%), working in the government sector (n=139, 51.9%), living with family members (n=225, 84.0%), and with a monthly household income of more than RM5000 (n=121, 45.1%).

Exposure to COVID-19 infection

The responses regarding our respondents' history of exposure to COVID-19 infection are illustrated in Table II. The majority of our respondents had not been infected by COVID-19 (n=152, 56.7%) nor classified as a Person under Investigation (PUI) or Person Under Surveillance (PUS) (n=144, 53.7%). A vast majority had also not been hospitalised or admitted to COVID-19 Treatment and Quarantine Centres (PKRC) due to COVID-19 infection (n=269, 97.0%), and reported no history of death among family members (n=221, 82.5%) or acquaintances (n=185, 69.0%) due to COVID-19 infection. Nevertheless, the majority of them had family members (n=207, 77.2%) or close acquaintances (n=257, 95.9%), who were infected by COVID-19, experienced COVID-19 cases in their neighbourhood (n=244, 91.0%) or at their workplace (n=226, 84.3%), and with experience of being tested for COVID-19 infection via RTK-Ag or PCR testing (n=227, 84.7%).

COVID-19 vaccination status

The details of respondents' COVID-19 vaccination status are illustrated in Table III. A vast majority of our respondents received at least 2 doses of COVID-19 vaccines (n=267, 99.6%), primarily the Pfizer Comirnaty Vaccine (n=186, 69.4%).

Table III. Vaccination status (n=268)

Question	Frequency, n	Percentage (%)
Vaccination status		
Partially vaccinated	1	0.4
Fully vaccinated	46	17.2
Received booster dose	221	82.5
Types of vaccine received		
Pfizer	186	69.4
Sinovac	47	17.5
Astra Zeneca	27	10.1
Johnson & Johnson	1	0.4
Mix	7	2.6

Table II. Exposure to COVID-19 infection

Questions	Frequency		P-Value
	Yes	No	
History of being infected by COVID-19	116 (43.3)	152 (56.7)	0.028
History of being a person under investigation (PUI) or person under surveillance (PUS)	124 (46.3)	144 (53.7)	0.222
History of hospitalizations or admission to PKRC due to infected with COVID-19	8 (3.0)	260 (97.0)	<0.001
History of family member being infected by COVID-19	207 (77.2)	61 (22.8)	<0.001
History of a close acquaintance being infected by COVID-19	257 (95.9)	11 (4.1)	<0.001
History of death among family members due to COVID-19	47 (17.5)	221 (82.5)	<0.001
History of death among close acquaintance due to COVID-19	83 (31.0)	185 (69.0)	<0.001
History of COVID-19 case around neighbourhood area	244 (91.0)	24 (9.0)	<0.001
History of COVID-19 case at workplace area	226 (84.3)	42 (15.7)	<0.001
History of RTK-Ag/PCR test	227 (84.7)	41 (15.3)	<0.001

Experience of purchasing & awareness of the existence of COVID-19 self-test kit

The responses regarding awareness of COVID-19 self-test kits are illustrated in Table IV. All respondents were aware of the existence of COVID-19 self-test kits (n=268, 100%), and the majority (n=259, 96.6%) had purchased them before. Most respondents (n=252, 91.0%) were able to identify the types of COVID-19 self-test kit available in the market, which include nasal and saliva specimens.

Table IV. Awareness of the existence of COVID-19 self-test kit (n=268)

Question	Frequency, n	Percentage (%)
Did you know about the existence of COVID-19 self-test kit?		
Yes	268	100.0
Did you know the type of COVID-19 self-test kit?		
Nasal specimen	2	0.7
Saliva specimen	22	8.2
Both	244	91.0

Table V. Willingness to pay for the COVID-19 Self-Test Kit (n=268)

Willingness to pay	Yes	No	
Willingness to pay for the COVID-19 Self-Test Kit	197 (73.5)	71 (26.5)	
Willingness to pay	**No**	**Yes, pay partially**	**Yes, pay fully**
Individuals have to spend their own money to pay for the COVID-19 self-test kit	69 (25.7)	97 (36.2)	102 (38.1)
Employer has to pay for the COVID-19 Self-Test Kit	41 (15.3)	80 (29.9)	147 (54.9)
Government has to pay for the COVID-19 self-test kit	41 (15.3)	99 (36.9)	128 (47.8)
Health insurance has to pay for the COVID-19 self-test	44 (15.3)	59 (22.0)	168 (62.7)

Willingness to pay for the COVID-19 self-test kit

The details on respondents' willingness-to-pay for COVID-19 self-test kits are illustrated in Table V. The majority of our respondents were willing to pay for the COVID-19 self-test kits (n=197, 73.5%). 74.3% (n=199) of the respondents agreed that individuals should spend their own money to pay for the COVID-19 self-test kits, either partially or fully. However, they also perceived that the employers (n=227, 84.7%), the government (n=227, 84.7%), and the health insurance providers (n=227, 84.7%) should also partially of fully fund the COVID-19 self-test kits.

Table VI illustrats the reasons why some respondents refused to pay for the COVID-19 self-test kits. Out of 71 respondents who disagreed to pay for COVID-19 Self-test kits, 70 of them provided their reasons (n=80), which included cost and affordability issues (n=52, 65.0%), the number of family members to subsidise (n=11, 13.8%), and the need to test frequently (n=10, 12.5%), as summarized in Table VI.

The extent of willingness-to-pay for COVID-19 self-test kits based on price differences is further illustrated in Figure I. Among the 198 respondents who answered this section, the majority of them were comfortable spending RM 3.00 to RM 6.00 for a set of COVID-19 self-test kit, with a mean maximum price of RM 9.16 (SE = 0.68) and a median maximum price of RM 6.00.

Table VI. Reasons of refuse to pay for COVID-19 self-test kit (No. of respondent answered = 70, no. of responses = 83)

Reason of unwillingness to pay	Frequency	Percent
Cost & affordability	52	62.7
The need to test frequently	10	12.0
The number of family members to subsidise	11	13.3
Unnecessary	7	8.4
The cost should be borne by the government and authorities	3	3.6

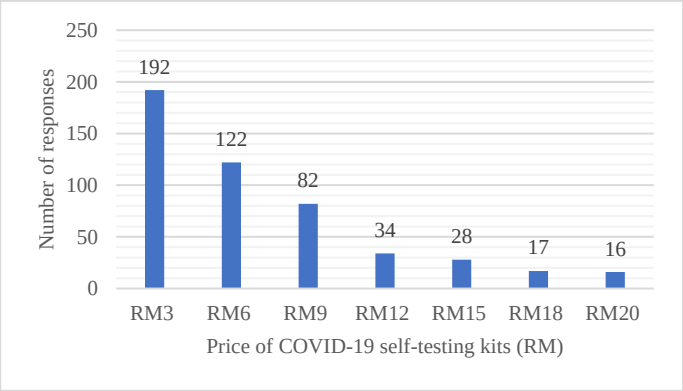

Figure I. The willingness of respondents to pay for COVID-19 self-test kit (n=198)

Attitude towards COVID-19 self-tests

Perspectives on attitudes towards performing COVID-19 self-tests under various situations are illustrated in Table VII (n=268). The majority of our respondents possessed a positive attitude towards COVID-19 self-tests; they were willing to take tests before interstate travel for work (n=221, 82.5%) or personal matters (n=214, 79.9%), before international travelling for work (n=228, 85.1%) or personal matters (n=225, 84.0%), after returning from interstate travel, and before starting work (n=231, 86.2%). They were also willing to perform COVID-19 self-tests prior to attending meetings or trainings sessions involving more than 30 participants (n=203, 75.7%), and importantly, when they are symptomatic (n=257, 95.9%) or when they became a closed contact (n=253, 94.4%).

Table VII. Attitude towards COVID-19 Self-Test Kit (n=268)

Question	Frequency		Percentage	
	Yes	No	Yes	No
Are you willing to take COVID-19 self-test for all of the followings:				
Before doing cross-state activities on work matters	221	47	82.5	17.5
Before doing cross-state activities on personal matters	214	54	79.9	20.1
Before doing cross-country activities on work matters	228	40	85.1	14.9
Before doing cross-country activities on personal matters	225	43	84.0	16.0
After returning from cross-state activities and before starting work	231	37	86.2	13.8
Before attending a meeting or training involving more than 30 participants	203	65	75.7	24.3
Before attending meetings or trainings involving participants from various districts or states	211	57	78.7	21.3
If symptomatic	257	11	95.9	4.1
If becoming a closed contact	253	15	94.4	5.6

Table VIII. Factors associated with willingness to pay for COVID-19 self-test kit (n=268)

Demographic Characteristic	n (%)	Willingness to pay, n (%)		p-value[a]
		Yes	No	
Age				0.300[a]
18-25	57 (21.3)	45 (78.9)	12 (21.1)	
26-35	60 (22.4)	47 (78.3)	13 (21.7)	
36-45	71 (26.5)	45 (63.4)	26 (36.6)	
46-55	70 (26.1)	52 (74.3)	18 (25.7)	
56-65	8 (3.0)	6 (75.0)	2 (25.0)	
65 and above	2 (0.7)	2 (100.0)	0 (0.0)	
Gender				0.013[b]
Male	66 (24.6)	41 (62.1)	25 (37.9)	
Female	202 (75.4)	156 (77.2)	46 (22.7)	
Race				0.073[a]
Malay	237 (88.4)	173 (73.0)	64 (27.0)	
Chinese	20 (7.5)	18 (90.0)	2 (10.0)	
Indian	9 (3.4)	5 (55.5)	4 (44.4)	
Minangkabau	1 (0.4)	0 (0.0)	1 (100.0)	
Suluk	1 (0.4)	1 (100.0)	0 (0.0)	
State of Residence				0.386[a]
Kedah	124 (46.3)	86 (69.4)	38 (30.6)	
Selangor	32 (11.9)	27 (84.4)	5 (15.6)	
Perak	28 (10.4)	23 (82.1)	5 (17.8)	
Wilayah Persekutuan Kuala Lumpur	17 (6.3)	11 (64.7)	6 (35.3)	
Pahang	14 (5.2)	9 (64.3)	5 (35.7)	
Pulau Pinang	12 (4.5)	10 (83.3)	2 (16.6)	
Johor	11 (4.1)	6 (54.5)	5 (45.5)	
Kelantan	11 (4.1)	8 (72.7)	3 (27.3)	
Terengganu	6 (2.2)	5 (83.3)	1 (16.7)	
Negeri Sembilan	4 (1.5)	4 (100.0)	0 (0.0)	
Sabah	4 (1.5)	4 (100.0)	0 (0.0)	
Melaka	2 (0.7)	2 (100.0)	0 (0.0)	
Sarawak	2 (0.7)	2 (100.0)	0 (0.0)	
Wilayah Persekutuan Labuan	1 (0.4)	0 (0.0)	1 (100.0)	
Location of Residence				0.491[a]
Urban	149 (55.6)	107 (71.8)	42 (28.2)	
Suburban	60 (22.4)	43 (71.7)	17 (28.3)	
Rural	59 (22.0)	47 (79.7)	12 (20.3)	
Education Level				0.470[a]
College/University	236 (88.1)	176 (74.6)	60 (25.4)	
Secondary School	31 (11.6)	20 (64.5)	11 (35.5)	
No Formal Education	1 (0.4)	1 (100.0)	0 (0.0)	
Occupation				0.013[a]
Government	139 (51.9)	104 (74.8)	35 (25.2)	
Private/Self Employment	78 (29.1)	58 (74.4)	20 (25.6)	
Retired	8 (3.0)	5 (62.5)	3 (37.5)	
Student	23 (8.6)	21 (91.3)	2 (8.7)	
Unemployed	20 (7.5)	9 (45.0)	11 (55.0)	
Living Status				0.236[a]
Alone	26 (9.7)	17 (65.4)	9 (34.6)	
With Family	225 (84.0)	165 (73.3)	60 (26.7)	
With non-family	17 (6.3)	15 (88.2)	2 (11.8)	
Monthly Household Income				0.071[a]
Less than RM1,000	10 (3.7)	5 (50.0)	5 (50.0)	
RM1,001-RM2,000	28 (10.4)	21 (75.0)	7 (25.0)	
RM2,001-RM3,000	34 (12.7)	19 (55.9)	15 (44.1)	
RM3,001-RM4,000	46 (17.2)	35 (76.1)	11 (31.4)	
RM4,001-RM5,000	29 (10.8)	22 (75.9)	7 (24.1)	
> RM5,000	121 (45.1)	95 (78.5)	26 (21.5)	

***[a]Chi-Square Test;* * P < 0.05 *[b]Fisher Exact Test;* * P < 0.05**

The level and determinants of the willingness of public to pay for the COVID-19 self-test kit

Table VIII illustrates the factors associated with respondents' willingness to pay for COVID-19 self-test kits. It was found that female gender (P=0.013) and students (P=0.013) were associated with higher odds of willingness to pay for COVID-19 self-test kits.

Table IX further illustrates the correlation between respondents' exposure to COVID-19 infection and their WTP for COVID-19 self-test kits. It was found that having close acquaintances infected with COVID-19 was significantly associated (P = 0.009) with willingness-to-pay for COVID-19 self-test kits.

Table IX. Correlation between exposure to COVID-19 infection and Willingness-To-Pay (WTP) for COVID-19 self-test kit (n=268)

Items	n (%)	Willingness to pay, n (%)		p-value[a]
		Yes	No	
History of being infected by COVID-19				0.838
Yes	116	86	30	
No	152	111	41	
History of hospitsalisation due to COVID-19 infection				1.000
Yes	8	6	2	
No	260	191	69	
History of family member being infected by COVID-19				0.869
Yes	207	153	54	
No	61	44	17	
History of close acquaintance being infected by COVID-19				0.009
Yes	257	193	64	
No	11	4	7	
History of death among family members due to COVID-19				0.467
Yes	47	37	10	
No	221	160	61	
History of death among close acquaintance due to COVID-19				0.178
Yes	83	66	17	
No	185	131	54	
History of COVID-19 case around neighbourhood area				0.227
Yes	244	182	62	
No	24	15	9	
History of COVID-19 case at workplace area				0.568
Yes	226	168	58	
No	42	29	13	
History of RTK-Ag/PCR test				0.125
Yes	227	171	56	
No	41	26	15	

DISCUSSION

This nationwide online survey outlines the fact that, in general, our respondents were highly aware of the need to perform COVID-19 self-tests and were generally willing to pay for the self-test kits. However, subgroup analysis revealed that only half of the respondents with monthly household income less than RM1,000 and 55% of Indian respondents were willing to pay for COVID-19 self-test kits. Publicity efforts by the government and non-governmental agencies across the nation, given the complexity and seriousness of the pandemic at the time of the survey, resulted in good penetration of information towards COVID-19 self-testing policies. Our results on awareness of COVID-19 self-tests were in fact, better than those of studies conducted in Indonesia and United Arab Emirates, in which only 15.53% and 25% of respondents were aware of COVID-19 self-testing, respectively [9,10].

Nevertheless, the extent of Willingness-To-Pay (WTP) based on price differences in our study did not differ significantly from the median WTP among respondents in the Indonesian study (USD 1.5, in approximate RM 6.00 during the period) but was higher than the median WTP reported in a study conducted in Nigeria (USD 1.2, in approximate RM 4.80). This may be explained by the fact that both Malaysia and Indonesia are classified as Upper Middle-Income countries, while Nigeria is a Lower Middle-Income Country, as reported by the World Bank at the time of study. This classification reflected differences in median WTP for COVID-19 self-test kits. It also reflects the affordability and perceived value of the COVID-19 self-test kits, as portrayed in our survey - when the survey was conducted, COVID-19 self-test kits were sold at the price as low as RM 3.00. We believe that this may have influenced the findings of WTP among our respondents.

The attitudes portrayed towards COVID-19 self-tests in our survey generally corresponded to the emergence of the Omicron variant in March 2022 [11], and the stipulations in the Standard Operating Procedures (SOP) for the 4th Phase of National Recovery Plan (Fasa Pemulihan Negara) at the time of the survey [12]. The Omicron variant was found to replicate around 70-fold faster than Delta variant, despite causing milder symptoms, and fewer death and complications [13]. This heightened risk perception likely contributed to a higher willingness to conduct COVID-19 self-tests when necessary. Another online nationwide study evaluating willingness to perform COVID-19 self-testing similarly told that in general, 89.3% of the respondents were willing to perform COVID-19 self-tests [14]. Although international and interstate travelling was permitted for fully-vaccinated individuals (with booster doses) except in areas where Enhanced Movement Control Order (EMCO) were implemented, the requirement to perform COVID-19 self-tests remained high in situations such as international travel, meetings, workshops, or when signs and symptoms of COVID-19 were suspected, as well as for close contacts and during quarantine periods for confirmed cases [12]. This context may synergistically resulted in our respondents' high willingness to perform self-tests to ensure daily activities, including work, school or business operations, would not be disrupted by COVID-19 infection, reflecting a greater willingness to adapt to the "new norm". Additionally, the requirement to perform self-tests was mainly attributed to work and organisational needs, or situations with apparent perceived risks, this could explain why the majority of our respondents perceived that COVID-19 self-test kits should also be at least

partially funded by their employers, healthcare insurance providers, or the government.

While methodological differences existed in evaluating WTP compared to other similar studies, the finding that female and students had higher odds to pay for COVID-19 self-test kits was somehow unexpected. However, it aligned with the observation that female had a higher risk perception towards COVID-19 infection as compared to males, leading to a greater willingness to invest in COVID-19 self-test kits [14,15]. The correlation between students and WTP for COVID-19 self-test kits may also have related to another study among Malaysian university students, which found that they exhibited high risk perception (indicated by high mean risk perception in the study) towards COVID-19 [16], thereby increasing their willingness to pay for the self-testing kits at an affordable price. Conversely, more commonly observed predictors, such as household income level, surprisingly did not show statistical significance in our survey compared to other studies [8].This could be explained by the general recognition of the importance of COVID-19 self-testing within our society, resulting in a willingness to pay for them – what varied was simply the extent of payment from self-pockets and whether they were partially funded by other parties (e.g. government or employers). Nevertheless, findings from this survey warrant further insights into targeted subsidisation.

While the demand for COVID-19 self-test kits may have declined as the pandemic transitioned into an endemic phase, the findings remain significant in several ways. First, the study provides valuable insights into consumer behaviour and pricing strategies that can guide policymakers in preparing for future pandemics or similar public health emergencies. The high willingness to pay (WTP) demonstrated in this study reflects the public's readiness to invest in accessible diagnostic tools when faced with infectious threats that may affect their daily activities. Such data offer guidance in crafting strategies to optimise the affordability and accessibility of rapid diagnostic tools during the initial phases of future pandemics, where rapid testing is crucial. Furthermore, it is important to note that the study also highlights the importance of pricing subsidies and contributions from employer or government, which can be generalised to other healthcare commodities. The behavioural predictors identified, such as risk perception and demographic factors, provide a foundation for targeted communication and resource allocation during health crises.

This study is not without limitations. Interpretations from this study may not fully represent the general Malaysian population, as our sample distribution were not stratified according to the proportions of Malaysian population across different states (the majority of the samples were from Kedah) or various demographic characteristics, resulting in a less homogenous sample. Furthermore, we did not evaluate the extent of WTP (as of different level of prices) across different factors and determinants, which is commonly seen in other similar studies among currently available literature. We also did not compute WTP estimates based on any econometric models, such as Tobit or Heckman selection models, which are more robust methods for determining WTP, especially when zero WTP cases occurred in this survey. Nevertheless, serving as a baseline study, we believe the findings from this study can establish a foundation for improvements in future research, including a more inclusive sampling approach and enhanced methodology to provide deeper insights for future studies. Furthermore, longitudinal studies to track changes in willingness to pay and attitudes towards self-testing over time are also warranted, which can help to assess the impact of public health interventions and changes in the situation.

CONCLUSION

This study depicts a high willingness among respondents to perform COVID-19 self-tests, with a willingness to pay for the self-testing kits at a mean maximum price of RM 9.16 (SE = 0.68) and a median maximum price of RM 6.00. While COVID-19 has gradually transitioned into an endemic phase at the time of writing, the WTP findings from this study serve as a valuable reference for price setting, differentiation, and subsidisation of self-test kits in preparation of any potential future emergence of similar pandemics.

CONFLICT OF INTEREST

No conflict of interest declared.

REFERENCE

[1] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet (London, England). 2020 Feb;395(10223):497–506. https://doi.org/10.1016/s0140-6736(20)30183-5

[2] World Health Organization. WHO Coronavirus (COVID-19) Dashboard. Available from: https://data.who.int/dashboards/covid19/cases?n=c

[3] Ministry of Health Malaysia. COVID-19 Dashboard. Available from: https://data.moh.gov.my/dashboard/covid-19

[4] World Health Organization. SARS-CoV-2 antigen-detecting rapid diagnostic tests: an implementation guide. Country & Technical Guidance - Coronavirus disease (COVID-19). 2020; 1–48. Available from: https://www.who.int/publications/i/item/9789240017740

[5] Ministry of Health Malaysia. COVID-19 Rapid Test Kit Antigen (RTK-Ag) Testing for Professional Use. 2022;19–21. Available from: https://covid-19.moh.gov.my/garis-panduan/garis-panduan-kkm/ANNEX-4g-Covid-19-RTK-Ag-21092022.pdf

[6] Ministry of Health Malaysia. Garis Panduan Pengurusan Kit Ujian Kendiri COVID-19. Available from: https://covid-19.moh.gov.my/semasa-kkm/2021/07/garis-panduan-pengurusan-kit-ujian-kendiri-covid-19-23072021

[7] Vaughan W, Darling A. The Optimal Sample Size for Contingent Valuation Surveys: Applications to Project Analysis. 2000. http://dx.doi.org/10.18235/0008824

[8] Kazungu, J., Mumbi, A., Kilimo, P., Vernon, J., Barasa, E., & Mugo, P.. Title Level and determinants of willingness to pay for rapid

COVID-19 testing delivered through private retail pharmacies in Kenya. 2021 http://dx.doi.org/10.1101/2021.10.10.21264807

[9] Thomas C, Shilton S, Thomas C, Batheja D, Goel S, Mone Iye C, et al. Values and preferences of the general population in Indonesia in relation to rapid COVID-19 antigen self-tests: A cross-sectional survey. Trop Med Int Heal. 2022;27(5):522–36. https://doi.org/10.1111/tmi.13748

[10] Jairoun AA, Al-Hemyari SS, Abdulla NM, Al Ani M, Habeb M, Shahwan M, et al. Knowledge about, acceptance of and willingness to use over-the-counter COVID-19 self-testing kits. J Pharm Heal Serv Res. 2022;13(4):370–7. http://dx.doi.org/10.1093/jphsr/rmac037

[11] Ministry of Health Malaysia. Penularan Sub-Lineage Variant Of Concern (Voc) Omicron Ba.2 Dan Kesan Kesihatan Awam. 2022. Available from: https://covid-19.moh.gov.my/semasa-kkm/2022/03/penularan-sub-lineage-variant-of-concern-voc-omicron-ba-2-dan-kesan-kesihatan-awam

[12] Council MNS. Pelan Pemulihan Negara (PPN) - SOP Fasa 4. 2022. Available from: https://covid-19.moh.gov.my/faqsop/pelan-pemulihan-negara-sop-fasa-empat

[13] Chavda VP, Bezbaruah R, Deka K, Nongrang L, Kalita T. The Delta and Omicron Variants of SARS-CoV-2: What We Know So Far. Vaccines. 2022;10(11). https://doi.org/10.3390/vaccines10111926

[14] Ng DL, Bin Jamalludin MA, Gan XY, Ng SY, Bin Mohamad Rasidin MZ, Felix BA, et al. Public's Willingness to Perform COVID-19 Self-Testing During the Transition to the Endemic Phase in Malaysia - A Population-Based Cross-Sectional Study. Risk Manag Healthc Policy. 2023. https://doi.org/10.2147/rmhp.s439530

[15] Alsharawy A, Spoon R, Smith A, Ball S. Gender Differences in Fear and Risk Perception During the COVID-19 Pandemic. Front Psychol. 2021. https://doi.org/10.3389/fpsyg.2021.689467

[16] Wong CY, Tham JS, Foo CN, Ng FL, Shahar S, Zahary MN, et al. Factors influencing COVID-19 vaccination intention among university students: A cross-sectional study in Malaysia. Biosaf Heal. 2023;5(1):37–44. https://doi.org/10.1016/j.bsheal.2022.12.005

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Original Research Article

Job Satisfaction: Among Pharmacy Enforcement Officers in Penang, Malaysia: A Pilot Study

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Keywords: Pharmacy Enforcement Officer, Job Satisfaction, Behavioural Integrity, Work related burnout.

ABSTRACT

Introduction: Job satisfaction is well known to have direct impact on employee motivation, which is reflected in their productivity. In this regard, job satisfaction among Pharmacy Enforcement Officers (PEO) is vital for job commitment in the Pharmacy Enforcement Division (PED), which includes enforcing laws pertaining to the sale of unregistered pharmaceutical products, unnotified cosmetics, and products adulterated with scheduled poisons that are harmful to consumers. **Objectives:** This study aimed to evaluate the job satisfaction level among PEO in Penang and identify the variables affecting it. **Methods:** A cross-sectional survey was conducted among 35 PEO in Penang. A validated self-administered questionnaire consisting of five sections was used to study the overall job satisfaction level and the factors affecting them. Descriptive analysis was used to analyse demographics and job satisfaction levels among PEO in Penang. Correlation analysis was used to measure the variables affecting job satisfaction. **Results:** The descriptive analysis revealed no significant results regarding job satisfaction. However, 77% of the PEO who responded were satisfied with their current job. It was found that salary, supervision, rewards, co-workers, communications, benefits, and nature of work affect job satisfaction levels. Correlation analysis revealed that work-related burnout and behavioural integrity showed positive correlation ($p < 0.05$ and $p < 0.01$) with job satisfaction among PEO in Penang. Logistic regression was conducted to investigate the impact of variables on job satisfaction among PEO. Work-related burnout and behavioural integrity significantly affected job satisfaction. **Conclusion:** The majority of the PEO were satisfied with their jobs, with work-related burnout and behavioural integrity identified as two major variables affecting job satisfaction in the PED. Additional positive findings from this study indicated that job satisfaction among officers was vital, as it fostered a positive attitude towards their work and improved the organizational performance, resulting from a committed workforce.

INTRODUCTION

The long-term success of any business or public agency depends on employees' satisfaction, which, when measured properly, reflects underlying work morale, organizational commitment sentiments, and some key aspects of organizational commitment sentiments [1,2]. The lack of job satisfaction will lead to increased employee turnover and loss of organizational knowledge; thus, job satisfaction remains a topic of great interest [3]. This is supported by a report [4] that cited issues affecting pharmacists' job satisfaction and commitment in the public workforce, as well as the likely turnover rate, which was highly affected by the compulsory service. According to Kariyawasam (2012), in a study of Job Satisfaction Survey of Police Inspectorate at Nugegoda Police Division, the, author deduced that neglecting job satisfaction in the police department caused poor performance and low productivity among officers, which concurrently jeopardized the reputation of the police department [5].

In Malaysia, the Enforcement Division is the body authorized to enforce laws pertaining to the control of medicine, pharmaceutical products, cosmetics products and the advertisement of medicine and medical services [6]. The Pharmacy Enforcement Branches focuses on activities to curb the sales of unregistered healthcare products and cosmetic

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products, as well as products adulterated with controlled schedule drugs under the poison list, which are harmful to consumers. Specifically, the operational routines include licensing, intelligence and operations, legislation, advertisement control, and pharmaceutical and consumer protection. High workloads from scheduled inspections, entry-point checks, market sampling, and conducting raids to seize and confiscate unregistered healthcare products, cosmetic products and adulterated products. Since every officer is required to be involved in all these activities, evaluating job satisfaction among Pharmacy Enforcement Officers is crucial. According to Hoath et al. (1998), a negative attitude among enforcement officer can affect the community's trust in the Enforcement Officers organization. High job satisfaction tends to lead to lower stress level and reduced burnout, and vice versa [7].

Furthermore, Judge et al. (2006) argued that job satisfaction had a profound impact on both the organization and the individual [8]. The author noted that job satisfaction could affect the work outcomes such as job performance, attendance, turnover decisions, retirement decisions, life satisfaction, physical and mental health, and the quality of marital interactions. These findings indicate that the job satisfaction is an important area of study for the development of organisations like Pharmacy Enforcement Division development and for the improvement of its officers.

This situation has motivated the idea to evaluate job satisfaction among Pharmacy Enforcement Officers in the Penang State Health Department, Malaysia. Current study was conducted among Pharmacy Enforcement Officers in Penang using a validated questionnaire to evaluate the job satisfaction level and the variables that significantly affect job satisfaction among Pharmacy Enforcement Officers (PEO) in Penang.

Background of Job Satisfaction

Various theories define job satisfaction. The simplest definition would be the level of likeliness towards one's job [9]. Evaluating job satisfaction is crucial as it can affect the performance of the organization, the development of community trust towards the Enforcement Officers organization, and the stress levels or burnout of the Enforcement Officers [7]. There is a correlation between the working environment and job satisfaction; a better working condition, including cooperative co-workers, leads to a high level of job satisfaction in the pharmacy enforcement organization, based on a study by Raziq et al. (2015) [10]. When Enforcement Officers are overloaded with work, it leads to burnout, significantly reducing their job satisfaction [11]. One's job performance and productivity are believed to be linked to job satisfaction [12]. High employee job satisfaction leads to positive behaviour in operations [13]. Simons, Tomlinson, and Leroy (2011) reported that behavioural integrity was important in prompting favourable follower attitudes toward their work (e.g., job satisfaction, affective organizational commitment, and intent to stay) [14]. The job characteristics in an organization may reflect perceptions of job satisfaction. However, according to Miller et al., the only strong factor is autonomy; when more enforcement officers feel independent in performing their duties, they have higher job satisfaction [15].

Work Related Burnout:

Job stress is believed to occur when a person feels job-related hardness, tension, anxiety, frustration, worry, and distress. Constant exposure to stress can be destructive to employee's mental and physical state, work quality, and to the respective organization [16]. Since the nature of the Pharmacy Enforcement job requires multitasking and exposes employees to high risks, managing job stress is crucial for achieving high job satisfaction. Additionally, job stress arises as people interact with each other within an organization or deal with organizational policies and environmental circumstances [17]. Although the outcomes of stress differ according to the circumstances and characteristic of the individuals involved, its consequences are consistently intense [18].

He and Lovrich et al (2002) described two major types of stress: organizational stress and operational stress [19]. Organizational stress refers to problematic aspects within the organization, such as lack of confidence in management, constant organizational or policy change, and poor communication among colleagues. The organizational stress experienced by officers may stem from the nature of the organization, such as its hierarchy and employee dynamics, for example, cooperation between colleagues, as mentioned by Burke &Mikkelsen, 2006 [20]. Operational stressors arises from the nature of the police work, including exposure to danger, physical threats during raids or inspections, facing unpredictable incidents, and long working hours [18].

Maslach, Schaufeli and Leiter (2001) defined burnout as a psychological syndrome in response to work-related stressors [21]. According to Freudenberger (1974), the term "job burnout" refers to a state where a person is psychologically worn out and exhausted from their job [22]. Evaluating stress in enforcement bodies is crucial, as this stress may affect the performance and professionalism of law enforcement officers, which in turn could lead to a breakdown in communication with the public [25].

Working Environment

Raziq et al.(2015) stated that the working environment can be defined from two perspectives: work and context [10]. "Work"

refers to how the job is conducted and completed, while "context" includes both the physical and social working environments. Meanwhile, Buhai, Cottini, and Nielsen (2008) mentioned that a company can enhance work efficiency by improving the physical working environment, leading to positive outcomes in productivity [24]. Therefore, organizations need to pay more attention to working environment; by creating a good working environment, employees will become more productive, ultimately increasing profits for organization [25]. Additionally, human-to=human communication and interactions play a more dominant role in overall job satisfaction compared to financial incentives. This statement is supported by a study among Taiwanese police officers [26], which showed significant positive job satisfaction when they were assessed on their relationships with colleagues and supervisors, as well as opportunities for promotion.

Behavioural Integrity (BI)

Becker (1998), who refined the definition of integrity, described it as a commitment in action to a morally justified set of principles and values [20]. Later, Simons (2002) expanded on this distinction and defined Behavioural Integrity (BI) as the perceived alignment between an actor's words and actions – how well that actor tends to keep promises, "walk the talk" and "practice what they preach" [27]. According to Simons (2002), behavioural integrity encompasses the perception that the actor's behaviour aligns with their personal statements regarding values, priorities, and management style. Behavioural integrity does not consider the moral content or the observer's acceptance of the actor's espoused values [27]. In other words, we may dislike leaders who enact values that we consider socially or morally unacceptable, but we will still acknowledge them for enacting those values honestly, thus displaying behavioural integrity [14]. This is because behavioural integrity focuses purely on leaders' words and actions [27], unlike moral integrity, which emphasizes moral and social content [28]. Therefore, this distinction must be clearly addressed, as the observer's own values (moral or social) may bias their perceptions of behavioural integrity [27]. Simons (2002) explained that a lack of BI's can be attributed to an individual, a group (leadership team), or a company. Another study reported that a leader's BI was important in prompting favourable follower attitudes toward their work, such as job satisfaction, affective organizational commitment, and intent to stay [14].

METHOD

Data Collection

This is a cross-sectional pilot study in which a validated questionnaire in English was distributed among 35 PEO in Penang. The questionnaire was provided in printed hardcopy format and was to be completed within one (1) month. The data collected will be stored confidentially for 3 years. The inclusion criteria included PEOs with a minimum of one (1) year of experience in enforcement, as those with less than a year of experience were considered to be in their probation period. Conversely, the exclusion criteria applied to officers holding the positions of Head of Branch and Head of Section.

Research Instruments

In this study, a questionnaire was used as the measuring instrument for data collection. The questionnaire consisted of closed-ended questions adapted from published articles. A quantitative questionnaire with each question utilizing a five-point Likert Scale was employed. The survey was prepared based on the following variables: Work-Related Burnout, Working Environment Factors, and Behavioural Integrity (Table I). The questionnaire used the scopes presented in Table II for each variable.

Sampling Method

The study used a descriptive measure using a cross-sectional design and random stratified sampling method to obtain the data. The study population involved approximately 50 officers from the Penang Pharmacy Branch. Using Raosoft method, the estimated minimum sample size was 35 respondents, with a 5% margin error and 50% response distribution. To protect the privacy and confidentiality of personal information and questionnaire responses, each respondent was assigned a coded questionnaire specifically for data collection. All responses (including consent forms and questionnaires) were collected and analysed using SPSS Inc. Software version 26.

Table I. Composition of losartan potassium-loaded buccal films.

No	Performance measurement	item	Question (Q)	Source
1	Job Satisfaction	8	**Section 2** Q1 to Q8	[13]
2	Work Related Burnout	21	**Section 3** Q1 to Q7 **Organizational Stress** Q8 to Q14 **Operational Stress** Q15 to Q21	[13]
3	Working Environment	18	**Section 4** **Working Equipment** Q1 to Q2 **Relationships with colleagues** Q3 to Q5 **Relationship with superiors** Q6 to Q9 **On-the-job training** Q10 to Q13 **Working hours** Q14 to Q15 **Safety**: Q16 to Q18	[14]
4	Behavioural Integrity	8	**Section 5** Q1 to Q8	[9]

Table II. Operationalisation of Variables

Variables	Scopes of Variables
Job Satisfaction	1. Pay 2. Supervision 3. Benefits 4. Contingent Reward 5. Operating Procedures 6. Dealing with co-workers 7. Nature of work 8. Communication with the organization
Work Related Burnout	1. Emotional exhaustion 2. Burnout 3. Frustration 4. Worn out 5. Routine 6. Exhaustion 7. Social life deterioration
	Organizational Stress 1. Favouritism 2. Excessive administrative duties 3. Constant changes in SOP/ guidelines 4. Staff shortages 5. Lack of resources 6. Unequal work 7. Internal investigation
	Operational Stress 1) Traumatic events 2) Managing social life 3) Occupational-related health 4) Physical condition 5) Lack of understanding from family and friends 6) Public's comment
Working Environment	1) Working equipment 2) Relationships with colleagues 3) Relationship with superiors 4) On-the-job training 5) Working hours 6) Safety
Behavioural Integrity	1) Words and actions 2) Promise 3) Practice vs Preach 4) Value 5) Priority 6) Certainty

Analysis of Data

Data analysis was conducted using SPSS Inc. Software version 26. This study used the primary data sources collected through the questionnaires. The data was analysed using bivariate chi square tests ($p<0.05$) and logistic regression analysis.

RESULTS

Survey data were analysed from 35 participants. Approximately more than half of the respondents (60.0%) were male, while 40.0% were female. A total of 97.1% of the cohort held a bachelor's degree in pharmacy and 2.9% had master's degrees. Regarding working experience, 20.0% had less than 5 years of experience as pharmacy enforcement officers; 71.0% had 5-10 years; and 8.6% had more than 10 years of service with the pharmacy enforcement organization (Table III).

Overall, about 77% of PEO in Penang were satisfied with their current job, while 23% were not satisfied. Analysis of responses from the 35 PEO in Penang revealed that salary, supervision, rewards, co-workers, communication, benefits, and the nature of work all had satisfaction levels exceeding 60.0%. In contrary, 65.7% of the respondents were not satisfied with the current operating procedures, as shown in the Figure I.

Table III. The Association of Job Satisfaction Level with Various Factors of Demographics

Demographics	Satisfied (%)	Not Satisfied (%)	Total (n)
Gender			
Male	16 (76.2)	5 (23.8)	21 (60.0)
Female	11 (78.6)	3 (21.4)	14 (40.0)
Race			
Malay	15 (83.3)	3 (16.7)	18 (51.4)
Chinese	11 (78.6)	3(21.4)	14 (40)
Indian	1 (50)	1 (50)	2 (5.7)
Others	1 (100)	0	1 (2.9)
Age (years)			
26-34	20 (76.9)	6 (23.1)	26 (74.3)
35-45	7 (77.8)	2 (22.2)	9 (25.7)
Academic qualification			
Bachelor	26 (76.5)	8 (23.5)	34 (97.1)
Master	1 (100)	0	1 (2.9)
Length of Service (years)			
< 5	6 (85.7)	1 (14.3)	7 (20)
5-10	19 (76.0)	6 (24.0)	25 (71)
>10	3 (100.0)	0 (0)	3 (8.6)
Working Section			
Entry Point	5 (71.4)	2 (28.6)	7 (20)
Operation & Intelligence	9 (90.0)	1 (10.0)	10 (28.6)
Investigation & Prosecution	4(80.0)	1 (20.0)	5 (14.3)
SKIF	4(80.0)	1 (20.0)	5 (14.3)
Licensing & Inspection	5 (62.5)	3 (37.5)	8 (22.9)

***(Data represented as mean ± standard deviation; n=3. For all the studies, $p < 0.05$)**

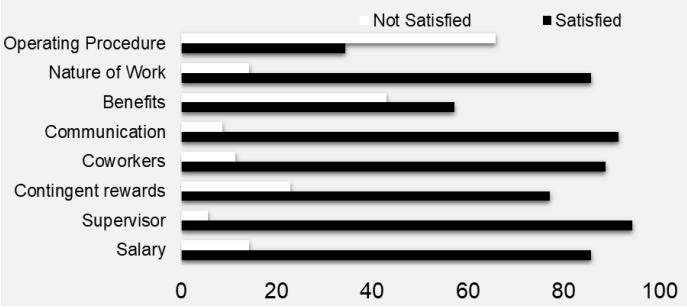

Figure I. Job Satisfaction indicator

Table IV. Correlation Analysis of job satisfaction against the tested variables

Level of Job Satisfaction (%)	Satisfied	BI	WRB	WE
Job Satisfaction	**Pearson Correlation**	**.392***	**-.642****	**.351***
	Sig. (2-tailed)	**.020**	**.000**	**.039**
	N	**35**	**35**	**35**

JS: Job Satisfaction, BI: Behavioural Integrity, WRB: Work Related Burnout, WE: Working Environment

Correlation Analysis

Among the three variables, all were correlated with job satisfaction at the $p<0.05$ level of statistical significance. Behavioural integrity and working environment had positive correlations, whereas work-related burnout had a negative correlation with job satisfaction, as shown in Table IV.

Regression Analysis

In addition, to determine the respective strengths of the determinants of job satisfaction between the dependent variable (job satisfaction) and the independent variables (work-related burnout, working environment, and behavioural integrity), a further analysis using regression was conducted. The results indicated that, out of the 3 determinants of job satisfaction, two factors (work-related burnout and behavioural integrity) were found to be significant ($p<0.05$) on job satisfaction (Table V). Higher beta value of the variable of work-related burnout indicated the heavy implication of this variable toward overall job satisfaction.

Table V. Regression Analysis

Variables	β (SE)	Wald	p-value	OR	95% CI for OR (lower, upper)
Work Related Burnout	1.05 (0.33)	9.67	0.003	2.85	1.47;5.51
Working Environment	0.34 (0.20)	2.60	0.10	1.39	0.93;2.10
Behavioural Integrity	0.33 (0.15)	4.65	0.03	1.40	1.03;1.90

****Significant at 0.05 level***

DISCUSSION

Based on our study, all three tested variables were independently correlated with job satisfaction. This aligned with the findings reported by Eric et al. (2017), who found that law enforcement was one of the important professions that dealt with a range of individuals from different levels of the society [37]. This is in agreement with a study carried out by Raziq et al. (2015), who reported that working environment and job satisfaction were directly proportional [10]. A positive working environment played a crucial role in high job satisfaction. Good working hours, job security & safety, relationship with colleagues and effective management led to high job satisfaction. The working environment was an important key factor used in many studies to evaluate job satisfaction. Thus, it is very important to identify and enhance the effectiveness of each element of working environment to improve job satisfaction of Pharmacy Enforcement officers.

Focusing on the regression, when the situation was multifaceted, work-related burnout contributed the highest beta value. This signified its greater impact on changes in the degree of job satisfaction. According to Martinussen, Richardsen, and Burke (2007), prolonged stress harmed individual's job-related health, commonly recognized as one of the possible outcomes of work stress, which was burnout [30]. Stearns and Moore (1992) found strong associations between occupational stress and employee burnout, with occupational stress being a strong predictor of higher levels of burnout [31]. Pines and Keinan (2005) reported a correlation between burnout and employees' attitude towards the police organization, leading to job dissatisfaction and intentions to leave [32].

The current pilot study also highlighted the individual influence on overall job satisfaction by ranking behavioral integrity as a contributing factor to job satisfaction. Other studies reported similar observations. Prottas (2008) tested the relationships between the behavioural integrity of managers, as perceived by employees, and employee attitudes (job satisfaction and life satisfaction), well-being (stress and health), and behaviours (absenteeism) [33]. The respondents were a representative sample of employed adults who participated in the 2002 National Study of the Changing Workforce. The author found that behavioural integrity was related to a higher job satisfaction, which prior research also found to be positively related to a various important outcome, such as employee commitment and job performance. He concluded that behavioural integrity was an important variable in accessing job satisfaction in a workforce setting. On a separate note, the author clarified that there were no substantial gender differences regarding perceptions of behavioural integrity or the strength of the relationships between behavioural integrity and job satisfaction.

Similarly, in 2012, the same group of researchers tested data from respondents who participated in the 2008 National Study of the Changing Workforce (NSCW) and concluded that behavioural integrity was positively related to job satisfaction [34]. Although some of the findings of this study using the 2008 NSCW study merely replicated what Prottas (2008) reported in his study using the 2002 data, the measures were also quite similar. However, the consistency in both studies provided confidence in the robustness of the relationship between behavioural integrity and job satisfaction. Hence, based on both studies, it was concluded that leaders with high behavioural integrity promoted better job satisfaction among their employees (Prottas, 2008).

In addition, Guchait, Simons & Pasamehmetoglu (2016) examined the mediating effect of job satisfaction between behavioural integrity and error recovery performance, where the data were collected among hotel employees in Turkey [35]. In their study, a significant positive relationship was found between behavioural integrity and job satisfaction among hotel employees. On the other hand, Joel (2016) demonstrated the importance of supervisors' behavioural integrity in Jewish day schools [36]. As previous research on behavioural integrity had been conducted in general business and hotel settings, this study discovered that the same was true within the school setting. It was reported that the behavioural integrity of the supervisor significantly predicted job satisfaction in Jewish days Schools.

In summary, it was clear that behavioural integrity was critical to the success of an organization because of its impact on employees' job satisfaction (Joel, 2016) [36]. As such, the research cited was heavily weighted towards the business world, hotels, and and schools; thus, this study aimed to evaluate the impact of behavioural integrity on job satisfaction in Pharmacy Enforcement Division.

CONCLUSION

The study investigated the impact of the three (3) variables - work related burnout, working environment, and behavioural integrity- as determinants of job satisfaction among Pharmacy Enforcement Officers in Penang. It was found that all three predictors had a significant positive correlation with the job satisfaction of the officers. The working environment and behavioural integrity were positively related to the job satisfaction of the officers. Meanwhile, work related burnout had a negative relationship. This study has important implications for the Pharmacy Enforcement Officers in Penang. The job satisfaction of these officers can provide many benefits to the organization and the country as a whole, given that the safety and well-being of the public are protected and safeguarded. Hence, the job satisfaction of the Pharmacy Enforcement Officers in Penang is crucial. In summary, job satisfaction among officers is vital for ensuring the long-term efficiency and effectiveness of their performance within the department. The research contributes to the body of knowledge regarding the important predictors of job satisfaction. The findings of this study are consistent with existing research that shows the three variables are significantly related to the officers' job satisfaction. Additionally, the research advances statistical methods in the study of job satisfaction. Future research could employ a mixed-method approach (quantitative and qualitative) to further explore the determinants of job satisfaction among Pharmacy Enforcement Officers in Penang.

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CONFLICT OF INTEREST

No conflict of interest declared.

REFERENCE

[1] Naseem, A., Sheikh, S. E., Malik, K. P.. Impact of Employee Satisfaction on Success of Organization: Relation Between Customer Experience & Employee Satisfaction. Int.J. Multidiscip. Sci. Engineer. 2011;2(5):41-46 https://api.semanticscholar.org/CorpusID:32048488

[2] Parker, S. K., Morgeson, F.P., & Johns, G. One Hundred Years of Work Design Research: Looking Back and Looking Forward. J Appl Psychol. 2017;102:403-420 https://doi.org/10.1037/apl0000106

[3] Roodin, P. &Medelson, M. (2013). Multiple Generation at Work: Current and Future Trends. J Intergener Relatsh 2013;11 (3): 213-222 https://doi.org/10.1080/15350770.2013.810496

[4] Gin Nie Chuaa , Lai Jiuan Yeeb , Bee Ai Simb , Keat Hin Tanc , Ng Khai Sinb , Mohammed Azmi Hassalia , Asrul Akmal Shafiea and Guat See Ooi. (2014). Job satisfaction, organisation commitment and retention in the public workforce: a survey among pharmacists in Malaysia. Int J Pharm Pract 2014; 22: 265–27. https://doi.org/10.1111/ijpp.12077

[5] Kariyawasam, B. S. T.. Factor Influencing Job Satisfaction of Police Inspectorate: A Study of Nugegoda Police Division. Unpublished dissertation Bsc Degree in Management in the General Sri John Kotelawala Defence University, 2013 http://dx.doi.org/10.13140/RG.2.2.12452.50566

[6] Zulkifli, Nur Wahida, Noorizan Abd. Aziz, Yahaya Hassan, Mohamed Azmi Hassali, Nur Liyana Zainal Bahrin, and Azlan Ahmad. "Are We on the Right Track?: Overview of Unregistered Drugs in Malaysia." J. Pharm. Pract. Community Med. 2016; 2(4):107–15. doi: http://dx.doi.org/10.5530/jppcm.2016.4.2 .

[7] Hoath, D. R., Schneider, F. W., & Starr, M. W. Police Job Satisfaction as A Function of Career Orientation and Position Tenure: Implications for Selection Community Policing. J Crim Justice. 1998; 26:337−347 https://api.semanticscholar.org/CorpusID:142601026

[8] Judge, T. A., Ilies, R., & Scott, B. A. Work-Family Conflict and Emotions: Effects at Work and at Home. Pers Psychol. 2006; 59:779-814 http://dx.doi.org/10.1111/j.1744-6570.2006.00054.x

[9] Spector, P.E. Job Satisfaction: Application, Assessment, Causes, and Consequences. Sage Publication. 1997; 2

[10] Raziq, A. &Maulabakhsha, R. Impact of Working Environment on Job Satisfaction. Procedia Econ. Financ. 2015; 23 :717 – 725 https://doi.org/10.1016/S2212-5671(15)00524-9

[11] Lambert, E. G., Qureshi, H., Frank, J., Klahm, C., & Smith, B. Job Stress, Job Involvement, Job Satisfaction, and Organizational Commitment and Their Associations with Job Burnout Among Indian Police Officers: A Research Note. J Police Crim Psychol. 2017 https://doi.org/10.1007/s11896-017-9236-y

[12] Yahaya,N.D., Hashim, R. & Ismail, N.M. Job satisfaction among the technical and operational personnel of the Royal Malaysia Police Communication Division. IEEE Business, Engineering & Industrial Applications Colloquium (BEIAC). 2012; 97 http://dx.doi.org/10.1109/BEIAC.2012.6226061

[13] Othman, R., Omar, N., Azam, A., Ibrahim, S., Farouq, W. A., Rustam, N. &Aris, N. A. (2014). Influence of Job Satisfaction and Codes of Ethics on Integrity Among Police Officers. Procedia Soc Behav Sci. 2014;145,:266–276 https://api.semanticscholar.org/CorpusID:144424062

[14] Simons, T. L., Tomlinson, E. C., & Leroy, H. Research OnBehavioral Integrity: A Promising Construct for Positive Organizational Scholarship. Cornell University School of Hotel Administration Collection 2011. https://api.semanticscholar.org/CorpusID:59058156

[15] Miller, H.A., Mire,S.& Kim, B. (2009). Predictors Of Job Satisfaction Among Police Officers: Does Personality Matter? J Crim Justice. 2009;37:419–426 https://doi.org/10.1016/j.jcrimjus.2009.07.001

[16] Maslach, C. (2003).Job Burnout: New Directions in Research and Intervention. Curr Dir Psychol Sci, 2003; 12(5):189-192 https://psycnet.apa.org/doi/10.1111/1467-8721.01258

[17] Kula, S. Occupational Stress, Supervisor Support, Job Satisfaction and Work-Related Burnout: Perceptions of Turkish National Police (TNP) Members. Police Pract. Res. 2016; 18(2), 146–159 doi: https://doi.org/10.1080/15614263.2016.1250630

[18] Stephens, C. & Long, N. Communication with Police Supervisors and Peers as a Buffer of Work-Related Traumatic Stress. J Organ Behav. 2000; 21:407-424 https://psycnet.apa.org/doi/10.1002/(SICI)1099-1379(200006)21:4%3C407::AID-JOB17%3E3.0.CO;2-N

[19] He, N. &Lovrich, N..Predicting Five Dimensions of Police Officer Stress: Looking More Deeply into Organizational Settings for Sources of Police Stress. Police Quarterly. 2002;5:43-62 https://doi.org/10.1177/109861110200500103

[20] Becker, T. E.. Integrity in Organizations: Beyond Honesty and Conscientiousness. Acad Manage Rev, 1998;23(1): 154-161 https://doi.org/10.2307/259104

[21] Maslach, C., Schaufeli, W. B., & Leiter, M. P. Job Burnout. Annu. Rev. Psychol. 2001; 52:.397–422 http://dx.doi.org/10.1146/annurev.psych.52.1.397

[22] Freudenberger, H. J.. Staff Burn-Out. A Journal of The Society for The Psychological Study of Social Issues. 1974; 30:159-165 http://dx.doi.org/10.1111/j.1540-4560.1974.Tb00706.x

[23] McCreary, D. R. & Thompson, M. M. Development of Two Reliable and Valid Measures of Stressors in Policing: The Operational and Organizational Police Stress Questionnaires. Int J Stress Manag. 2006; 13:494–518 http://dx.doi.org/10.1037/1072-5245.13.4.494

[24] Buhai, S., Cottini, E., &Westergard, N. (2008). The Impact of Workplace Conditions on Firm Performance. Tinbergen Institute Discussion Paper. 2008; 3 https://api.semanticscholar.org/CorpusID:53487236

[25] Chandrasekar, K. Workplace Environment and Its Impact on Organisational Performance in Public Sector Organisations. Int. J. Enterp. Comput. Bus. Syst. 2011; 1(1) https://ijecbs.com/January2011/N4Jan2011.pdf

[26] Kuo, S. Y. (2015). An Occupational Stress, Job Satisfaction, and Affective Commitment to Policing Among Taiwanese Police Officers. Police Quarterly. 2015; 18, :27-54 https://doi.org/10.1177/1098611114559039

[27] Simons, T. L. Behavioral Integrity: The Perceived Alignment Between Managers' Words and Deeds as a Research Focus. Cornell University School of Hotel Administration Collection. 2002 http://dx.doi.org/10.1287/orsc.13.1.18.543

[28] Mayer, R. C., Davis, J. H., &Schoorman, F. D. An Integrative Model of Organizational Trust. Acad Manage Rev, 1995; 20 (3):709-734 https://doi.org/10.2307/258792

[29] Simons, T., Leroy, H., &Collewaert, V. How Leader Alignment of Words and Deeds Affects Followers: A Meta-analysis of Behavioral Integrity Research. J. Bus. Ethics. 2014;132:831–844 doi: https://doi.org/10.1007/s10551-014-2332-3

[30] Martinussen, M., Richardsen, A. M., Burke, R. J. Job Demands, Job Resources, and Burnout Among Police Officers. J Crim Justice. 2007; 35:239-249 https://api.semanticscholar.org/CorpusID:144409180

[31] Stearns, G. M., & Moore, R. J. The Physical and Psychological Correlates of Job Burnout in the Royal Canadian Mounted Police. Can. J. Criminol. Crim. Justice. 1993; 35:127-148 https://psycnet.apa.org/record/1993-43674-001

[32] Pines, A. M. &Keinan, G. (2005). Stress and Burnout: The Significant Difference. Elsevier Pers. Individ. Differ. 2005;39:625–635 https://psycnet.apa.org/doi/10.1016/j.paid.2005.02.009

[33] Prottas, D. J. (2008). Preceived Behavioral Integrity: Relationships with Employee Attitudes, Well-Being and Absenteeism. J. Bus. Ethics. 2008;81:313- 322 https://doi.org/10.1007/s10551-007-9496-z

[34] Prottas, D. J. Relationships Among Employee Perception of Their Manager's Behavioral Integrity, Moral Distress and Employee Attitudes and Well-Being. J. Bus. Ethics. 2012;113: 51-60 https://www.jstor.org/stable/23433874

[35] Guchait, P., Simons, T. L., &Pasamehmetoglu, A. Error Recovery Performance: The Impact of Leader Behavioral Integrity and Job Satisfaction. Cornell University School of Hotel Administration Collection. 2016;57(2), :150-161 https://doi.org/10.1177/1938965515613858

[36] Joel, A. The Impact of Teacher's Perceived Behavioral Integrity of their Supervisor on Teacher Job Satisfaction in Modern Orthodox Jewish Day Schools. Unpublished Degree of Doctor of Education in the Azrieli Graduate School of Jewish Education and Administration Yeshiva University, 2016 https://hdl.handle.net/20.500.12202/460

[37] Eric G. Lambert1 & Hanif Qureshi 2 & James Frank3 & Charles Klahm4 & Brad Smith4 (2017), Job Stress, Job Involvement, Job Satisfaction, and Organizational, Commitment and Their Associations with Job Burnout Among Indian Police Officers: a Research Note, J Police Crim Psych 2018;33: 85–99 (2018). https://doi.org/10.1007/s11896-017-9236-y

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Original Research Article

Stability study of an extemporaneous furosemide oral suspension prepared using commercially available tablets with X-Temp® Oral Suspension System

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ABSTRACT

Introduction: Furosemide is a widely used loop diuretic for managing conditions such as oedema and hypertension. In paediatric patients, especially in the absence of commercially available liquid formulations, extemporaneous oral suspensions are often prepared. This study aimed to evaluate the stability of furosemide oral suspensions formulated at two different concentrations, made from commercial tablets using the X-Temp® Oral Suspension System. **Methods:** Furosemide suspensions were prepared at concentrations of 2 mg/mL and 10 mg/mL using the X-Temp® system, then packaged in amber HDPE bottles. The suspensions were stored under refrigeration (5 ± 3°C) or at room temperature (30 ± 2°C) for a duration of up to 90 days. A comprehensive evaluation protocol, including visual inspections, pH measurements, and HPLC assays, provided a multi-faceted assessment of the samples' stability over the 90-day period. The inclusion of microbiological testing at each interval further reinforced the safety profile of the product. A validated HPLC method was used to determine furosemide content in the oral suspension, ensuring the accuracy, precision, and reliability of the analytical data provided by the system. **Results:** The results showed no statistically significant changes in the assay of furosemide suspension at concentrations of 2 mg/mL and 10 mg/mL over 90 days ($n = 3$, $p > 0.05$). In addition, the stability studies revealed that furosemide in X-Temp® suspension was physically and microbiologically stable throughout the study period. HPLC analysis results shows that all the samples maintained drug concentrations within the specified range. Therefore, it can be concluded that furosemide tablets can be compounded extemporaneously using the X-Temp® Oral Suspension System at concentrations between 2 mg/mL and 10 mg/mL. The resulting suspensions remain stable for up to 90 days when stored in amber HDPE bottles at either 5 ± 3°C or 30 ± 2°C. **Conclusion:** This study provides important insights into the stability of extemporaneous furosemide oral suspensions compounded using the X-Temp® Oral Suspension System. The findings offer valuable guidelines for the preparation, storage, and use of furosemide in X-Temp® suspensions in paediatric care, highlighting the need for careful consideration of storage conditions to ensure therapeutic efficacy.

INTRODUCTION

Furosemide, a potent loop diuretic, is a cornerstone in the treatment of conditions such as oedema associated with heart failure, liver cirrhosis, and renal diseases, as well as in managing hypertension [1]. Despite the availability of furosemide in tablet and intravenous forms, there is limited access to liquid formulations suitable for paediatric patients, who often require precise dosing and may have difficulty swallowing solid dosage forms [1]. This gap necessitates the preparation of extemporaneous oral liquid formulations, particularly in paediatric care.

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The pharmacokinetics of furosemide in children differ significantly from those in adults due to the immature organ systems in younger patients [2,3]. These differences underscore the importance of stable and consistent formulations to ensure effective therapeutic outcomes. Given the lack of a commercially available liquid formulation, extemporaneous preparation is often the only viable option for paediatric patients. However, the sensitivity of furosemide towards factors such as pH, light, and temperature [4,5] raises concerns about the stability of the preparation, which could potentially lead to degradation and reduced efficacy.

The X-Temp® Oral Suspension System, a ready-to-use suspending vehicle, offers a practical and efficient option for compounding pharmacists, providing a safe and time-saving alternative. To explore its potential, this study was conducted to evaluate the stability of furosemide oral suspension at two different concentrations, prepared from commercial tablets using the X-Temp® Oral Suspension System. This system is specifically designed to facilitate the preparation of stable and uniform oral suspensions. By systematically evaluating the physicochemical and microbiological properties of these formulations under various storage conditions, this research aims to provide evidence-based guidelines for the preparation, storage, and administration of furosemide in X-Temp® suspensions, with a particular focus on paediatric applications.

METHOD

Oral suspensions were prepared from commercially available tablets, each containing 40 mg of furosemide (Pharmaniaga Frusemide Tablet 40 mg, Malaysia). The X-Temp® Oral Suspension System, marketed by Pharm-D Sdn. Bhd. (Malaysia), was the commercial suspending system utilized in this study. This system is commonly employed in hospitals to support the extemporaneous preparation of oral liquids and aqueous formulations with insoluble components.

Preparation of furosemide in X-Temp® suspension

In this study, two concentrations of furosemide suspension were prepared: 2 mg/mL and 10 mg/mL. For each concentration, forty bottles containing 100 mL of the suspension (totalling 4000 mL) were prepared. Before levigating, the required amount of X-Temp® Oral Suspension System was measured, and the furosemide tablets were ground into a powder using a mortar and pestle. A small portion of X-Temp® Oral Suspension System was initially mixed with the powder to create a smooth paste. The remaining X-Temp® Oral Suspension System was then gradually incorporated into the paste while stirring continuously until a uniform liquid was obtained. Subsequently, the mixture was transferred to a graduated container, and the mortar and pestle were rinsed thoroughly using the X-Temp® Oral Suspension System. The final volume of 4000 mL was achieved by adding more X-Temp® Oral Suspension System. To simulate actual dispensing conditions, the prepared bulk suspension was transferred into 40 amber high-density polyethylene (HDPE) bottles, each containing 100 mL, and sealed with white polypropylene (PP) screw caps.

Stability Evaluation

In the stability study, two concentrations of furosemide in X-Temp® suspension, 2 mg/mL and 10 mg/mL, were prepared and stored under two different conditions to simulate the dispensing environments. The first group was kept at room temperature, specifically 30 ± 2°C with a relative humidity of 75 ± 5%, while the second group was stored under refrigeration at 5 ± 3°C. Each group consisted of 18 bottles, and the samples were maintained for 90 days. To evaluate the stability of the samples, aliquots from both the 2 mg/mL and 10 mg/mL concentrations were collected at various time points: Day 0, Day 15, Day 30, Day 45, Day 60, Day 75, and Day 90.

(i) Physical Stability

The assessment of physical stability through visual inspection was the first step in ensuring the quality of oral suspensions. It involved observing the suspension for any changes in colour, flavour, and clarity, which were indicative of its stability. A stable preparation was defined as one in which these physical characteristics did not change significantly over time. Additionally, the measurement of specific gravity was an important physical test that compared the weight of the sample to that of water [6], providing insight into the concentration and consistency of the suspended drug. This test was conducted at a controlled room temperature to ensure its accuracy and reliability. The specific gravity values for concentrations of 2 mg/mL and 10 mg/mL were expected to fall within the range of 1.01 to 1.07 g/mL, as per the established in-house specifications. This range was critical for confirming that the oral suspension maintained the appropriate density and composition throughout the study period.

(ii) Chemical stability

The concentration of furosemide in the samples is a critical parameter and the specification limit was set to be within 90.0% to 110.0% of the labelled amount to ensure efficacy and safety [7]. The analysis was performed using High-Performance Liquid Chromatography (HPLC), and the retention time (RT) of furosemide in both the reference standard solution and the sample solutions was compared to confirm the identity of the compound. Concurrently, the peak area of furosemide, as the compound of interest, was calculated to provide a quantitative measure of its concentration. This dual assessment of RT and

peak area underpinned the capability of HPLC in ensuring the quality of pharmaceutical products.

The concentration of furosemide in the oral suspension was determined using the formula below:

Assay (%)

$$= \frac{(\text{Area for sample} \times \text{Concentration of reference standard} \times \text{reference standard purity} \times 100)}{(\text{Area for standard} \times \text{concentration of sample})}$$

The limit test for 4-chloro-5-sulfamoylanthranilic acid, also known as furosemide related compound B, was a quality control measure in the detection of degradation product for this study. The calculation of the percentage of 4-chloro-5-sulfamoylanthranilic acid in the oral suspension was performed based on the formula shown below:

Percentage of 4-chloro-5-sulfamoylanthranilic acid (%) (furosemide related compound B) in limit test:

$$= \frac{r_u}{r_s} x \frac{C_s}{C_u} x\ 100\%$$

Where

r_u = peak response of furosemide related compound B in the sample solution

r_s = peak response of furosemide related compound B in the standard solution

C_s = concentration of USP Furosemide Related Compound B RS in the standard solution (mg/mL)

C_u = nominal concentration of furosemide in the sample solution (mg/mL)

The pH values of the samples were measured at each time point by 57 tilized 57 a digital pH meter (Metrohm Model 913, Metrohm, Switzerland). The study outcomes were documented appropriately.

Analytical Method and Equipment

The quantification of furosemide was performed using HPLC equipped with a UV/Vis detector (Agilent, United States). The furosemide reference standard used was a working standard 57tilized57ize against a primary reference standard obtained from the European Directorate for the Quality of Medicines & HealthCare (EDQM).

Table I. HPLC Operating Conditions.

Description	Parameters
Type of Column	Zorbax Exclipse® XDB-C8
Column size	4.6 mm × 150 mm, 5 µm
Detection	UV 238 nm
Flow rate	1.0
Injection volume	10 µL
Mobile phase	0.021 M Potassium Dihydrogen Orthophosphate (KH2PO4) pH 7.00 with Cetrimide and Propan-2-ol (62:38 v/v)

Using the British Pharmacopoeia as a guide, a HPLC assay method was established based on the internal HPLC procedure [6]. The compound of interest was eluted with a mixture of 0.021 M potassium dihydrogen orthophosphate (KH2PO4) at pH 7.00, combined with cetrimide and propan-2-ol (62: 38, v/v) as the mobile phase. The diluent used in the preparation of reference standard and test sample was a combination of 40% propan-2-ol and 60% 0.021 M potassium dihydrogen orthophosphate (KH_2PO_4) at pH 7.00 with cetrimide. The furosemide peak in the sample chromatograph was compared to the furosemide peak of the reference standard chromatograph. The operating conditions applied in the reversed-phase HPLC assay analysis were tabulated in Table I.

The methods employed In this study were previously validated in a short-term stability investigation of extemporaneously prepared furosemide oral suspension using the same formulation. The validation process for the analytical methods encompassed specificity, linearity, accuracy, precision, and system suitability.

Identification and assay of furosemide using HPLC

(i) Preparation of reference standard

Approximately 100 mg of furosemide reference standard was dissolved in roughly 70 mL of diluent in a 100 mL amber volumetric flask and subjected to sonication for 5 minutes. The solution was brought to a final volume of 100 mL to yield the standard stock solution. A 10 mL portion of the standard stock solution was then diluted to 50 mL, and 5 mL of the diluted solution was diluted again to 50 mL using diluent. Prior to injection into the HPLC system, the solution was filtered through a 0.2 µm syringe filter into the an amber autosampler vial.

(ii) Preparation of Test Sample

To prepare a stock solution with a concentration of 2 mg/mL, a weighed quantity of the furosemide suspension containing 10 mg of furosemide was mixed with 70 mL of diluent. The solution was capped and subjected to sonication in a water

bath for 5 minutes before being diluted to 100 mL with the diluent. A total of 10 mL of the solution was then diluted to 50 mL using the diluent and filtered through a 0.2 µm syringe filter into an amber autosampler vial for chromatographic analysis.

To prepare a stock solution with a concentration of 10 mg/mL, a weighed quantity of the furosemide oral suspension containing 50 mg of furosemide was mixed with 70 mL of diluent. The solution was capped and subjected to sonication in a water bath for 5 minutes before being diluted to 100 mL with the diluent. The sample solution was diluted to 100 mL with the diluent. From this solution, 10 mL was further diluted to 50 mL with diluent, another 10 mL from the resulting solution was again diluted to 50 mL with diluent and filtered through a 0.2 µm syringe filter into an amber autosampler vial for chromatographic analysis. The resulting concentration of the standard and sample solutions prepared was 0.02 mg/mL.

Limit Test of 4-chloro-5-sulfamoylanthranilic acid (furosemide related compound B)

A series of test solutions was prepared for the quantification of 4-chloro-5-sulfamylanthranilic acid in the study samples. A system suitability solution was prepared with 0.1 mg/mL of furosemide and furosemide related compound A, and 0.015 mg/mL of furosemide related compound B as standard solution. A sensitivity solution of 0.0015 mg/mL of furosemide related compound B was also prepared for the limit test analysis. The sample test solution at a concentration of 1 mg/mL was prepared for the limit test. Matrix solution and diluent were also included in the limit test analysis for peak comparison. All sample solutions were subjected to filtration through a 0.2 µm syringe filter before being injected into the HPLC system. The limit test of furosemide related compound B was analysed through reversed-phase HPLC. The operating conditions applied in the limit test were summarised in Table II.

Table II. HPLC Operating Conditions for Limit Test.

Description	Parameters
Type of Column	Zorbax SB-CN
Column size	4.6 mm × 250 mm, 5 µm
Detection	UV 254 nm
Flow rate	1.0
Injection volume	10 µL
Mobile phase	17.3% Acetonitrile 82.7% Mobile phase mixture [Acetonitrile: Glacial acetic acid: Water (22:1:22)]

Microbiological stability

To ascertain whether the samples conformed to the microbiological attributes of non-sterile pharmaceutical, microbiological evaluation was performed on the samples in accordance with BP2024. According to BP2024 [6], the microbiological test parameters were set as Total Aerobic Microbial Count (TAMC) below 2×10^2 CFU/g, Total Combined Yeasts and Moulds Count (TYMC) below 2×10 CFU/g, and absence of Escherichia coli (E. coli) in 1 g.

(i) Microbial Enumeration Tests

The spread plate technique was employed to determine the TAMC and TYMC. A 10 g sample was diluted in 90 mL of buffered sodium chloride-peptone solution (pH 7.0). A 1:10 dilution was prepared, and a 1% w/v solution of polysorbate 80, used to inactivate antimicrobial agents, was added to the mixture. Serial tenfold dilutions (10^{-1}, 10^{-2}, etc.) were then prepared using the same diluent to achieve a colony count between 25 and 250. From these dilutions, 0.5 mL of each was transferred onto two Petri dishes containing Soybean-Casein Digest Agar (TSA) and two dishes with Sabouraud Dextrose Agar (SDA). The solution was evenly spread across the surface, and the plates were allowed to dry. Subsequently, the TSA plates were covered, inverted, and incubated at 30 – 35°C for 3 – 5 days to assess total aerobic bacterial and fungi, while the SDA plates were incubated at 20 – 25°C for 5 – 7 days to evaluate yeast and mould. The plates were then inspected for signs of microbial growth. A negative control was prepared concurrently using sterilized diluent in place of the sample for each medium.

(ii) Tests for Escherichia coli

A 10 g sample of furosemide oral suspension was diluted in 90 mL of buffered sodium chloride-peptone solution (pH 7.0). A 1:10 dilution was prepared, and 1% w/v polysorbate 80, an antimicrobial inactivator, was added to the mixture. To inoculate 100 mL of Soybean-Casein Digest Broth, 10 mL (equivalent to 1 g or 1 mL) of the diluted sample was used. The broth was homogenized and left to incubate at 30 – 35°C for 18 – 24 hours. After the incubation period, the broth was agitated to ensure proper mixing, and 1 mL of the Soybean-Casein Digest Broth was transferred into 100 mL of the MacConkey Broth. This was then incubated at a temperature range of 42 – 44°C for 24 – 48 hours. Following this, the MacConkey Broth was shaken, and a loopful was streaked onto MacConkey Agar plates using a sterile inoculating loop. The plates were incubated inverted at 30 – 35°C for 18 – 72 hours. Colony growth was examined for the presence of red nonmucoid colonies on the MacConkey Agar. The isolates were identified using Gram staining and biochemical tests, with further

confirmation using the API 20E (bioMérieux) identification system.

Statistical Analysis

The assay of furosemide oral suspension was performed in triplicate, and the results were presented as mean ± SD (Standard Deviation) and analysed using one-way ANOVA. GraphPad Prism X and Microsoft Excel 2019 were utilised to conduct statistical analysis.

RESULTS AND DISCUSSION

Furosemide oral suspensions at the concentrations of 2 mg/mL and 10 mg/mL were compounded from commercially available furosemide tablets using the X-Temp® Oral Suspension System, a commercially produced suspending agent. The extemporaneous suspension was prepared through a straightforward and reproducible process, following current good manufacturing practices for pharmaceutical compounding. Validation of the method was performed to ensure that it was congruous with its intended purpose, thereby providing accurate and precise results. Following the ICH Q2 guidelines, a structured approach to validation was employed, which included assessing parameters such as specificity, linearity, range, and precision [8]. The analysis fulfilled all specification criteria during the validation process, further confirming the reliability of the method in the quantification of furosemide in oral suspension formulations. A summary of method validation is tabulated in Table III.

Table III. ***Results of Method Validation.***

Test Parameter	Acceptance Criteria (6) (8)
Specificity	
Identification	
Comparison with a known reference material	Positive control: furosemide peak at RT 13.0 min Negative control: absence of peak at RT 13.0 min
Assay	
Placebo / Matrix analysis	No interfering peak from excipients Placebo Effect NMT 1.5 %
Linearity & Range	r2 ⩾ 0.995; 0.016 - 0.064 mg/mL Y-intercept at 100% working concentration ⩽ 2.0 %
Accuracy	% Recovery within 95% to 105 %
Precision (Repeatability)	RSD ⩽ 2.0 %
Precision (Reproducibility)	RSD ⩽ 2.0 %
Precision (Intermediate Precision / Ruggedness)	RSD ⩽ 2.0 %
System Suitability	
a.System Specificity	RSD ≤ 2.0 %
b. Peak identification	k' ≥ 1.5 USP Tailing Factor < 2 Column efficiency ≥ 2000

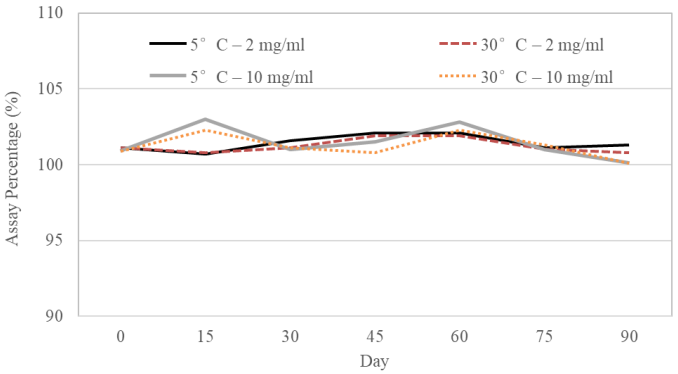

Figure I. Stability study on the percentage of furosemide in X-Temp® suspension over 90 days for both preparations of 2mg/ml and 10mg/ml at 5oC and 30oC respectively (n = 3, p-value > 0.05). (Specification: 90% - 110% of labelled amount)

The stability of furosemide in X-Temp® suspension was studied at two different concentrations – 2 mg/mL (low dose) and 10 mg/mL (high dose) – under both room temperature conditions (30 ± 2°C) and refrigerated conditions (5 ± 3°C). Stability studies revealed that furosemide in X-Temp® suspension, at both low and high doses, remained stable under two storage conditions for at least 90 days. As shown in Figure I, the furosemide level in the samples remained consistent and fell within the established specifications. The results obtained could provide a reference point for the formulation of furosemide in X-Temp® suspension, considering its stability at both low and high dose concentrations.

The physical, chemical, and microbial stability profiles of the furosemide in X-Temp® suspension (2 mg/mL and 10 mg/mL under two different storage conditions) over 90 days are presented in Table IV and Table V. The assay of the 2 mg/mL suspension ranged from 100.7% to 102.1%; for the 10 mg/mL suspension, the result ranged from 100.1% to 103.0%. From the data analysis, all the assay percentages showed no significant difference between the group of samples and remained consistent throughout the 90-day stability study.

(i) Physical Stability

Throughout the 90-day study period conducted at 2 distinct storage temperatures (5 + 3°C and 30 + 2°C), no significant alterations were identified regarding the colour, flavour, or clarity of suspension. In terms of the specific gravity, there was only negligible change observed during the stability study period.

(ii) Chemical Stability

All samples from both 2 mg/mL and 10 mg/mL were assayed at specific study intervals. The findings reveal that furosemide content in both 2 mg/mL and 10 mg/mL samples were in the range of 100.0% to 103.0% of the labelled amount. Based on the results obtained throughout the 90-day stability study, it

Table IV: Stability Profile of Furosemide in X-Temp® Suspension 2 mg/mL

Test	Specifications	Storage condition	Days						
			1	15	30	45	60	75	90
Visual Appearance	Colour: White to Off-white Clarity: Opaque Flavour: Orange	5 ± 3°C	Off-white & Opaque; Orange	Off-white & Opaque; Orange	Off-white & Opaque; Orange	Off-white & Opaque; Orange	Off-white & Opaque; Orange	Off-white & Opaque; Orange	Off-white & Opaque; Orange
		30 ± 2°C	Off-white & Opaque; Orange	Off-white & Opaque; Orange	Off-white & Opaque; Orange	Off-white & Opaque; Orange	Off-white & Opaque; Orange	Off-white & Opaque; Orange	Off-white & Opaque; Orange
Physical Properties	pH: 4.0 – 4.4	5 ± 3°C	4.255	4.260	4.256	4.259	4.258	4.254	4.213
		30 ± 2°C	4.255	4.266	4.253	4.253	4.244	4.229	4.232
	Specific gravity: 1.01 – 1.07 (g/mL)	5 ± 3°C	1.0356	1.0361	1.0382	1.0390	1.0392	1.0373	1.0375
		30 ± 2°C	1.0356	1.0377	1.0348	1.0380	1.0371	1.0368	1.0375
Assay* (%)	90.0 % – 110.0 %	5 ± 3°C	101.1 ± 0.79	100.7 ±1.42	101.6 ±0.22	102.1 ± 0.41	102.1 ± 0.41	101.1 ± 0.76	101.3 ± 0.21
		30 ± 2°C	101.1 ± 0.79	100.8 ± 1.36	101.1 ± 0.37	101.9 ± 0.37	101.9 ± 0.08	101.0 ± 0.62	100.8 ± 0.57
Related Substances (%)	Furosemide Related Compound B - Not more than 1.5%	5 ± 3°C	0.01	0.02	0.02	0.01	0.02	0.004	0.008
		30 ± 2°C	0.01	0.03	0.02	0.01	0.03	0.02	0.02
Microbial limit	Aerobic microbial: < 200 CFU/g	5 ± 3°C	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
	Yeasts & moulds: < 20 CFU/g	30 ± 2°C	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
	Escherichia coli: Absent in 1 g								

Note: *Assay percentage is expressed as mean ± standard deviation of triplicate (n = 3, $p < 0.05$).

Table V: Stability Profile of Furosemide in X-Temp® Suspension 10 mg/mL

Test	Specifications	Storage condition	Days						
			1	15	30	45	60	75	90
Visual Appearance	Colour: White to Off-white Clarity: Opaque Flavour: Orange	5 ± 3°C	White & Opaque; Orange	White & Opaque; Orange	White & Opaque; Orange	White & Opaque; Orange	White & Opaque; Orange	Off-white & Opaque; Orange	Off-white & Opaque; Orange
		30 ± 2°C	White & Opaque; Orange	White & Opaque; Orange	White & Opaque; Orange	White & Opaque; Orange	White & Opaque; Orange	Off-white & Opaque; Orange	Off-white & Opaque; Orange
Physical Properties	pH: 4.0 – 4.4	5 ± 3°C	4.217	4.239	4.227	4.237	4.229	4.217	4.205
		30 ± 2°C	4.217	4.254	4.233	4.239	4.236	4.226	4.188
	Specific gravity: 1.01 – 1.07 (g/mL)	5 ± 3°C	1.0479	1.0474	1.0478	1.0488	1.0480	1.0467	1.0472
		30 ± 2°C	1.0479	1.0484	1.0468	1.0480	1.0473	1.0468	1.0469
Assay*	90.0 % – 110.0 %	5 ± 3°C	100.9 ± 0.86	103.0 ± 1.00	101.0 ± 0.55	101.5 ± 0.52	102.8 ± 0.40	101.0 ± 0.23	100.1 ± 0.65
		30 ± 2°C	100.9 ± 0.86	102.3 ± 1.80	101.1 ± 0.55	100.8 ± 0.26	102.3 ± 0.58	101.3 ± 0.39	100.1 ± 0.13
Related Substances	Furosemide Related Compound B - not more than 1.5%	5 ± 3°C	0.10	0.09	0.09	0.08	0.08	0.09	0.08
		30 ± 2°C	0.10	0.10	0.10	0.10	0.10	0.12	0.12
Microbial limit	Aerobic microbial: < 200 CFU/g Yeasts & moulds: < 20 CFU/g *Escherichia coli*: Absent in 1 g	5 ± 3°C	Conforms Conforms	Conforms Conforms	Conforms Conforms	Conforms Conforms	Conforms Conforms	Conforms Conforms	Conforms Conforms
		30 ± 2°C							

Note: *Assay percentage is expressed as mean ± standard deviation of triplicate (n = 3, $p < 0.05$).

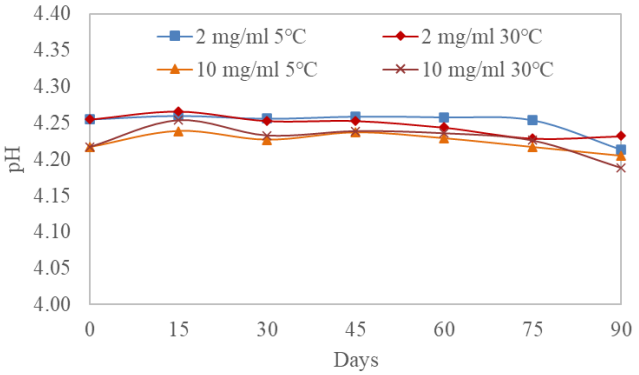

Figure II: pH of furosemide in X-Temp® suspension over 90 days.

could be inferred that furosemide remained stable when suspended in X-Temp® Oral Suspension System. The difference between the results in the 2 mg/mL and 10 mg/mL samples at both storage conditions was statistically proven to be insignificant, with a p-value of 0.856 ($p > 0.05$) and an F-value of 0.257. The current findings were in agreement with the studies conducted by Svirskis et al. (2020) [9] and Wahab et al. (2020) [13]. In those studies, the physical and chemical stability of furosemide in the commercial vehicle Ora-Blend® was examined. The pH of the suspending system ranged from 4.2 to 7.7, and the formulations were prepared at a concentration of 2 mg/mL. The studies found that extemporaneous formulations of furosemide in Ora-Blend® products were physically and chemically stable over 30 days at 4°C and 25°C. Ora-Blend® SF has an almost identical formulation to X-Temp® Oral Suspension, with a pH buffered to an acidic range of 4.0 – 4.5. Consequently, the results from both studies were unsurprisingly similar. The pH of the furosemide in X-Temp® suspension remained relatively stable throughout the 90-day study, as depicted in Figure II. Both formulations exhibited a consistent pH with a minimal decrease of 0.01 - 0.04 pH units observed from the initial measurement to 90 days.

Building upon the findings of Wahab et al. (2020), which demonstrated that X-Temp® could serve as an appropriate vehicle for furosemide compounded suspension, the current study extended the stability assessment to 90 days. In addition to monitoring the assay percentage of furosemide, the study included a limit test for 4-chloro-5-sulfamoylanthranilic acid, a significant degradation product of furosemide. The content of furosemide and its related compound B were determined quantitatively in this study design. The results indicate that furosemide remains stable in X-Temp® under both refrigerated and real-time storage conditions for the duration of the 90-day study period.

The X-Temp® Oral Suspension System utilise a buffering system consisting of Citric Acid and Monosodium Phosphate. The pH value of furosemide in X-Temp® suspension was stable and remained at around 4.2. According to Kovar et al. [10], furosemide has been observed to undergo acid-catalysed hydrolysis in acidic environments, leading to the breakdown into 4-chloro-5-sulfamoylanthranilic acid and furfuryl alcohol. This instability does not occur in basic conditions, which is essential for the stability of furosemide [4]. Interestingly, despite the general instability in acidic media, stability studies of furosemide in X-Temp® suspension for both concentrations (2 mg/mL and 10 mg/mL) in the present study had shown that even in a low pH system, furosemide remained stable over a period of 90 days. Stability was shown through the limit test (Figure III), which demonstrated that the concentration of the degradation product, 4-chloro-5-sulfamoylanthranilic acid, remained significantly low and well within the acceptable specification limit of 1.5% [7]. Theoretically, changes in pH are often associated with drug degradation [11]. Due to the absence of any considerable pH changes in the extemporaneous preparations in the current study, it could be deduced that no drug degradation had occurred in the formulation.

Furosemide is also known for its photosensitivity, which poses a challenge for its storage and stability [5]. When exposed to light, an aqueous solution of furosemide can undergo photo-induced hydrolysis, consequently resulting in the formation of a yellow solution consisting of the degradation products 4-chloro-5-sulfamoylanthranilic acid and furfuryl alcohol [12]. This degradation not only affects the appearance but can also compromise the efficacy of the medication, which is critical for patients relying on its therapeutic benefits. The use of amber-coloured HDPE bottles in the present study provided a protective barrier against light, effectively shielding the furosemide in X-Temp® suspension from light sources that would otherwise trigger degradation. By safeguarding the medication from light-induced degradation, these bottles ensured that furosemide retained its efficacy throughout the study period, whether stored under refrigerated conditions or at room temperature.

The present research suggests that a furosemide oral suspension utilising the X-Temp® Oral Suspension System to suspend furosemide offers a promising treatment alternative for patients, particularly children, who have difficulty swallowing tablets.

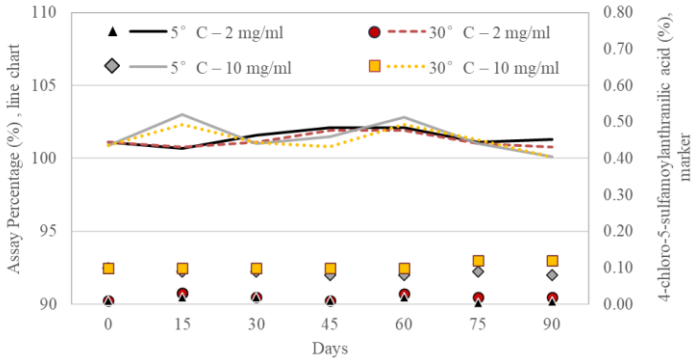

Figure III: Stability Profile - Assay on % of furosemide against 4-chloro-5-sulfamoylanthranilic acid limit test over 90 days for both preparations of 2mg/ml and 10mg/ml at 5ºC and 30ºC respectively.

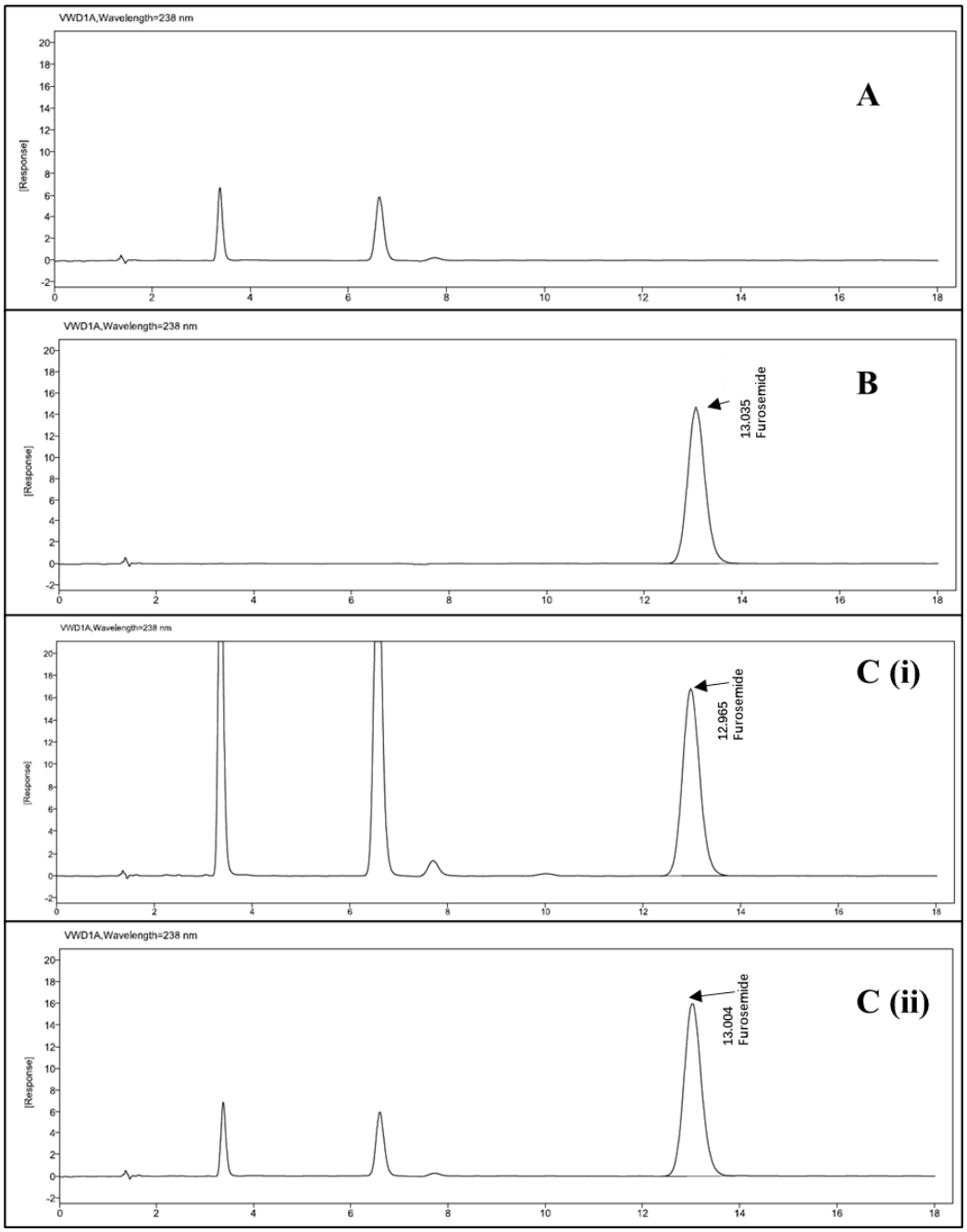

Figure IV: HPLC Chromatograms of (A) X-Temp® Oral Suspension System, (B) Furosemide Reference Standard, (C) Furosemide in X-Temp® Suspension (i) 2 mg/mL (ii) 10 mg/mL.

The study finds that an oral suspension with a concentration as low as 2 mg/mL and as high as 10 mg/mL can remain stable for up to 90 days, regardless of whether it was kept at room temperature or refrigerated, potentially enhancing the accessibility of the medication and ease of administration.

The chromatograms (Figure IV) illustrated the selectivity of the HPLC method utilised in this research, showing insignificant interference from the excipients present in the formulation. The chromatograms of the analysed samples at various time points during the stability study showed that there was no additional peak correlated to any potential degradation products.

Microbiological Stability

Based on the results in Table 4 and 5, none of the study samples exhibited any microbial growth throughout the entire study duration. The microbial analysis indicated that TAMC, TYMC,

and E. coli were not detected, which evinced the adherence to the established quality requirements. This was indicative of the potential of the X-Temp® Oral Suspension System in maintaining the microbial stability of the suspension over the course of the study. The suspensions were maintained at around pH 4.2, which contributed to the effectiveness of the preservatives and provided an environment that hindered microbial growth. This aspect is of pivotal importance since the shelf-life of many extemporaneous formulations is often restricted by the susceptibility to microbial growth, on top of the stability of the active component itself.

CONCLUSION

Furosemide oral suspensions consisting of 2 mg/mL and 10 mg/mL of furosemide were readily formulated from commercially available tablets using the X-Temp® Oral Suspension System. The compounding exhibited reassuring stability for up to 90 days while preserving all the quality characteristics. Based on the results, it can be concluded that furosemide in X-Temp® suspension at concentrations ranging from 2 mg/mL to 10 mg/mL demonstrates physical, chemical, and microbiological stability under refrigeration and at room temperature for a minimum of 90 days when stored in amber HDPE bottles. This formulation, prepared using the X-Temp® Oral Suspension System, offers a promising alternative in terms of efficacy, safety, and reliability for hospital pharmacy services to optimise paediatric diuretic therapy.

The stability study results indicated that the X-Temp® Oral Suspension System could serve as a stable suspending vehicle for compounding various active pharmaceutical ingredients indicated for a wide range of medical applications. In addition to providing a stable formulation, it offers several other benefits, such as being alcohol-free, colorant-free, and sugar-free.

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CONFLICT OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

REFERENCE

[1] Batchelor, H.K. & Marriott, J.F. Formulations for children: Problems and solutions. Br J Clin Pharmacol, 2015; 79(3): 405-418. https://doi.org/10.1111/bcp.12268

[2] Kearns, G.L., Abdel-Rahman, S.M., Alander, S.W., Blowey, D.L., Leeder, J.S., & Kauffman, R.E. Developmental pharmacology—Drug disposition, action, and therapy in infants and children. The New England Journal of Medicine, 2003; 349(12):1157-1167. https://www.nejm.org/doi/full/10.1056/NEJMra035092

[3] Costello, I., Long, P.F., Wong, I.K., Tuleu, C. & Yeung, V. Paediatric drug handling. Pharmaceutical Press, London. 2007

[4] Ghanekar, A.G., Gupta, V.D. & Gibbs, C.W. Stability of furosemide in aqueous systems. J Pharm Sci, 1978; 67(6):808-810. https://doi.org/10.1002/jps.2600670621

[5] Moore, D.E. & Sithipitaks, V. Photolytic degradation of frusemide. J. Pharm. Pharmacol, 1983;35(8): 489-493. https://doi.org/10.1111/j.2042-7158.1983.tb04816.x

[6] British Pharmacopoeia Commission. British Pharmacopoeia 2024 Volume V. Appendix XVIB. London, The Stationery Office. 2023

[7] USP. Furosemide Oral Solution. In: USP-NF. 2022 [cited May 1, 2022]. Available from https://doi.org/10.31003/USPNF_M34560_03_01

[8] International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, ICH Harmonised Tripartite Guideline, Q2 (R2). [cited May 1, 2024]. Available from https://database.ich.org/sites/default/files/ICH_Q2-R2_Document_Step2_Guideline_2022_0324.pdf

[9] Svirskis, D., Jaffer, J., Agarwa, P., Khan, A., Kaur, J., Cheng, A. & Hanning, S. Alcohol-free extemporaneous formulations of furosemide are chemically and physically stable in Ora-Blend products for 30 days. Int J Pharm Compd, 2020;24(3):246-251. https://pubmed.ncbi.nlm.nih.gov/32401745/

[10] Kovar, K.A, Wojtovicz, G.P. & Auterhoff, H. Hydrolysis of diuretic sulphonamides. Archiv der Pharmazie, 1974; 307(74): 657-662. https://doi.org/10.1002/ardp.19743070902

[11] Shoosanglertwijit, J., Kaewnopparat, S., Yongmaitreesakul, B., Pattayananthavej, S., & Kaewnopparat, N. Physical, chemical, and microbiological stability of extemporaneous furosemide suspensions. Asian Biomed, 2011; 5(5):681-686. https://intapi.sciendo.com/pdf/10.5372/1905-7415.0505.089

[12] Giannetti, M., Canale, V.C., Micheli, L., Fiori, M., Mazzuca, C. & Palleschi, A. An insight into the degradation processes of the anti-hypertensive drug furosemide. Molecules, 2023; 28(1):381. https://doi.org/10.3390/molecules28010381

[13] Wahab, M. F. B. A., Amir, A. B., Razi, S. S. B. M., & Ramli, N. B. The Stability Study of Extemporaneous Preparations Prepared in The Outpatient Pharmacy of Tuanku Fauziah Hospital Stored in Patient's Setting. Pharm. Res Reports, 2020; 40. https://research.pharmacy.gov.my/sites/default/files/publication/PRR%20Vol3%202020%20Issue2.pdf#page=46

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Can We Balance the Scale - Understanding the Landscape of Medicine Shortages and Surpluses Across Healthcare Facilities in Malaysia

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Li Ling Yeap*, San Min Soh, Wei Xian Yeoh, Guo Huei Tan, Jia Nuo Hee, Khuen Yen Ng, Pui San Saw

Abstract P16

Understanding The Contributing Factors and Impact of Burnout on Malaysian Pharmacists in Their Respective Healthcare Organisations (Government and Private): A Study Protocol

Freda Jia Xin Jong, Mei-Hua Lin, Kun Yun Lee, Mark Wing Loong Cheong, Pui San Saw, Shaun Wen Huey Lee, Siew Li Teoh

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ORAL PRESENTATION

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Abstract 001

Revolutionising Medication Reconciliation For Elderly Care With SafeMeds Application: A Study Protocol

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ABSTRACT

Background: Pharmacists in Malaysian public hospitals face challenges such as staff shortages and time constraints, impacting patient care. The high patient load, especially among the growing elderly population with complex medication needs, hinders thorough medication reviews. The elderly in Malaysia, facing increased comorbidity, use multiple medications, leading to polypharmacy and medication-related problems. Additionally, the ageing process makes elderly patients more susceptible to adverse drug reactions due to metabolic changes and reduced drug clearance. Existing time pressures exacerbate these issues, emphasising the urgent need for an innovative solution. The proposed SafeMed app aims to address these challenges by offering a user-friendly platform to enhance medication safety and improve elderly patient care in Malaysian hospitals. **Method and Design:** The SafeMeds mobile application's development will adhere to a systematic methodology: identifying user requirements through literature reviews and consultations, followed by meticulous design and development. A pilot study will assess usability and guide modifications, leading to a randomised controlled trial among hospital pharmacists. Data analysis will evaluate SafeMeds' effectiveness in improving reconciliation outcomes. The study will conclude with evidence-based recommendations for the application's adoption and implementation in healthcare settings, ensuring a comprehensive approach within a limited framework. **Conclusion and Discussion:** We hypothesise that the SafeMed application will improve medication-related challenges and improve care for elderly patients in Malaysian public hospitals. Its innovative features will streamline pharmacists' review processes, reducing the risk of adverse drug reactions. The application will also enhance medication safety and reduce the workload on pharmacists, aligning with United Nations Sustainable Development Goal 3 whose initiative contributes to the pursuit of healthy lives and well-being for individuals of all ages. **Trial registration:** Ethical approval has been obtained from Taylors University Ethics Committee, ID NO: 202127-9811.

Abstract 002

A Comparison Retrospective Study On The Efficacy of Azvudine And Traditional Chinese Medicine In The Treatment of COVID-19

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ABSTRACT

Background and objective: Coronavirus disease (COVID-19) has become a global pandemic and posed serious threats to the general population. Many therapeutic drugs are employed for the COVID-19 treatment. However, there is a paucity of data on comparison of the currently available drugs with Traditional Chinese Medicine in terms of their efficacy. The objective of this study is to compare the efficacy of Azvudine (FNC) and Traditional Chinese Medicine (TCM) in the treatment of mild and moderate cases of coronavirus disease (COVID-19). **Methods:** Patients admitted in a public hospital in Zibo City, China between November 2022 and June 2023 for treatment of COVID-19 either with Azvudine (FNC) or Traditional Chinese Medicine (TCM) or a combination of FNC + TCM were enrolled in this retrospective study. **Results and Discussion:** A total of 307 confirmed cases of COVID-19 fulfilling the inclusion criteria, and having definite outcomes were included. The mean age of participants was 64.9 (±16.9) years and males, n=176 (57.3%) outnumbered females. The duration of negative nucleic acid conversion (NANC), an indicator of drug efficacy and clinical improvement, was significantly lower for patients in the group receiving a combination therapy of FNC + TCM (6.80 days, $p < 0.001$). The time to chest CT improvement was significantly reduced in the combination treatment group (8.81 days, $p < 0.001$). Similarly, the duration of hospital stay was also significantly lower i.e. 12 days at $p < 0.035$ in the group receiving the combination treatment as compared to the groups receiving either FNC monotherapy or TCM alone. **Conclusion:** FNC combination with TCM has a significant clinical efficacy in the treatment of mild and

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moderate cases of COVID-19, which is worthy of further larger scale study and clinical application.

Abstract 003

The Use of ATLAS, a Generative AI Tool in Preparing Pharmacy Students for OSCEs

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ABSTRACT

Background and Objective: Students often require more practice to prepare for high-stakes clinical examinations, such as Objective Structured Clinical Examinations (OSCEs). ATLAS (Authentic Teaching & Learning Application Simulations) is a prototype that harnesses cutting-edge Large Language Model technologies to enable patient avatars in the software to offer human-like responses and real-time, tailored feedback of the users' clinical and communication skills. It has the potential to develop clinical skills such as history-taking and clinical reasoning. This study aimed to evaluate the usability and acceptability of ATLAS. **Methods:** A quasi-experimental study was conducted in a Year Two pharmacy unit across Monash campuses in Malaysia and Australia. Students volunteered to practise with patient avatars simulating community pharmacy settings before their OSCEs. Data encompassing ATLAS attempt counts, OSCE scores, and tool perceptions were systematically collected and analysed. **Results and Discussion:** 385 students participated in the survey, with 91.4% practising at least one history-taking case. The cohort in Malaysia responded more positively to the tool than the Australian. Overall, students perceived the tool as realistic, engaging, interactive, and able to maintain their interest. Students desired more scenarios to practise with. They agreed that the tool effectively taught them patient-friendly language and an empathetic approach. However, they disagreed that the feedback was less offensive than that of traditional tutors. Median OSCE scores improved with increased ATLAS practice from 0.80 with no attempts to 0.90 after six attempts. Regression analysis showed a significant impact of ATLAS usage on OSCE marks (p=0.01). **Conclusion:** ATLAS shows potential for clinical skill development by providing a realistic environment for safe, unrestricted practice, addressing the challenges of organising face-to-face practice sessions, which can be both costly and labour-intensive.

Abstract 004

Exploring the Potential of Incorporating Community Pharmacists in Tuberculosis Management

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ABSTRACT

Background and Objectives: The Public-Private Mix (PPM) has been advocated as one of the catalysts to accelerate efforts in tuberculosis (TB) control and prevention. Community pharmacists can play a role in improving TB case detection and treatment outcomes, but these roles have not been explored in Malaysia. This study aimed to evaluate the perspectives of various stakeholders towards the potential of community pharmacy-based TB services in Malaysia. **Method:** A qualitative study was performed. Thirty-two participants from three groups of stakeholders: policymakers, healthcare professionals (pharmacists, doctors, clinicians), and the community (TB survivors, TB patients, people with latent TB infection, non-governmental organisations, and the public) participated in a one-on-one semi-structured interview. All interviews were transcribed verbatim and analysed using an inductive thematic content analysis approach rooted in grounded theory. **Results and Discussion:** Three main themes were identified in this study: (1) The Service gap in the TB care cascade; (2) The expansion of the professional role of community pharmacists in improving access to TB services; and (3) The availability of resources to facilitate community pharmacy-based TB services. Findings suggested that community pharmacists could play an active role as the point of referral and as the supervisor in monitoring TB-directly observed therapy (TB-DOT). Participants also agreed collective support is needed to strengthen PPM for community pharmacists to expand their professional role and service in TB management. **Conclusion:** Community pharmacy-based TB interventions were viewed as a novel and potential strategy for contributing to the National TB Control Program, where community pharmacists could potentially improve the accessibility to TB services in primary care settings. Educational interventions for TB awareness to all members of society are the fundamental cornerstones to enhance the understanding of

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the urgent need to address the service gaps in TB care through community pharmacists.

Abstract 005

Exploring Factors Influencing Acceptance of Digital App Usage for Medication Adherence Enhancement in Type 2 Diabetes Mellitus

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ABSTRACT

Background and Objectives: Non-adherence to antidiabetic treatment remains suboptimal. Digital applications (apps) have demonstrated positive impacts on adherence and glycemic outcomes. However, the factors influencing type 2 diabetes mellitus (T2DM) patients' acceptance of using apps to improve adherence are still unclear. Therefore, this study aimed to explore the perspectives of T2DM patients in using apps for medication adherence enhancement. **Method:** By employing a qualitative phenomenological approach, 25 semi-structured in-depth interviews were conducted. All interviews were audio-recorded and transcribed verbatim. Thematic analysis was utilised to identify the factors. **Results and Discussion:** Three primary themes affecting perceived usefulness emerged: medication, patient, and healthcare professional-related factors. Three key themes affecting perceived ease of use emerged: patient, app, and family-related factors. Patients perceived that digital apps were beneficial for individuals with poor adherence, complex medication regimens and forgetfulness issues, especially if recommended by healthcare professionals with additional family support. However, concerns regarding effective implementation were raised because of the technical challenges encountered by late middle-aged T2DM patients, suggesting a combination approach integrating digital technology and conventional patient education and counselling. **Conclusion:** This study highlighted the factors influencing patients' acceptance of digital health solutions to improve medication adherence. The proposed factors serve as a guide for strategic interventions to effectively encourage the use of digital health technology among T2DM patients.

Abstract 006

Comparison of Direct Proportion Approach (Investigated) versus Conventional Method (Standard) For Dose Adjustment of Carbamazepine

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ABSTRACT

Background and Objectives: Therapeutic Drug Monitoring (TDM) is extremely useful and significant for drugs with a narrow therapeutic index. One of the common drugs requiring TDM is carbamazepine. Conventional pharmacokinetic approach in drug dosage adjustment presents a problem of applying a rather complex formula and multiple steps in calculating the dosage adjustment. Direct proportion method involves two variables such as dose and concentration in the calculation while conventional pharmacokinetic approach requires multiple variables such as dosing interval, clearance, concentration at steady state, salt factor and bioavailability. This study aimed to determine the magnitude of difference and the level of agreement between the conventional pharmacokinetic equation method (standard) and the direct proportion approach in CBZ dose adjustment. **Method:** This was a retrospective study conducted at Therapeutic Drug Monitoring Department, Sultan Abdul Halim Hospital, Kedah, Malaysia. A sample size of 5 which required CBZ dose adjustment based on their concentration from 1st January 2022 to 31st December 2022 was included into the study in which the median age was 36 years old with a median weight of 74kg. Males represented 80% of the population. Calculations of actual cases requiring CBZ dose adjustment in hospital were done using both Conventional pharmacokinetic approach and Direct proportion method. The final answers were then compared using SPSS to check for statistical significance. Statistical analysis included one sample T test and Bland Altman analysis. **Results and Discussion:** The propose dose adjustments were identical using the conventional (multiple steps) approach and the direct proportional method (1 step), p = 1.00. One sample T test was used to analyze the mean differences of proposed dose adjustments based on direct

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proportion method to a value of zero (no difference). The mean differences of proposed dose adjustments were non statistically significant ($p > 0.05$). Bland-Alman analysis showed good agreement of the proposed dose adjustments by direct proportion method with the conventional (standard) approach, $p = 1.00$. **Conclusion:** The results from this study gave strong assurance and evidence that direct proportion method could be used safely as an alternative to the conventional pharmacokinetic equation method (standard) in the calculation of new maintenance dose for CBZ.

Abstract 007

Complementary and Alternative Therapies (CATs) are Positively Perceived and Highly Utilised by Epilepsy Patients on Anti-Epileptic Drugs (AEDs)

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ABSTRACT

Background and Objectives: The main objective in epilepsy treatment is to control seizures, minimize adverse effects, and enhance quality of life. Dissatisfaction with anti-epileptic drugs (AEDs) may drive patients with epilepsy (PWEs) to seek alternative treatment like complementary and alternative therapies (CATs), possibly impacting on AED adherence. The aims of this study were to assess perception and utilization on CATs and its association with adherence. **Method:** A cross-sectional study was carried out at neurology clinics in three government hospitals in Peninsular Malaysia. The perception and utilization of CATs were assessed using a validated questionnaire, while Malaysian Medication Adherence Scale (MALMAS) evaluated adherence. Using SPSS 26, descriptive statistics and chi-square test were utilized to determine the association between CAT usage and adherence. **Results and Discussion:** Eighty-six PWEs were selected through convenience sampling (mean age = 33.9 ± 11.3 years; 59.3% female; 51.2% unmarried; 94.2% Malay). Eighty percent admitted to using CATs. The most common being prayers (64.0%), massage (44.2%), structured exercise such as yoga (29.1%) and vitamins and supplementations (22.4%). While 40.7% disagreed that CATs can provide quick and additional relief in treating epilepsy, the majority agreed that CATs are cheaper than modern medicine (31.4%), easily accessible (55.8%), promoting self-healing (37.2%), and solely for treating minor illnesses (43.0%). Additionally, 45.3% acknowledged that people generally use CATs due to fear of discomfort from allopathic treatment. Nevertheless, a high level of AED adherence (41.9%) was recorded i.e. all MALMAS questions were fully-scored. Encouragingly, no significant association was observed between AED adherence and CAT usage ($p > 0.05$). **Conclusion:** Despite the positive perception and high utilization of CATs by PWEs, their usage was unrelated to adherence. Healthcare professionals should regularly monitor potential interactions between CATs and AEDs to ensure the effectiveness of AEDs and prevent adverse effects.

Abstract 008

Investigating HbA1c reduction and incidents of reported hypoglycaemia between human insulins versus analogue insulins among type 2 diabetic mellitus patients - A Single Centre, Retrospective Study

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ABSTRACT

Background and Objectives: Two types of exogenous insulin are available within the realm of diabetes treatment: human insulins and analogue insulins. Studies have shown that both human insulins and analogue insulins performed similarly in reducing blood glucose without significant changes in the frequency of serious hypoglycaemic episodes. This study aimed to determine the magnitude of difference in

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terms of HbA1c reduction and explore the incidents of reported hypoglycaemia among T2DM patients receiving human insulins (premixed) and analogue insulins (premixed). **Method:** This was a retrospective study conducted in one primary public health clinic in the state of Perak, Malaysia. All type 2 diabetes patients who fulfilled the inclusion criteria were identified and recruited for analysis. Sugar profiles and incidents of reported hypoglycaemia in patients receiving human insulin and analogue insulin were compared. The results were analysed by using Independent t-test and Chi-square test with IBM SPSS Statistics (Version 29) to determine statistical significance. **Results and Discussion:** No significant HbA1c reduction was noted among patients receiving human insulin therapy. Instead, the results showed an increased HbA1c level of 0.11 %, p = 0.347. Meanwhile, for the analogue insulin group, a reduction of HbA1c by 0.99 % was observed, p = 0.004. A total of 13 (37.14%) incidents of hypoglycaemia were reported among patients receiving human insulin. On the other hand, 3 (8.57%) incidents of hypoglycaemia were reported in patients receiving analogue insulin. **Conclusion:** Premixed human insulins and analogue insulins might not perform similarly in terms of reducing HbA1c and incidents of hypoglycaemia. Analogue insulin was associated with better HbA1c control and significantly lesser incidents of reported hypoglycaemia. Optimal control of postprandial blood sugar is equally important.

Abstract 009

Breastfeeding-Friendly Community Pharmacists to Support Mothers for Successful Lactation and Combating Anxiety and Depression: A Protocol of Pilot-Testing Study in Malaysia

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ABSTRACT

Background and Objectives: Breastfeeding rates in Malaysia are lower than the Ministry of Health's and World Health Organisation's targets, only 47% exclusively breastfed infants compared to 58% and 70% set targets respectively. The role of community pharmacists is limited in pregnant and breastfeeding women. This study aimed to evaluate the impact of pharmacist-led interventions on breastfeeding practices among pregnant and postpartum women. The objectives include enhancing breastfeeding intention and self-efficacy in pregnant women and reducing anxiety and depression while improving self-efficacy in breastfeeding mothers. **Method:** The study will involve training community pharmacists as breastfeeding-friendly pharmacists. Subsequently, a mixed-method approach, consisting of two studies, will then be conducted to evaluate the pharmacist-led interventions for pregnant and breastfeeding mothers. Study 1 targets pregnant women, whereby the intervention will increase their intention to breastfeed and self-efficacy. Study 2 targets breastfeeding women, whereby the intervention will reduce their anxiety and depression as well as increase their intention to continue breastfeeding and self-efficacy. For both studies, the cross-sectional study design will evaluate the pre-post improvement following the intervention. Follow-up evaluations will be conducted up to 2 months postpartum to assess breastfeeding practices, supplemented by qualitative feedback on the intervention's feasibility and effectiveness. **Results and Discussion:** Pharmacists will be trained to be more breastfeeding-friendly. Expected outcomes include improved breastfeeding intention and self-efficacy in pregnant women (Study 1), and enhanced postpartum mental health, self-efficacy, and breastfeeding continuation in mothers (Study 2). Follow-up results and qualitative feedback will inform the intervention's effectiveness and feasibility, leading to improved future interventions. **Conclusion:** Community pharmacists, as the most accessible healthcare professionals, can offer critical breastfeeding support in primary care settings. This model will further inform a scalable approach to improving breastfeeding rates and maternal well-being in Malaysia, aligning with national health objectives and global breastfeeding recommendations.

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Abstract 010

Assessing the Magnitude of Blood Pressure Reduction in Newly Diagnosed Patients Treated with Perindopril or Amlodipine Monotherapy at Various Dosages – A Retrospective, Multicenter Observational Study

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ABSTRACT

Background and Objectives: Hypertension is a well-established modifiable risk factor for the spectrum of cardiovascular diseases. What is being missed from available clinical practice guidelines in managing hypertension is the absence of data on the magnitude of reduction (%) or mean BP reduction potential of individual antihypertensive agents. This study aimed to identify the magnitude of BP reduction of the two most common antihypertensive agents (perindopril and amlodipine) at various dosages used in public primary care clinics in Malaysia. **Method:** This was a multicentre, retrospective and observational study that identified the magnitude of the BP reduction of perindopril and amlodipine from 1st January 2017 to 30th of September 2019. The study was conducted at six primary public health clinics in the Northern Region of Malaysia. **Results and Discussion:** A significant reduction of mean SBP was observed after three months of treatment with perindopril 4 mg OD. Mean SBP was reduced significantly by 5.47% (95% CI: 4.15-12.15, $p < 0.001$). However, there was no statistically significant reduction in mean DBP ($p = 0.368$). Amlodipine 5mg OD reduced both mean SBP and DBP significantly. Mean SBP was reduced by 8.48% after 3 months of treatments ($p < 0.001$) while mean DBP was reduced by 4.65% ($p < 0.001$). Amlodipine 10mg OD reduced mean SBP and DBP significantly. Mean SBP was reduced significantly by 9.04% ($p < 0.001$). Mean DBP was reduced significantly by 7.22% ($p = 0.001$). **Conclusion:** The mean BP reduction by perindopril 4mg OD in the study population was 5.47%/1.23%. Amlodipine 5mg OD, and 10mg OD reduced mean BP in the study population by, 8.48%/4.65%, and 9.04%/7.22% respectively. The result of this study shall provide the mean BP reduction of both commonly used antihypertensive agents.

Abstract 011

Development and Validation of the Malay HIV Knowledge Questionnaire (HuSKQ-Malay) Among Human Immunodeficiency Virus Infected Individuals in Malaysia

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ABSTRACT

Background and Objective: In people living with the human immunodeficiency virus (PLWH), self-care is important, as it empowers PLWH to attain better control of their health. To date, no questionnaire has been developed to assess knowledge on human immunodeficiency virus self-care. Hence, our aim was to develop and validate the Malay HIV Knowledge Questionnaire (HuSKQ-M) among PLWH. **Methods:** The HuSKQ-M was initially developed in English based on literature review and input from an expert panel. It was then translated into Malay and piloted among ten PLWH. The final version of the HuSKQ-M had 29 items in 3 domains: physical health, psychological functioning, and social relationship. It was then administered to PLWH [CD4 count of > 200cells/mm3], who understood Malay, aged ≥ 21 years, on treatment for > 3 months; from March to October 2022, at a tertiary hospital in Malaysia at baseline and 2 weeks later. Each participant took approximately 15 minutes to answer the questionnaire. **Results & Discussion:** 149/168 PLWH participated (response rate=88.7%). Majority were male (88.6%) with a median age of 41.0 years. Kaiser-Mayer-Olkin measure of sample adequacy was 0.835 and Bartlett's Test of Sphericity was 0.000 indicating an adequate sample size to perform factor analysis. Exploratory factor analysis revealed that the HuSKQ-M had 4 domains: (1) misconception and understanding HIV; (2) transmission and prevention; (3)

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treatment and management; (4) stigma and consequences. The overall Cronbach alpha was 0.892 (individual domains ranged [0.0-100.0]. The HuSKQ-M was able to discriminate the knowledge level of patients with and without postgraduate education (64.6±22.1 vs 83.2±8.6, $p < 0.05$). At retest, 102/149 PLWH participated (response rate = 68.5%) and 26/29 items were not statistically significant, indicating adequate reliability. **Conclusions:** The HuSKQ-M was found to be a valid and reliable questionnaire for evaluating HIV self-care knowledge in Malaysia.

Abstract 012

Factors associated with unused medicines: a cross-sectional study

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ABSTRACT

Background and Objective: The presence of unused medicines significantly impacts the economy and environment. Understanding the factors associated with this issue is crucial. This study aims to identify these factors influencing the accumulation of unused medications. **Methods:** A cross-sectional survey was conducted using face-to-face interviews and a structured questionnaire. Participants were recruited through convenience sampling in Kuala Lumpur and Selangor, Malaysia. Multivariate logistic regression analysis was employed to examine the associations between factors and unused medicines. **Results:** Among 1184 participants, 84% (995) reported having unused medicines. About a quarter of respondents kept unused medicines in the cabinet, and another quarter disposed of them in the trash or toilet. Individuals using medications for acute illnesses were significantly more likely to have unused medications compared to those with chronic conditions (Odds Ratio [OR] = 29.8, 95% CI 7.03-126.56). Additionally, participants who paid for their medicines (OR = 6.0, CI 3.81-9.49) and those unwilling to participate in a Medicine Return Programme (MRP) (OR = 2.5, CI 1.26-5.03) were more likely to have unused medications. The primary reasons for having unused medicines were non-adherence (69%, $p < 0.05$) and improvement in health conditions leading to medication discontinuation (79%, $p < 0.05$). **Conclusion:** The study revealed a high prevalence of unused medicines. To address this issue, potential measures include promoting rational prescribing practices, optimizing medication dispensing quantities, educating patients on adherence, and expanding the reach and awareness of MRP programs in private healthcare facilities.

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Abstract P01

A Comparative Study of Deproteinisation Techniques for Extracting Polysaccharides from *Rosa roxburghii* Fruits

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ABSTRACT

Background and Objectives: *Rosa roxburghii* fruits are known for their health benefits. Its polysaccharides can be extracted using water. However, the presence of proteins in the water extract poses a challenge to achieving high-quality polysaccharides. The study aimed to determine the best deproteinisation techniques for polysaccharides from *R. roxburghii* fruit and to evaluate its purity. **Method:** *R. roxburghii* fruits were collected, sun-dried and powdered based on the previous study. The powdered sample was extracted with water at 80 ℃ for 4 hours. The crude extract was filtered and decolourised using polyamide resin. The decolourised extract was then concentrated using a rotary evaporator at 60 ℃. The concentrated extract was then deproteinised using (i) NaCl-gelatin method, (ii) trichloroacetic acid method, or (iii) cellulose semi-permeable membrane method. The polysaccharide recovery of the deproteinised extract was calculated and compared. **Results and Discussion:** Our study showed that the cellulose semi-permeable membrane had the best ultrafiltration efficiency of polysaccharides from *R. roxburghii* fruits and the highest polysaccharides recovery ratio. **Conclusion:** The deproteinisation method using cellulose semi-permeable membrane has the highest quality, and is cost-effective, simple to perform, eco-friendly, and scalable. This study provides new insights into the technique of purifying the polysaccharides from *R. roxburghii* using a cellulose semi-permeable membrane. This achievement may add value to the comprehensive application of *R. roxburghii*.

Abstract P02

GCMS Analysis And Antimicrobial Activities of Different Extracts Of *Clitoria Ternatea*

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ABSTRACT

Background: *Clitoria ternatea* (CT), belongs to the family Fabaceae, which is a highly valued medicinal plant. Locally this is also known as the Butter pea flower. This plant (flower part) is found to contain different kinds of metabolites. These metabolites could help in the treatment of various kinds of diseases. The aim of the present work was to carry out GCMS and antimicrobial evaluations of different flower extracts of CT. **Methods**: The dried CT flower was macerated in methanol and fractionated into different solvent extracts like hexane, chloroform, and ethyl acetate. GCMS analysis was carried out, and compounds were identified by the NIST 2008 library, whereas in vitro antimicrobial activities were performed by well diffusion methods. **Results& Discussion:** A total of 10 and 17 compounds were identified in methanolic and hexane extracts, respectively. Oxalic acid, isobutyl nonyl ester, is found to be present in the highest concentration (18.81%) and identified at RT 5.13 in methanolic extract, whereas 2-Ethylacridine is found to be present in the highest concentration (23%), identified at RT 44.04 min in hexane extract. An antibacterial study shows that methanolic extract and ethyl acetate fraction were found to exhibit border antibacterial effects. Apart from this, this ethyl acetate fraction also shows good scavenging activity in another study conducted in the same lab. **Conclusion**: LCMS analysis successfully planned to explore the different metabolites present in the ethyl acetate fraction, which can help to isolate pure antimicrobial compounds.

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Abstract P03

Impact of Drug Pricing on Medication Adherence: A Narrative Review

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ABSTRACT

Background and Objective: The escalating costs of pharmaceuticals pose a formidable challenge to healthcare, influencing patients' ability to adhere to prescribed treatment plans. This review analyzes the relationship between drug pricing and medication adherence, highlighting the urgent need for deeper understanding of this interaction in contemporary healthcare. **Method:** The review employs a narrative approach, shaping concepts and keywords aligned with the research question: "What is the relationship between drug pricing and medication adherence?" A systematic search, utilizing Medical Subject Headings (MeSH) terms, conducted on the PubMed database, and inclusion and exclusion criteria are applied for article selection. **Results and Discussion:** Pharmacoepidemiologic analyses unveil the impact of drug pricing on medication adherence. Studies on hypertension, antiplatelet and anticoagulant therapies, heart failure, and peripheral arterial disease illustrate varied adherence rates based on drug pricing. Factors such as financial incentives, refill reminder programs, and out-of-pocket costs play crucial roles, revealing disparities across different patient populations. The discussion synthesizes findings from diverse studies, emphasizing the role of single-pill formulations, financial programs, and strategic drug choices in mitigating the impact of drug pricing on adherence. Collaboration among healthcare professionals, policymakers, and pharmaceutical companies emerges as a key recommendation to address drug pricing challenges comprehensively. **Conclusion:** In conclusion, this review provides valuable insights into strategies for enhancing medication adherence amid rising drug prices. The findings underscore the importance of tailored interventions, proactive healthcare, and collaborative efforts to create a more equitable and sustainable healthcare system. The multifaceted nature of the issue necessitates a comprehensive approach to improve patient outcomes and accessibility.

Abstract P04

Effectiveness Of Medication Coverage Checking Tool In Reducing Non-payment For Insurance and Corporate Patients At KPJ Ipoh Specialist Hospital

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ABSTRACT

Background and Objectives: Managing medicine coverage in private hospitals is complex, particularly in identifying and collecting payments for non-covered medications. At KPJ Ipoh, 62.5% of patients are covered by insurance or Managed Care Organisations (MCOs), each with unique health coverage policies that pharmacy staff are required to interpret. Over 2500 patients were contacted in 2019 to make payment on uncovered medicine after being notified by insurance or MCO companies which disrupted pharmacist flow in the pharmacy. The medicine coverage checking tool was created to enhance patient satisfaction, reduce the workload on staff calling patients, improve the efficiency of medication payment processes and reduce the patient's financial burden of non-covered medication costs. **Method:** A comprehensive review of outpatient pharmacy data spanning five years (2019-2023) to analyse the costs associated with uncovered medications and the total outstanding payments due to non-payment. The patient satisfaction and time taken to check coverage prior to and post-implementation of the tool were measured. A root cause analysis was conducted to also determine the reason for many non-covered medicines released to the patients. **Results and Discussion:** Lack of clear guidelines and staff knowledge to identify non-covered medicine was identified through root cause analysis as a major contributor to previous inefficiencies. The implementation of the medicine coverage tool led to significant reductions in the costs of non-covered medications and improved patient satisfaction. This tool effectively decreased the time spent on post-discharge payment collections and minimised financial losses. **Conclusion:** Future steps include continuous updating of the coverage checking tool to keep pace with changes in insurance policies and exploring further enhancements in staff training and patient communication to sustain the benefits of this tool. This approach not only improves operational efficiency but also significantly boosts patient satisfaction and financial outcomes for the hospital. This solution can also be scaled to another private hospital as well.

Abstract P05

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Therapeutic Potential of Compound 9b Against Carbonic Anhydrase IX in Colorectal Cancer

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ABSTRACT

Background and Objectives: Hypoxia is a typical feature of malignant tumors as these cells can adapt to a hypoxic environment by expressing carbonic anhydrase IX (CAIX). Sulfonamide is one of the main CAIX inhibitors. However, their inhibitory selectivity needs to be strengthened. Therefore, in this study, we synthesized compound 9b, which has the structure of benzenesulfonamide, and studied its effects on the third most common cancer in the world, colorectal cancer. **Method:** Molecular docking was performed to verify the target of compound 9b. MTT assay was performed in human colorectal cancer, SW480 cells, for anti-proliferative activity under normoxic and hypoxic conditions, and the assay was also conducted in human normal colon, NCM460 cells, for toxicity. The mechanism of cytotoxicity was studied by Annexin V-FITC/PI staining, mitochondrial membrane potential, lipid reactive oxygen species (ROS) assay, transmission electron microscopy, and Western blotting. **Results and Discussion:** Molecular docking showed that compound 9b could stably bind to the zinc atom in the active pocket of CAIX. Compound 9b exhibited good anti-proliferative activity on SW480 cells, under normoxic and hypoxic conditions, with IC_{50} values of 17.03 ± 1.09 μM and 10.90 ± 0.46 μM respectively. Interestingly, it showed low toxicity on normal colon, NCM460 cells, with the IC_{50} of more than 40μM. This compound inhibited SW480 cells in the G2/M phase and induced apoptosis in a concentration-dependent manner with the percentage being higher in hypoxic than in normoxic conditions. **Conclusion:** Compound 9b specifically targets CAIX and induces apoptosis dose-dependently in SW480 cells, suggesting the potential anti-tumor effects of compound 9b in colorectal cancer.

Abstract P06

Evaluating Management of Headaches at Community Pharmacies in a District of Perak, Malaysia Using Simulated Client Method

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ABSTRACT

Background and Objectives: Minor ailments are medical conditions that can be reasonably diagnosed and managed by patients themselves or healthcare professionals. One of the most encountered minor ailments is migraine. Community pharmacies are well recognised as first-line settings to provide healthcare consultation. Community pharmacists play an important role in simple diagnosis and providing accurate and appropriate treatment to clients in managing minor ailments. The study aimed to investigate the practice of managing headaches in community pharmacies. **Method:** A migraine case scenario was developed. The researcher acted as the simulated client and visited community pharmacies located in the Manjung district, Perak. After each visit, the information gathered was immediately recorded in a data collection form. The data collection form was prepared based on "Pharmacists' Patient Care Process", a framework endorsed by the Joint Commission for Pharmacy Practitioners in 2014, OBRA'90, and was reviewed by 2 pharmacy experts. **Results and Discussion:** The simulated client visited 29 community pharmacies. The most frequently asked question was the nature of the headache experienced (79.3%), followed by medication allergy history (51.7%). None of the respondents asked for the aura symptoms. None of the respondents identified the possibility of an ibuprofen overdose migraine. All of the 29 respondents suggested medications to treat the condition. The most common information delivered in dispensing was the dose of medication (96.6%) and frequency of medication to be taken (96.6%). None of the respondents mentioned the duration of the therapy and storage of the medication. The average dispensing time was 3.5 minutes. An average of one product was dispensed. **Conclusion:** Getting a treatment for headaches in community pharmacies was time-saving. However, most pharmacists or pharmacy assistants at the studied location did not practice all the components stipulated in the patient care process. Continuous

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professional training should be emphasised to ensure all aspects of the patient care process are addressed.

Abstract P07

Effect of Tocilizumab on Clinical Outcomes and Safety among Critically-ill Coronavirus Disease 2019 (COVID-19) Patients: A Retrospective Case-Control Study

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ABSTRACT

Background and Objective: Tocilizumab is a high-cost immunomodulatory agent that has been innovatively repurposed as an off-label treatment for Coronavirus Disease 2019 (COVID-19). Global research on its clinical application and safety in COVID-19 yielded mixed results. This prompted a need to verify previous findings locally. Our study aimed to compare the effect on clinical outcomes and safety of Tocilizumab-treatment (TOC) versus Standard-of-Care (SOC) in critically ill COVID-19 patients. **Method:** A retrospective case-control study was conducted among critically ill COVID-19 patients admitted to a Malaysian secondary care hospital between April 2020 to June 2021. Patients were randomly sampled into a TOC or SOC cohort using a 1:6 ratio propensity score (PS) matching. Information on patients' demographic, laboratory and clinical status was retrospectively reviewed from medical records. The study endpoints were clinical outcomes (all-cause in-hospital mortality, 6-point ordinal scale clinical improvement, organ support-free and inflammatory markers improvement). Complications developed post-study inclusion were monitored as safety evaluations. Comparisons between TOC and SOC were made using bivariate, multivariate as well as survival analyses. **Results and Discussion:** A total of 182 PS-matched patients were included with 26 TOC-patients and 156 SOC-patients. Our study demonstrated insignificance in mortality, clinical improvement and organ support-free after Tocilizumab administration (p> 0.05). Despite these, Tocilizumab did show a protective effect by reducing inflammatory markers, specifically C-reactive protein (CRP) [AOR 3.727 (95% CI: 1.061 to 13.090; p=0.040)]. The frequency of complications developed was balanced between TOC and SOC (p>0.05). **Conclusion:** Tocilizumab significantly reduced CRP level and showed a comparable safety profile as control. However, the CRP reduction did not improve overall survival or other clinical benefits. With the high acquisition cost of Tocilizumab, this study provided insights to guide future clinical justification for its prudent use in COVID-19, particularly when transitioning into the post-pandemic era.

Abstract P08

Comparison of INR Control in Non-Valvular Atrial Fibrillation Patients on Warfarin: A Multicentered Retrospective Cohort Study in Sarawak, Malaysia

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ABSTRACT

Background and Objectives: Anticoagulation control in non-valvular atrial fibrillation is challenging in both rural and urban hospitals in Malaysia. Time in Therapeutic Range (TTR) is a useful tool for measuring anticoagulation management. Limited data on TTR comparison between rural and urban hospitals. This study aims to compare the anticoagulation control between rural (Kanowit Hospital, Lundu Hospital and Marudi Hospital) and urban (Miri Hospital) and to determine the independent predictors associated with TTR ≥ 70%. **Method:** This multicenter retrospective cohort study examined patients receiving warfarin at Anticoagulation Medication Therapy Adherence Clinic (ACMTAC) service in 2021. Patient demographics, clinical characteristics, INR values and TTR in four facilities were analyzed. TTR was calculated using Rosendaal's method. Multivariate logistic regression was used to determine the independent predictors associated with TTR ≥ 70%. **Results and Discussion:** 114 patients

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were included, 21.1% (n=24) of patients from Kanowit Hospital, 26.3% (n=30) from Lundu Hospital, 21.9% (n=25) from Marudi Hospital and 30.7% (n=35) from Miri Hospital. The mean TTR± SD of all hospitals was 73.18±17.78%. The mean TTR± SD for rural and urban hospitals was 71.23±17.5% and 77.6±17.8%, respectively. There was no statistically significant difference between rural and urban hospitals (p=0.267). Lower episodes of warfarin missed dose and INR test deranged are identified as the predictors of TTR ≥ 70%. (AOR=0.31, 95% CI: 0.14, 0.72, p =0.006) and AOR=0.40, 95% CI: 0.24, 0.69, p<0.001 respectively. **Conclusion:** This study reported that anticoagulation control in rural and urban hospitals is similar. Pharmacists involvements is crucial in reducing the warfarin missed dose and INR test deranged to achieve good coagulation control.

Abstract P09

Knowledge, Attitude And Practice (KAP) Towards Antibiotic Use and Its Resistance Among The General Public In Klang Valley, Malaysia

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ABSTRACT

Background and Objectives: Antibiotics use has increased significantly throughout the years leading to a high percentage of misuse and overuse in Malaysia which causes an increased trend of antibiotic resistance (ABR). Our hypothesis is the general public has a low level of KAP towards antibiotic use and its resistance. This study aims to determine the knowledge, attitude and practice (KAP) towards antibiotics use and its resistance among the general public in Klang Valley, Malaysia. **Method:** A cross-sectional study was conducted using a pre-validated questionnaire that comprised sections of socio-demographic details, questions regarding knowledge of antibiotics use, attitude of the public and practices towards the antibiotic's use including Klang Valley residents who were ≥18 years and could speak English language. Prior to the distribution of questionnaire, participants were asked about their English language proficiency and understanding. Upon, meeting the all requirements, the questionnaire was distributed among the study participant's through email and social media. All collected data was analysed by SPSS software using version 27.0. Chi-square test was used to determine the association between socio-demographic variables and KAP whereas Spearmen test was used to identify the correlation between KAP. **Results and Discussion:** A total of 408 participants were recruited and the study found that half of participants (53.4%) had a moderate level of KAP towards the antibiotic use. The results were also statistically significant within the residing area particularly due to higher educational levels that enhanced their KAP towards antibiotic use. **Conclusion**: This study provided us with baseline evidence about the KAP regarding antibiotic use among the general public in Malaysia. Hence, it will be useful in guiding further interventions to improve awareness about antibiotics use and enhance antimicrobial stewardship in our community.

Abstract P10

Medication Discharge Times at Hospital Pharmacy: To Take Home

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ABSTRACT

Background & Objectives: Efficient medication discharge is crucial for patient well-being and healthcare operations. This study was conducted at Regency Specialist Hospital, Johor, to determine medication discharge times, total time spent in pharmacy, and explore satisfaction with medication waiting times, aiming to enhance future pharmacy and related operations in line with forward-thinking pharmacy practices. **Method:** This observational study extracted data from Electronic Medical Record system and a satisfaction survey focused on medication waiting times. It was conducted among inpatients across all hospital wards from

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1st November 2023, to 2nd December 2023. Logistic regression was used to estimate adjusted odds ratios and 95% confidence intervals for factors affecting the 90-minute target medication discharge time. **Result & Discussion:** Of the 247 inpatient participants, approximately 58% (n=142) were female, 75% (n=186) had insurance coverage, 38% (n=93) were prescribed four or more medicines, 82% (n=202) were in adult wards, and 66% (n=163) were of Chinese ethnicity. Most participants, approximately 85% (n=209), were satisfied with the medication waiting times at pharmacy counter, which met their expectations, with an average waiting time of 12.0 (sd=7.1) minutes. The mean medication discharge time, from screening upon prescription receival to medication receipt stage, was 101.5 (sd=52.7) minutes, with approximately half (n=129) exceeding 90-minute target. Notably, only 12% of discharge time spent in pharmacy department, suggesting most of the discharge processing time took place outside of pharmacy department, particularly in payment-related processes involving nurses, doctors and charges incurred by patients. After adjusting for confounders, the 90-minute target medication discharge time was not associated with characteristics of patients or mode of payment. **Conclusion:** This study highlights that extended medicine discharge process time is influenced by factors beyond pharmacy operations, including administrative issues and patient-specific factors, warranting attention. To improve overall efficiency, innovative approaches are necessary to streamline transitions in the discharge process.

Abstract P11

Use of Biodegradable Face Masks And Its Effects Towards The Environment: A Systematic Review

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ABSTRACT

Background and Objectives: During the COVID-19 pandemic, the usage of face masks has surged, indirectly causing an increase in environmental pollution due to improper disposal. This review aimed to determine the feasibility of face mask filters from biodegradable materials with respect to filtration efficiency, air permeability and degradation ability. **Method:** The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement were adapted in the review. Two databases, Scopus, and Web of Science were used. Original articles in English, between 2019 to 2022 were included in the search. The search term keywords were related to biodegradable, mask, "personal protective equipment", degradation, filters and environment. The search terms used were [biodegradable AND (mask* OR "personal protective equipment")]. After retrieving an initial number of articles, further screenings were done to exclude articles that did not meet the inclusion criteria. **Results and Discussion:** 57 articles were initially retrieved that were then screened on the title, abstract and removing duplicates. A full-text screening was conducted, leaving 14 articles for the review. All 14 articles reviewed showed the biodegradable masks achieved filtration efficiency of at least 86% or higher for particle sizes ranging from 0.2µm up to 3.0µm. Seven of the articles had data regarding air permeability tests which showed a range of pressure drop, from 59Pa to 119Pa. Five of the articles contained data regarding the degradation ability which revealed the component materials were able to degrade completely within at least a month when exposed to the environment. **Conclusion:** Biodegradable face masks can filter out foreign particles well with the added benefit of being able to degrade within a month. Biodegradable face masks may replace non-biodegradable masks to reduce environmental burden.

Abstract P12

Evaluating Pharmacists' Research Skills and Their Perception on Research Impact in Johor Government Healthcare Settings

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ABSTRACT

Background and Objectives: While advancement in pharmacy practice is recently needed, research has become a vital aspect of evidence-based pharmacy practice that will further improve overall healthcare outcomes. Exploring

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additional factors affecting pharmacists' research skills and their impact can help foster a stronger research culture. This study aims to evaluate pharmacists' confidence and competence in research and their perception towards research impact. **Method:** A multicenter, cross-sectional survey was conducted among registered pharmacists working in government healthcare facilities across Johor, Malaysia, from December 2023 to January 2024. The cluster random sampling method was applied to minimise selection bias. A validated online questionnaire was used to evaluate their confidence and competence while their perception of research impact was gauged using a validated questionnaire based on the Payback Framework by Donovan & Hanney (2011). Both descriptive and inferential statistics were applied for data analysis. **Results and Discussion**: A total of 377 pharmacists participated in the study, with an average tenure of 9.3 years (SD: 5.1). The majority (82.5%) had previously been involved in research. A significant correlation was found between confidence and competence scores ($p<0.001$; $r=0.92$). Demographic characteristics, years of service, geographical location, and type of facilities did not affect competence levels. Higher competence levels were observed among those with postgraduate degrees, research interests and involvement in research mentorship programs ($p<0.05$). Pharmacists exhibited a moderate perception of research impact, with 55.6% recognising an increase in service quality, 48.5% noting individual satisfaction, and 51.1% acknowledging quality improvement awareness due to their research. Thematic analysis identified inadequate training, time constraints and lack of collaboration as major challenges hindering research engagement. **Conclusion**: Concerted efforts are needed to help pharmacists appreciate their research impact better and contribute more effectively to the advancement of pharmacy practice and patient care.

Abstract P13

Review on the Safety, Efficacy and Cost Effectiveness of Pharmacists-Led Deprescribing Program for Geriatric Patients

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ABSTRACT

Background and Objective: This review focuses on pharmacist-led deprescribing initiatives aimed at improving medication management in the geriatric population. Through comprehensive searches of major databases, studies specifically addressing deprescribing in geriatric populations and led by pharmacists were identified. Both original research and review publications investigating the safety, effectiveness, and economic viability of pharmacist-led deprescribing were included. The objective of this review is to assess the impact of pharmacist-led deprescribing programs on medication management in the geriatric population and to evaluate their economic implications. **Method:** Studies were identified through thorough searches of major databases, with a specific focus on pharmacist-led interventions targeting deprescribing in geriatric populations. The inclusion criteria encompassed both primary research and review articles investigating the safety, effectiveness, and economic viability of pharmacist-led deprescribing. Relevant studies were analysed to assess the impact of pharmacist-led deprescribing initiatives on medication management and to evaluate their cost-effectiveness. **Results and Discussion:** The results indicate that pharmacist-led deprescribing initiatives are associated with significant cost savings and improvements in quality-adjusted life years (QALYs), particularly in the context of nonsteroidal anti-inflammatory drugs (NSAIDs) and sedative-hypnotics for geriatric patients. These interventions have been found to be both more effective and less expensive, making them a cost-efficient strategy for optimising medication management in the geriatric population. Overall, pharmacist-led deprescribing programs have demonstrated effectiveness in enhancing health outcomes, promoting medication adherence, and reducing healthcare costs for geriatric patients. **Conclusion:** In conclusion, pharmacist-led deprescribing initiatives represent a valuable approach to optimising medication management in the geriatric population. The findings of this review underscore the importance of pharmacist-led interventions in improving medication safety, efficacy, and cost-effectiveness for older adults. Moving forward, further research and implementation of pharmacist-led deprescribing programs are warranted to maximise their potential benefits for geriatric patients and healthcare systems alike.

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Abstract P14

Comparison of four methods in computing area under the concentration-time curve (AUC24) of vancomycin versus integration approach (standard) in hemodynamically stable patients- A single-centered retrospective study

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ABSTRACT

Background and Objectives: The updated guidelines recommend two approaches to estimate the AUC24 for patients receiving vancomycin; Bayesian-derived AUC24 monitoring or the first-order pharmacokinetic analytic equations. Bayesian approach is complex and unfamiliar to most pharmacists or clinicians. Several methods were developed to estimate AUC24 for vancomycin. However, which approach can produce a more accurate AUC24 remained unanswered. The main objectives of this study were to identify the method that able to provide a more accurate values of AUC24 and to explore the agreement of AUC24 estimated by the investigated methods to the integration model (standard). **Method**: We conducted a retrospective analysis using the Electronic Hospital Information System from a tertiary hospital in Malaysia. Data pertaining to patients who received vancomycin treatment from 1st January 2021 to 31th of December 2022 were retrieved for analysis. **Results and Discussion:** The mean AUC24 of Simpson's Rule integrated method (standard) versus 2-Point trapezoidal, 3-Point trapezoidal, Pharmacokinetic Method 1(PK1) and Pharmacokinetic Method 2 (PK2) showed a statistically significant difference by 91.05 ± 40.88 mg·h/L, 116.95 ± 33.71 mg·h/L, 119.60 ± 40.91 mg·h/L and 38.73 ± 59.56 mg·h/L respectively, $p < 0.05$. None of the methods agree with the Simpson's Rule integrated method. The 2-Points, 3-Points, PK1 and PK2 methods also appeared to have some imprecision versus the Simpson's Rule Integration method, as 40%, 67.5%, 65 % and 12.5% of AUC24 estimates were outside the upper and lower agreement level of ±100 mg*h/L, respectively. **Conclusion**: The present study failed to demonstrate agreement of calculated AUC24 by the four methods to the Simpson integration approach (standard). All the approaches underestimated the AUC24. Among the four methods, there is a modest variance of 38.73 mg*h/L in the PK2 values, which aligns most closely with the accuracy of Simpson's rule integration.

Abstract P15

Can We Balance the Scale - Understanding the Landscape of Medicine Shortages and Surpluses Across Healthcare Facilities in Malaysia

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ABSTRACT

Background and Objective: Medicine surpluses and shortages are critical global concerns and have been identified as a national priority. They can occur at various levels of the supply chain. Addressing these issues within and across healthcare facilities is a promising avenue. The full scope of these challenges within our healthcare facilities is still unknown. The aim of this study was to understand the current landscape of medicine wastage and shortages across healthcare facilities in Malaysia, with a focus of identifying strategies to address both issues holistically. **Methods:** A cross-sectional online survey was conducted among registered pharmacists working across healthcare facilities in both public and private sectors in Malaysia. The questionnaire was adopted from the validated European Association of Hospital Pharmacists (EAHP) Medicines Shortages Surveys, and consisted of: (I) respondent demographics; (II) medicine shortages; (III) medicine surpluses; and (IV) potential solutions. **Results and Discussion:** The study received 112 responses between January to May 2023. Most respondents (89.3%) had less than 10 years of experience as pharmacists, with 41.1% practicing in community pharmacies. A significant proportion (83%) reported experiencing medicine shortages, predominantly in community pharmacies (30.4%) and public hospitals (29.5%). Surpluses were reported by 42.4% of respondents, primarily in community pharmacies (14.1%) and public hospitals (12.9%). Pharmacists agreed that Malaysia should implement a medicine shortage notification system similar to the USFDA (95%). Medicine redistribution was widely employed during both shortages

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(16%) and surpluses (45%). However, redistribution usually occurred within the establishment chain (e.g. KKM). While it is a viable short term effort, it can be tedious and often not fruitful (46%). **Conclusion:** Medicine shortages and surpluses co-occur at varying degrees in healthcare facilities across Malaysia. Pharmacists have employed multiple approaches, yet in silos, emphasizing the urgent need for a unified strategy involving both public and private sectors to address these challenges holistically.

Abstract P16

Understanding The Contributing Factors and Impact of Burnout on Malaysian Pharmacists in Their Respective Healthcare Organisations (Government and Private): A Study Protocol

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ABSTRACT

Background and Objectives: Globally, one in every two pharmacists experiences burnout. Burnout among pharmacists significantly affects healthcare delivery and organisational efficiency. The phenomenon of burnout has been relatively well studied in physicians and nurses, but not pharmacists. This study aims to identify the factors contributing to burnout and the resources that can mitigate it among Malaysian pharmacists using the Job Demand-Resource (JD-R) model, and to assess its impact on productivity and economic burden in healthcare organisations. **Method:** This multi-phase research will involve patient-facing pharmacists across Malaysia from both the government and private sectors. Study 1 will involve semi-structured, 1-to-1 interviews with 120 pharmacists to explore factors contributing to burnout and strategies for mitigation. Study 2 will assess the prevalence of burnout, its contributing factors, and mitigating resources among different groups of pharmacists through a cross-sectional survey involving a nationally representative sample of 2,400 pharmacists. The study will apply the JD-R model to develop a burnout framework for Malaysian pharmacists utilising a structural equation model (SEM). Study 3 will develop an economic model to quantify the direct, indirect, and turnover costs of burnout of pharmacists in Malaysia. **Results and Discussion:** The qualitative interviews will provide a preliminary understanding of burnout in pharmacists, including the similarities and differences of burnout factors and resources across different pharmacy sectors. The cross-sectional survey will complement the qualitative findings with a larger and nationally represented sample, validating the burnout factors and resources identified through the JD-R burnout framework. Study 3 will reveal the economic impact of burnout, including healthcare expenses, reduced productivity, and turnover costs. **Conclusion:** This research will produce valuable insights and a theoretical model affecting pharmacists' mental health in Malaysia. The findings will inform strategies to improve mental health and work environments, enhancing healthcare delivery and reducing the economic burden of burnout.

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