

Issue

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IRIS

International Review of Interdisciplinary Sciences

An International Research Journal

IN FOCUS

Getting Right Down to the Bone: Can Leave Extracts Induce Bone Regeneration in the Fight against Osteoporosis?

THROUGH OUR LENS

Children have Higher Odds of Developing Adverse Drug Reactions

Yemeni Sidr Honey shows Better Wound Healing Properties than Manuka Honey

POINTS OF VIEW

ChatGPT in Higher Education: More Harm than Good?

RESEARCH AND REVIEW PAPERS

Review Of Herbal Products For Treating Common Cold

Anxiety Level, Sleep Quality and Physical Activity among Malaysian University Students in the Klang Valley during COVID-19 Pandemic

Factors Affecting Poor Performance Among First Year Medical Students: A Qualitative Survey

Fall Among Geriatric Patients: Prevalence, Risk Factors and Clinical Outcomes

Preliminary Evaluation of Halal Status in Respiratory, Immunological Products and Vaccines in Malaysia

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FOREWORD



The driving purpose behind research should be the desire to discover new knowledge with the aim of benefiting humanity. Thus, it is apt that the cover story of our inaugural issue of the International Review of Interdisciplinary Sciences, or IRIS for short, be focused on Dr. Intan's research against osteoporosis. Or more specifically her FRGS funded study on the potential of

the kaduk leave extract on regenerating bone tissue, which has shown some promising results. This study best exemplifies the true benefit of research - in trying to help humanity despite the various challenges we face and to advance our species and our ecosystem collectively.

This further strengthens the motive behind the Editorial Board in its tireless work to produce this inaugural issue of IRIS. It is the Board's hope that this journal will continue to inspire young researchers with the joy of discovery and create a platform for the exchange of ideas for the collective good. IRIS is purposefully designed to be multidisciplinary as we believe the solutions to the problems mankind face today and tomorrow is complex and requires creative approaches from everyone, and across all disciplines.

With that in mind, I welcome readers to peruse this issue and find out more about the exciting studies that is being undertaken by young and motivated researchers from across institutions and regions. Among the studies features in this issue are the microbial properties of Yemeni sidr honey, medication delivery services, management of coronary artery disease patients, and discovery of the more efficient methods of extracting protein from lab bacteria for industrial use. Finally, I encourage you to share a copy of IRIS with someone you think would benefit from it or feel free to write to us to see how you can contribute as well. Thank you.

YBhg. Prof. Emeritus Dato' Dr. Mohamad Abd Razak

DSNS, MD, MS (ORTH.), PH.D (HONS), AM FELLOW OF SPINE SURGERY

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Getting Right Down to The Bone

Government funds research into the potential of natural leave extracts in inducing bone regeneration in the fight against osteoporosis



Did you know that osteoporosis is a largely ignored health condition? The “silent disease” occurs without symptoms until it is almost too late when a bone becomes brittle enough to break or fracture without force. According to Code Blue – a digital media that publishes free market approach in the development of patient-centric and community-focused health and social sector – 77 per cent of Malaysian women are living with post-menopausal osteoporosis that are undiagnosed.

The condition weakens the bones to the point where they break easily; often, it affects the hip bone, back bone, and wrists. This can happen over a period of years as the bones start losing strength. This is where research plays an important role in finding ways to regenerate bones, increase bone formation, and decreases bone resorption.

Head of Research Management Unit of the university’s Centre for Research and Graduate Studies, Assoc. Prof. Ts. Dr. Intan Zarina Zainol Abidin aims to make a difference with her research that uses an alternative non-toxic product as the cell’s inducer for bone healing therapy which reduces adverse side effects unto patients.

When bone loss is at a severe stage, and requires treatment, patients usually undergo bone healing therapy which use standard drugs such as bisphosphonate. These can create a number of side effects which include oesophageal ulcer and even bleeding after the administration of drugs within 24 to 70 hours. This occurrence is what urged Dr. Intan and her team of researchers to come up with an alternative course of treatment using natural products.

Her research titled, “Determination of Cellular Mechanism in Bone Regeneration using Natural Stem Cells Inducer from *Piper*

sarmentosum (kaduk) Leave Extracts”, studies the development of bone cells from blood stem cells when induced with kaduk leave extracts. Stem cells are cells that have the ability to divide for indefinite periods of time and are able to induce the development of specific cells.

Kaduk, scientifically known as *Piper sarmentosum*, is largely found in countries with tropical climate. Malaysia, with its fortunate location within the equator, is the perfect place to cultivate this plant within ideal weather and soil conditions. The plant is known for its antioxidant, antiplasmodial, antituberculosis, anti-inflammatory, anticarcinogenic and hypoglycaemic properties. In previous studies, it has been found to possess bone healing properties and was able to increase bone strength in rats as test subjects.

“Past research has found that kaduk leave extract have a lot of medicinal value. However, the mechanism of bone regeneration at the cellular level remains unknown. Our objective with this research is to assess its potential as a non-toxic natural inducer that can transform blood stem cells into osteoblasts,” says Dr. Intan.

Osteoblasts are the bone cells responsible for synthesising bone matrix proteins and minerals during early bone formation, controlling

bone formation and mineralisation throughout life. They are found where new bone formation is occurring.

The results of the study were encouraging as they found that the extracts do indeed transform blood stem cells into osteoblasts which concluded that kaduk leave extracts might be a promising alternative medicine for cell therapy to combat bone diseases such as osteoporosis or even bone repair.

Given the importance of this study, Dr. Intan's research secured a Fundamental Research Grant Scheme (FRGS) award of nearly RM100k from the Ministry of Higher Education.

Her co-researchers include Prof. Ts. Dr. Shahrul Hisham Zainal Ariffin from Universiti Kebangsaan Malaysia, Assoc. Prof. Dr. Zaidah Zainal Ariffin from Universiti Teknologi MARA and Anis Nabilah Johari from Universiti Kebangsaan Malaysia.

Part of their research was also published in high impact journals such as Scientific Reports. The research was also awarded with the Best Oral Paper Award in the 11th Kuala Lumpur International Agriculture Forestry and Plantation Conference.

"Although the results of our research prove that kaduk extracts are indirectly involved in bone formation, there are no studies on whether ingesting these plants directly can help strengthen bones.

These require further clinical research. There are also other studies that are looking into the effect of kaduk leaves on animals suffering from osteoporosis," adds Dr. Intan. With more research, kaduk extracts can be generated into supplements that will be substantial in replacing toxic products in therapy.

"Not many are aware that the population in Malaysia suffering from bone disease is high. Aside from osteoporosis, patients also suffer from osteopetrosis which is a rare disorder that causes bones to grow abnormally and become overly dense. I believe that we will be able to facilitate the repair process with the help of stem cells and kaduk extract," said Dr. Intan.

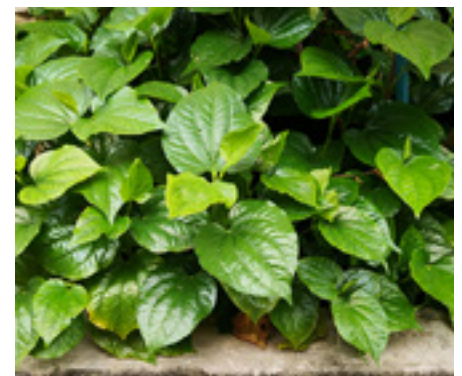
Dr. Intan further explains that her research is merely an *in vitro* experiment (experiments that researchers perform outside of a living organism) that requires more studies before it can qualify for clinical experiments to test on patients.

Studies have shown that bone loss begins from the age of 30-40 and is followed by an immediate decrease in bone mass and density. However, the intake of calcium has a significant effect on bone loss in women. Research has found that calcium supplementation slows the rate of bone loss in postmenopausal women especially those with a low dietary intake of calcium. Moreover, consuming calcium supplements together with vitamin D have also shown to reduce the risk of hip fractures in elderly patients.

However, adults ages 19 through 50 should not get more than 2,500mg calcium in a day, this includes food and supplements, while. Adults over the age of 50 should not exceed 2,000mg in a day. This is because too much calcium in the form of supplements have the potential to increase the risk of kidney stones, constipation, calcium build-up

in blood vessels, and difficulty to absorb iron and zinc.

In conclusion, as our bones support our entire weight, it is important for us to maintain its health. Losing strength in our bones is inevitable as we age, but with the help of calcium, vitamin D, the right nutrition and balanced exercise, the process can be slowed down to a much later stage in life. By then, thanks to the help of new research, better treatment options would be available to treat osteoporosis and other bone diseases sufficiently.



The Kaduk Plant - a non-toxic alternative to bone formation

The wild herb, kaduk or scientifically known as *Piper sarmentosum* and are often confused with betel leaves. Comparatively, kaduk also known as wild pepper, lacks the intense taste of betel leaves and are significantly smaller in size. The plant serves to aid digestion and treat fever in traditional medicine.

Leaves and roots can be placed on the forehead to relieve headache and soup from boiled kaduk water is used to relieve muscle and bone pain. Its leaves may also be pounded and used as a wash to relieve foot fungal itch. The roots of the plant treats ailments such as toothache, coughing, asthma, fungal dermatitis and more.

In fact, the leaves and roots aren't the only parts of the plant that are useful for traditional medicine. Its small fruits help to bring up mucus and other material from the

respiratory tract. The plant's benefits also extend to treating antimalarial effects and anti-clotting action.

A study that was conducted by a team of researchers led by Physiology Medical Lecturer Dr. Nik Aloesnisa Nik Mohd Alwi from Universiti Sains Malaysia in

a popular dish known as otak-otak, which is fish cake made of ground fish mixed in spices.

Osteoporosis - the world's silent disease

The word osteoporosis itself means "porous bone" which creates a condition where the person

Though it is a disease that affects more women than men, the International Osteoporosis Foundation estimate that 1 in 5 men will experience a bone fracture related to osteoporosis in their lifetime. Men who are at a higher risk developing the disease include



Source: <https://www.spineuniverse.com/>

collaboration with other researchers from Universiti Kebangsaan Malaysia found that kaduk leaves decrease high blood pressure among hypertension patients who regularly consumed the dish in their meals. This was due to the antioxidants found within the leaf extracts.

As a Malaysian cuisine, kaduk is used to increase the aroma in cooked meals. They are also eaten raw in nasi ulam, which is a rice salad dish popular within the Malay and Nonya community. Its raw shoots are dipped in sambal, its flowers are dried as a spice whereas its fragrant leaves are used to wrap fish or meat. This includes wrapping

gradually loses bone material, making their bones gradually more fragile and more likely to break.

As it is a "silent disease", the symptoms are not easily identified until a fracture occurs. However, if there has been a gradual loss of height of 6cm (2.5 inches) from when you were a young adult, you may have had a spinal fracture. Fractures can also lead to persistent lower or upper back pain in the bones and/or muscles.

Other symptoms include developing a stooped posture which causes clothes to not fit properly or having brittle fingernails.

those with unhealthy lifestyle habits such as smoking and having inadequate physical exercise as well as those regularly consuming medications such as glucocorticoids.

Osteoporosis Treatment

Unfortunately, there is no cure for osteoporosis but with treatment, patients will be able to protect and strengthen their bones. Some of the healthcare providers in charge of treating osteoporosis include endocrinologists, geriatricians, gynaecologists, and occupational therapists.

To treat osteoporosis, healthcare

providers find ways to slow or stop bone loss to prevent fractures. These include exercise, increasing the intake of calcium and vitamin D supplements as well as taking medications. Therapy includes using weight and strength-bearing exercises, resistance workouts, and gentle exercises that focus on posture and balance. Those recovering from fractures are medicated with painkillers, or hot or cold treatments to reduce pain.

If patients are currently taking medications that may cause bone loss, doctors would then lower the dose of that medication or switch the patient to another medication. Some medications that help with bone preservation or that help slow down bone loss include bisphosphonates, calcitonin, oestrogen, and hormone therapy, sclerostin inhibitor and more. In men, testosterone therapy helps to increase bone density.

Once patients begin treatment, their bone density may be monitored in either bone density scans or blood and urine tests to show how well the patient's bone is renewing itself. The bone renewal process is a slow one and should be continued to see its results in the long term.

Long term treatment, however, may incur side effects such as irritation to the food pipe, swallowing problems, and stomach pain. Therefore, doctors recommend taking a break from treatment also known as a 'treatment holiday' to recuperate.

History of broken bones and how they are treated in the past and present

Technology advancements have made inefficient orthopaedic treatment more efficient, affordable, quicker, and more effective for the treatment of bones issues. To appreciate this imminent advancement, let's have a look at how broken bones were treated before.

The technique of pouring plaster

of Paris mixture around an injured limb has been used in Arabia for many centuries and was only brought to the attention of European medicine in the 18th century. Arab surgeons used plasters made of mill dust mixed with egg, a mixture of gums, egg white and lime. Plaster of Paris bandages were then introduced by Antonius Methijssen, a military surgeon in Holland back in 1876.

In present times, synthetic casts usually made from a material called fiberglass are used more often than plaster casts. They are more porous and allows doctors to take an x-ray of the injured area without removing the cast. Fiberglass casts also weigh less compared to plaster casts.

Until about 150 years ago, open fractures resulted in either death or immediate limb amputation. Today, open fractures are treated with external fixation which requires doctors to insert metal screws or pins into the bone above and below the fracture site. The pins and screws project out of the skin where they are attached to metal and carbon fibre bars.



Assoc. Prof. Ts. Dr. Intan Zarina Zainol Abidin, Head of Research Management Unit

Upon obtaining her PhD in Universiti Kebangsaan Malaysia, Dr. Intan joined as a post doctorate researcher at its Faculty of Science and Technology with specialisations in Biotechnology (Stem Cell and Cell Biology).

During her time there, she furthered her research in the field of stem cells. Her research interest included the differentiation of stem cells towards other types of cells and the effect of plant extracts on isolated stem cells.

Her research has been published in more than 30 journals including in Web of Science, and Scopus. She has also been appointed as a reviewer by several international and national journals. In 2020, she was awarded as a Professional Technologist by the Malaysia Board of Technologists (MBOT).

She currently acts as the Principal Investigator for an FRGS grant and UoC Research Grant Scheme and is also a co-researcher for several external grants.

Upon 2 years of starting her career in University of Cyberjaya, she managed to secure a Ministry of Higher Education (MOHE) grant to fund her research on the development of bone cells from blood stem cells when induced with kaduk leave extracts. In 2020, she was appointed as a Postgraduate Coordinator involved in postgraduate management in matters pertaining to Malaysian Qualifications Agency (MQA) among others.



More than 1 out of 4
older people (aged 65+) falls
each year

X2

Falling once
doubles your chances of
falling again



1 out of 5 falls
causes a serious injury
such as broken bones or a
head injury

Source: International Osteoporosis Foundation

Children have Higher Odds of Developing Adverse Drug Reactions

Title: Adverse Drug Reactions (ADR) Among Malaysian Paediatric Populations and Performance of Medication Safety Signal Detection Methods

Student: Beldona Hema Rekha,
Master of Medical Science

Supervisor: Dr. Shairyzah Ahmad Hisham

After she became a mother, Hema Rekha started to realise that paediatric medication that are prescribed on a day-to-day basis are not studied for safety and efficacy. Dosages are prescribed merely based on a child's body weight estimation. This motivated her to implement her research project which analysed the safety of drugs that are marketed for children in order to highlight the importance of how drugs are prescribed to children as well as how paediatric adverse drug reactions are determined.

According to this study, children aged 1 to 12 years old most frequently reported to experience adverse drug reactions (ADR). Some of these reactions can include drug induced growth disorders or skin reactions such as erythema. In children aged 2 to 11 years, attention deficit hyperactivity disorder (ADHD) medications have also been reported to cause weight loss, sleep problems and decreased appetite. In relation to this, the study was carried out to determine the association between patient factors (age group, gender and ethnicity)



and ADRs experienced by the paediatric population in Malaysia. This study was also conducted to evaluate the performance of medication statistical safety signal detection methods.

The study was conducted with data obtained from the National Centre for Adverse Drug Reactions Monitoring and utilised a 5-year ADR data of paediatric patients from birth up to 12 years of age. Adverse reaction reports were recorded using a data collection form and analysed.

The ADRs were manually reviewed and selected for disproportionality analysis. Disproportionality measures known as the Proportional Reporting Ratio (PPR), Reporting Odds Ratio (ROR), Bayesian Confidence Propagation Neural Network (BCPNN) and Multiitem Gamma Poisson Shrinker (MGPS) were applied on each drug reported. The generated safety signals were further analysed for performance related test-characteristics based on the standard drug label.

The study revealed that during a 5-year study period, 484 serious paediatric cases were reported to the National Pharmaceutical Regulatory Agency. According to the results, children between the ages of 1 to 12

years of male gender and of Malay race have higher odds of developing ADRs. The results also showed that that male children are more likely to experience nervous and respiratory system disorders due to medicines.

Examples of the serious ADRs reported in this study include anaphylactic reaction to NSAIDs (paracetamol and ibuprofen) and antibiotics (amoxicillin and benzylpenicillin); Stevens-Johnson Syndrome (SJS) to antibiotics (amoxicillin, ampicillin and phenoxymethyl penicillin) and anti-epileptics (carbamazepine and lamotrigine). The presence of serious ADRs such as SJS, and anaphylaxis in children indicate that caution is needed while prescribing antibiotics and anti-epileptics.

This study also demonstrated that active drug safety surveillance systems are essential to detect ADRs and safety signals associated with it among paediatric patients. In addition, the use of multiple methods of disproportionality enhances the detection of safety signals. Of all the disproportionality measures, PPR, ROR and MGPS were found to be the most effective methods in signal detection.

Antibiotic Resistance: A Threat to Global Health

Title: A Cross-sectional Study on Knowledge, Attitude, Awareness, and Practice of Antibiotic Use and Antibiotic Resistance Among Students at University of Cyberjaya

Student: Afroza Sultana, Master of Medical Science

Supervisor: Dr. Mohamad Jahidul Islam, Assoc. Prof. Dr. Shamima Abdul Rahman

Afroza started looking into the use of Antibiotics after she found out how Antibiotics resistance can lead to the spread of infections that become difficult to treat and increase mortality as well as mortality rates. Realising how crucial it was, she developed and executed the following study to gauge the awareness as well as use of antibiotics using the UoC community as a yardstick for future studies and improvement in the quality of treatments.

Since its discovery, antibiotics have helped treat or prevent bacterial infections. Some of the most common antibiotic treated infections include acute cough, rhinosinusitis, otitis media, sore throat, and non-specific infections.

It is a widely used and widely purchased medicine. Even late in the pandemic, prophylactic antibiotic were widely used to prevent hospital-acquired infections during COVID-19 treatment.

However, due to the misuse and overuse of antibiotics, many suffer from antibiotic resistance. The COVID-19 pandemic has brought on a greater impact on the matter as antibiotics used to treat bacterial co-infections resulted in antibiotic-resistant bacteria. Antibiotic resistance, caused by resistant bacteria, make it difficult to ensure the safety of patients during emergency medical procedures, surgery and organ transplants.

Some of the causes of antibacterial resistance include self-medication, improper prescriptions, inappropriate ingestion, and excessive use of antibiotics. The outcome of antibacterial resistance include poorer clinical prognosis, and a greater burden on healthcare resources which leads to longer hospital stays, increased healthcare costs and even mortality.

To find out if the general public is aware of antibiotic resistance, a

cross-sectional study was conducted among students at University of Cyberjaya using a questionnaire-based analytical survey. 54 per cent of the study sample were Malaysian students whereas the rest were international students.

The study found out that most of the students in the study were well aware of the global antibiotic resistance. Students from the medical programme were able to answer all the questions better and had a more informed attitude towards dealing with the problem of antibiotic use and antibiotic resistance.

Medical students performed better in all knowledge-related questions (higher percentages of right answers) and had more awareness about the issues of antibiotic usage and antibiotic resistance (had higher percentages of correct answers in all questions related to attitude). As a result, they demonstrate a sound understanding and a positive behavioural attitude regarding the responsible use of antibiotics.

The study also found that 10 per cent of the respondents had self-medicated themselves with antibiotics in the past. However, non-compliance with the prescribed treatment was reported despite the modest self-medication. A significant amount of the respondents agree that antibiotic use and resistance should be better publicised for public awareness.



Wound Healing and Antimicrobial Activities of Yemeni Sidr Honey in Comparison with Manuka Honey



this contribute to 50% to 75% of hospital mortality. In many cases of poor healing, the most common bacteria found in the wound area is known as *Escherichia coli* (*E. coli*).

Though there are a number of synthetic antimicrobial and wound healing agents, some of them are associated with adverse effects that have caused various other health problems.

As an alternative, research has found honey to be a natural product for treating skin tissue infections and wound healing.

To find out more, a study was conducted to assess and compare the wound healing and antimicrobial activities of Yemeni sidr honey and manuka honey. Past researchers have invested a massive effort to reveal the effectiveness of manuka honey from New Zealand in several application fields, such as wound healing, antimicrobial activities, antioxidant properties, antiviral, anticancer, and other pharmacological properties.

On the other hand, there has been limited scientific reports and insufficient investigation on Yemeni sidr honey on its antimicrobial mechanism of action as it is not known worldwide. The possible bioactive phytochemical compounds found in both honey types that may exhibit antibacterial properties according to previous literature include methylglyoxal in manuka honey, hydrogen peroxide in Yemeni sidr honey, phenolic acids and

flavonoids such as p-coumaric acid, gallic acid, ferulic acid, myricetin, and rosmarinic acid.

The disc diffusion method was used to determine the antimicrobial susceptibility of honey samples against *E. coli*. The disc diffusion method includes a number of steps including having the bacterial suspension spread evenly on an agar plate. The honey concentration is then placed on the surface of the inoculated plate and is then incubated aerobically at 37 degree Celsius for 24 hours.

The results of the study indicated both types of honeys (700 mg/disc) had antibacterial properties against *E. coli*. However, Yemeni sidr honey exhibited better wound healing properties as it is more effective in enhancing the proliferation and migration of human and mouse skin fibroblast cells.

Other factors that contribute to the antibacterial activities of honey include low pH, osmotic pressure, bee defensin-1 (an antibacterial peptide derived from bees), low protein content, and hyper-osmolality impact. The pH of honey ranges between 3.5 and 5.5, while most bacteria grow best at neutral pH ranging from 6.5 to 7.5. The high sugar content of honey results in high osmotic pressure and causes water to flow out from the bacterial cells through osmosis. As a consequence of the dehydration and high osmotic pressure, the bacteria cells start to shrink and cannot grow in the hypertonic sugar solution. Phytochemical diversity, phenolic and flavonoid contents, and the high carbon-to-nitrogen ratio are other contributing factors to the antimicrobial activities of honey.

Student: Asma

Mohammed Ahmed Al-Sayaghi,
Master of Medical Science

Supervisor: Dr. Abdelkodosse
Mohammed, Prof. Dr. Mohammed
Abdullah Alshawsh

Asma became interested in natural remedies such as honey, after realising that not everyone around the world may have access to modern medication. Furthermore, some modern medication may have adverse side effects depending on how one reacts to it. Honey, which is more readily available can be an alternative solution, hence why Asma felt the to develop this study and analyse its results.

Microbial infections on human wounds are a major health problem globally. These infections are usually caused by unsanitary environments. Wound infections are a major complication of injuries, particularly burns, and

ChatGPT and Higher Education

by Assistant Professor Dr Prihadi Kususanto,
Faculty of Psychology and Social Sciences (FPSS), University of Cyberjaya

ChatGPT, an acronym for "Chat Generative Pre-trained Transformer," is an artificial intelligence (AI) language model created by OpenAI. It is specifically designed to generate human-like text in response to prompts, utilizing deep learning techniques to produce coherent and fluent responses to natural language inputs. Furthermore, the model is fine-tuned for a variety of natural language processing endeavors, such as language translation, text summarization, question answering, and text generation.

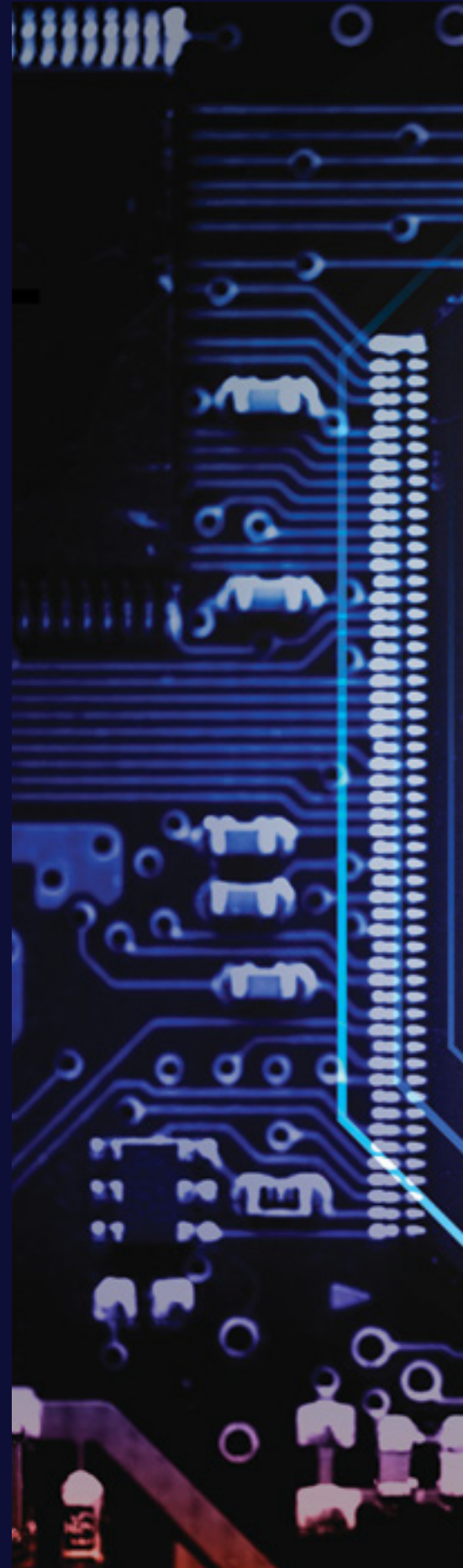
In general, anyone can use ChatGPT by opening it online and give it a prompt or question, and it will generate a response in human-like language. It is quite surprising to see how much the programme have learned, and how it responds to the questions we gave, as it can adjust its response based on how we want it to be. This is an example of how the programme responds to a question related to mental health theories, **"Explain the interpersonal theory of suicide in a maximum of 40 words."**

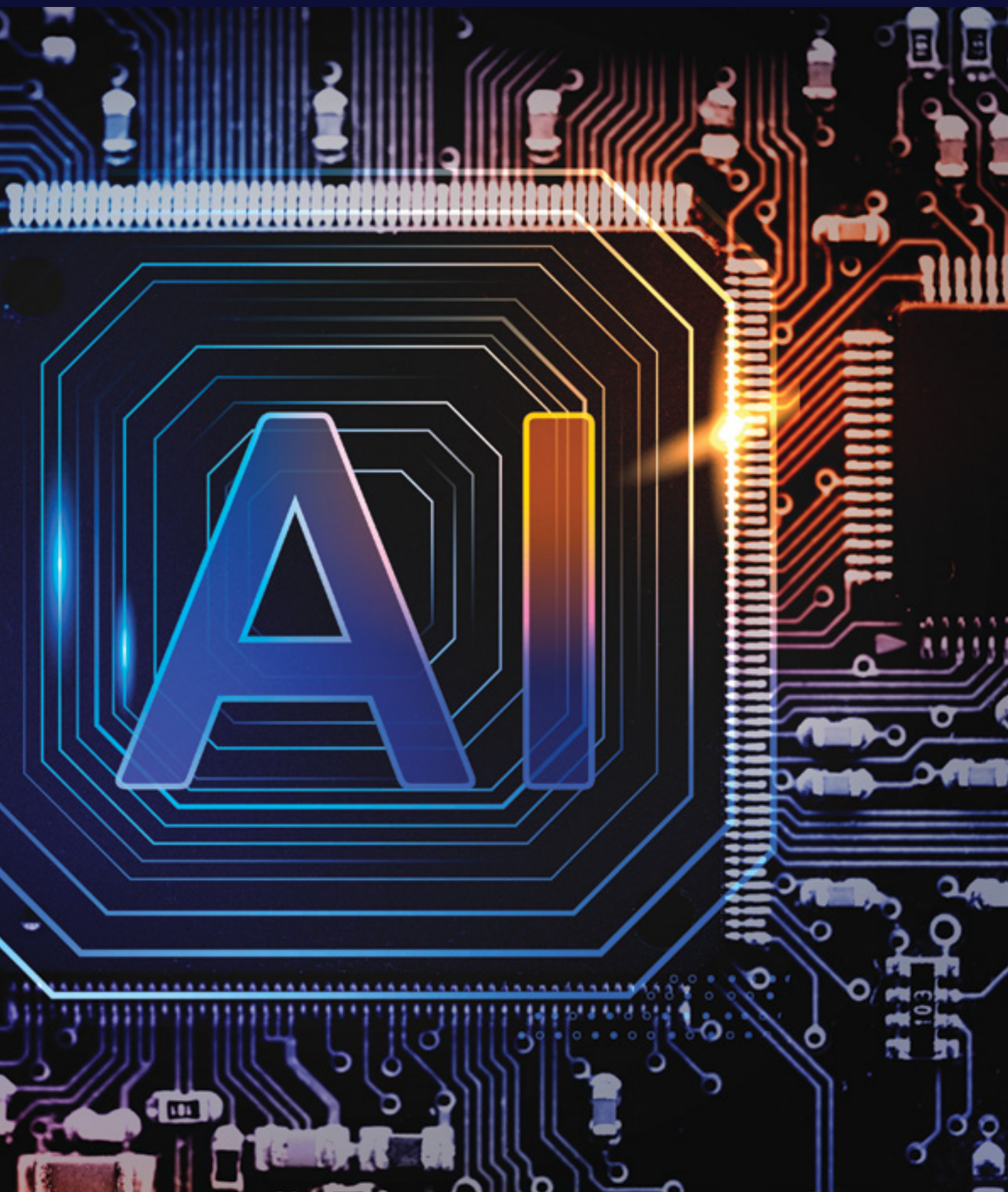
Interpersonal theory of suicide posits that suicide is preceded by a feeling of being alone and disconnected from others, which leads to a feeling of hopelessness and ultimately suicide.

As the respond did not sound 'academic' enough, we alter the prompt into: **Explain the interpersonal theory of suicide in a maximum of 40 words with psychology jargons**, and it gave us a respond as follows:

Interpersonal theory of suicide suggests that suicide is a consequence of a perceived lack of social connectedness, which leads to feelings of hopelessness and a sense of thwarted belongingness, ultimately resulting in the act of suicide.

Assuming that the question is given by a student who wants to know further about the implication of the theory, we entered the prompt "give an example





of the implication of interpersonal theory of suicide in a maximum of 50 words, and its response was:

One implication of the interpersonal theory of suicide is that individuals who have a strong sense of social connectedness, strong relationships, and a sense of belonging may be less likely to experience suicidal thoughts and behaviors. Therefore, interventions focused on building social connections and fostering a sense of belongingness may be effective in reducing suicide risk.

Assuming that we would like to explain the theory to a person from the non-psychology community with more informal lingo, we altered the prompt into **“Explain the interpersonal theory of suicide in a maximum of 40 words in an informal tone,”** and it generates the response as follows:

Interpersonal theory of suicide says that suicide happens because people feel alone and disconnected from others, this leads to feeling hopeless and ultimately to suicide.

Further, we simply tested the capability of the engine to cite the previous findings, so we altered the prompt into:

“The Interpersonal Theory of Suicide, first proposed by Joiner (2005), posits that suicide is preceded by a feeling of being alone and disconnected from others, which leads to a feeling of hopelessness and ultimately suicide. This theory proposes that individuals with a sense of thwarted belongingness and perceived burdensomeness are at risk of suicide. It suggests that suicide is not a result of a single factor, but rather the combination of these two factors along with the acquired capability for suicide (Joiner, 2005). According to this theory, people who feel disconnected from others and hopeless are at the highest risk of suicide, interventions that focus on building social connections, fostering a sense of belongingness, and addressing hopelessness can be effective in reducing suicide risk.”

While some educators might look at the artificial intelligence engine such as ChatGPT as a threat to their profession, and even ban it from public schools in New York City because “it does not build critical-thinking and problem-solving skills, which are essential for academic and lifelong success,” we can actually approach it as a tool that might enhance the students’ learning. Especially at the university level, where students have developed enough cognitive skills to interpret the AI-generated responses in a critical way.

Advanced educators who perceive that the engine hinders learning might come from the point of view that the students need to be trained to think critically, while less-advanced educators with the same attitude towards the engine might simply think that the engine can

provide answers to their quizzes and the students would not have to study. With all due respect to these groups of educators, we might want to remember that there was a time when some school teachers banned the use of calculators, and told students, “You won’t be carrying calculator everywhere you go.”

The LOTS and the HOTS

In 1956, Benjamin Bloom proposed an idea that the cognitive processes can be divided into two types called Lower Order Thinking Skills (LOTS) and Higher Order Thinking Skills (HOTS). LOTS refers to basic cognitive processes such as remembering, understanding, and applying information. These are the foundational skills that are necessary for more advanced thinking. On the other hand, HOTS refers to more advanced cognitive processes such as analyzing, evaluating, creating, and metacognition. In the case of the learners at the university levels, we obviously expect the learning to be conducted in a way that stimulates HOTS from the students. Therefore, educators at this level should not expect that their quizzes or exams can be answered by asking their seniors or simply by googling, as it does not imply the use of critical thinking skills. Thus, the next question will be how will higher education benefit from AI-based engines like ChatGPT and improve the students’ HOTS.

Ask (correctly) and you shall receive

As illustrated in the examples at the beginning of this article, the engine offered different answers for the same questions when they are asked in a different manner. Therefore, it is important for the learner to critically think how the questions should be imposed to the programme. While the AI might have learned from multiple sources, it might not have the same ‘understanding’ of the context of our inquiry. Therefore, prompting it “Write an introduction of a study on sense of empowerment and social support” might not give you the response that you would want unless you added elements like “in the Malaysian context” or “with citations from studies between 2018 and 2021.”

In other words, the engine might only be useful when we know how to prompt the correct question, and that requires HOTS.

We have tried to use it in the class of “Clinical Research Methods” for master’s students. We asked the students to open the site, and answer our HOTS questions related to the subject. We found that the students felt that the engine helped them to give them the rough idea to explore further. From the point of view of this educator, we personally see ChatGPT can be useful to enhance learning. But how? Is it ethical? Isn’t it cheating? *Well, ask (research questions) and you shall receive.*

Review of Herbal Products for Treating Common Cold

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Introduction

Have you ever had symptoms of roughness or soreness of the throat, development of nasal discharge, sneezing, and irritation of the upper respiratory tract before? Well, most people in the world have and those are the classic symptoms of the common cold. The common cold is an infection of the upper respiratory tract (URT) caused by approximately more than 200 different viruses. In 2004, the United States Census Bureau, International Data Base reported that approximately 1 billion of cold cases are reported each year, mostly affecting children. In Malaysia, the extrapolated incidence of the common cold in 2004 almost reaches 5.5 million cases. The next question that has been around for hundreds of years is whether or not there is a cure. We have certainly come very far in treating the condition. Over-the-counter (OTC) medications, as well as nutritional supplements and herbal medicines can alleviate symptoms and sometimes shorten the duration of infection. However, because colds and the flu are caused by viruses, they have no real cures. The role of herbal medicines in treating the common cold has been a massive topic discussed worldwide and the emerging use of these remedies with the evidence to support and against their uses will be discussed further in this review.

Objective

The use of herbal medicine in treating common colds is widespread but yet controversial. So far, there are at least more than 20 herbs have been identified to have potential beneficial effect in treating common cold. The aim of this review is to provide updated evidence regarding the use of these remedies.

Methods

The search for relevant articles related to herbal medicines use in common cold began in the OVID database. Under the subject heading "Common cold", 2115 articles were obtained. The next search was done using the subject heading "Herbal medicine". Under this umbrella term, 454 articles were obtained. Then, the two search terms were combined to yield more specific results. As a result, 4 articles were obtained but only one was relevant to the topic discusses. OVID database was also used as a search tool for more specific herbs such as Echinacea, ginger, garlic, goldenseal and ginkgo.

The search was continued using the National Library of Medicine-owned Pudmed database. Using the same subject headings and combination, the search yielded 11 articles. Searches were also done for specific type of herbs as in the previous search by the OVID database.

ScienceDirect was also used as a search tool to locate articles related to this topic. Search terms used include "common cold", "immune system", and "herbal medicine". The search yielded hundreds of full-text articles but most of them are animal studies. However, some of these studies are still accepted as references since they provide proven scientific evidence for the herbal medicines.

Throughout the search process, only articles written in English, and published not more than 10 years (1995-2005), were accepted. Some of the abstracts were accepted

because of the current information they provided and some articles which involved studies in animals were also accepted because they provide preliminary data on herbal medicines related to this topic.

Literature review

This literature reviews will focus on evidence-based use of herbal medicines in common cold. The review will address each common herb or plant with the evidence to support and against their uses separately. Echinacea will be the focus of this review since it is the most extensively studied herb for common cold. Herbs without any evidence to support its use will be discussed in another subheading. This review will also discuss the role of pharmacists in use of herbal medicines in general, and specifically for common cold. The implication of use of the herbals to pharmacy practice will be discussed in the final section.

ECHINACEA

At a glance

Echinacea played an important role in Native American (Giles et al., 2000) and it has been used for centuries. This is not an argument for efficacy, but it does indicate some degree of safety. The plant is grown in the central and eastern United States and is cultivated in Europe (Percival 2000, Barrett et al., 2004).

Common names are American coneflower, black Susan, purple coneflower, and narrow-leaved coneflower (Giles et al., 2000). Extracts of *Echinacea* contain varying concentrations of flavonoids, polysaccharides, derivatives of caffeic acid, polyacetylenes, alkylamides, and alkaloids (Erickson 2001). These compounds were commonly prescribed until the introduction of sulfa drugs in the 1930s (Giles et al., 2000). Types of *Echinacea* commonly used are *E. purpurea*, *E. pallida*, and *E. angustifolia*. Both the plant's upper parts and roots are used (Islam and Carter 2005). *E. angustifolia* has long been considered to have the greatest immunostimulating activity but as *E. purpurea* is the easiest to grow commercially and it has become the most used species in the United States (Giles et al., 2000). *Echinacea* is best known for its effects on immune system (Barrett 2003) but in general, the herb is used for treating the common cold, coughs, bronchitis, and inflammation of the mouth and pharynx (Percival SS 2000, Barrett et al., 2004). Powers (2004) reported that *Echinacea* could also be used for wound healing. Herbal texts list the use of *Echinacea* by at least 13 tribes of Native Americans for the treatment of very widely diverse conditions as sore mouth and gums, cough, dyspepsia, toothache, bowel complaints, hydrophobia, and snakebite (Sampson W 2005). However, until now there is no clear consensus about whether or not *Echinacea* can benefit human health (Barrett et al., 2002, Ohara et al., 1998) and also lack of safety and efficacy data in children (Barrett 2004, Taylor et al., 2003). On the other hand, there are also no published data to support contraindications of its use (Andrea et al., 2005).

Evidence supporting its use

A study was done to verify the efficacy and safety of an herbal medication containing an extract of a mixture of *Baptisia tinctoriae radix*, *Echinaceae pallidae/purpureae radix* and *Thuja occidentalis herba* (SB-TOX) in the treatment of upper respiratory tract infections. A total of 91 adults (mean age 42.1±13.0 years) were randomized to receive 19.2 mg of SB-TOX (n=31), 9.6 mg SB-TOX (n=29) or placebo (n=31) three times daily for 3–12 days. Since a “running nose” is the main symptom of a common cold, the total number of facial tissues used throughout the clinical duration of their cold was the primary efficacy parameter. No adverse events were reported. This study confirms the efficacy and safety of the herbal remedy in the treatment of the common cold. Patients recover more rapidly, within just a few days, and the effect was dose-dependent. Even the highest dosage did not produce any safety concerns. Based on these results and overall, it is recommended that treatment is initiated as soon as possible after symptom onset and with a high dose (Naser et al 2005).

Goel et al (2004) test the efficacy of a highly standardized formulation Echnilin (a formulation containing alkamides, cichoric acid, and polysaccharides from freshly harvested *Echinacea purpurea* plants) in reducing

the severity and duration of symptoms of common cold. In this randomized, double-blind, placebo-controlled trial involving 282 subjects aged 18-65 years, the total daily symptom scores were found to be 23.1% lower in the *Echinacea* group than in placebo in those who followed all elements of the study protocol (P<0.01). Therefore, the study concluded that early intervention with a standardized formulation of *Echinacea* resulted in reduced symptom severity in subjects with naturally acquired upper respiratory tract infection.

A review article compiling clinical trials on *Echinacea* from 1966-1999 concluded that the efficacy of *Echinacea* for treating common cold symptoms remains unclear, yet it appears to be a safe alternative for suitable patients. *Echinacea* appears to be well tolerated with a low frequency of adverse effects, such as mild dyspepsia, headache, and dizziness. In human and animal experiments, preparations given orally or parenterally produced immunostimulating effects such as increased white blood cells count, activation of phagocytosis and elevation of body temperature. Other actions are antiviral, antiinflammatory, and antibacterial properties, which were consistently reported from in vitro experiments. *Echinacea* appears to be well tolerated with a low frequency of adverse effects, such as mild dyspepsia, headache, and dizziness (Giles 2000). From studies in the English language, it is uncertain which part of the plant (root, aerial portion), of which species (*E. purpurea*, *E. angustifolia*, *E. pallida*), in which formulation (squeezed sap, hydroalcoholic extract, dried powder extract, etc.) offers the most evidence for efficacy (Giles et al., 2000).

Another review article published in the same year also concluded that *Echinacea* is indeed effective in reducing the duration and severity of symptoms, but that this effect is noted only with certain preparations (Percival 2000).

Evidence against its use

Grimm and Muller (1999) concluded in their randomized-controlled trial, that treatment with fluid extract of *Echinacea purpurea* did not significantly decrease the incidence, duration or severity of colds and respiratory infections compared to placebo. Results from the 8-week period found no significant differences between treatment groups in the number of infections in each category of severity determined by the investigators. Side effects were observed in 11 patients (20%) of the *Echinacea* group and in seven patients (13%) of the placebo group (p = 0.44).

Barrett et al. (2002) assessed the efficacy of dried, encapsulated, whole-plant *Echinacea* preparation as an early treatment for the common cold, in a community-based trial involving 148 subjects. This randomized-controlled trial involved the use of an encapsulated mixture of unrefined *Echinacea purpurea* herb (25%) and root (25%) and *E. angustifolia* root (50%) taken in 1-g doses six times on the first day of illness and three times on each

subsequent day of illness for a maximum of 10 days. The primary measurements are severity and duration of self-reported symptoms of upper respiratory tract infection. The study found that Echinacea preparations provided no detectable benefit or harm.

In another randomized, placebo-controlled trial, the effects of pressed juice of the above-ground plant parts of *E. purpurea* were studied. The juice was administered for 7 days before and after RV-39 inoculation, on rhinovirus colds. The results of the study suggest that Echinacea was not effective for preventing rhinovirus infection as defined by laboratory criteria. Among those who were infected and receiving Echinacea, there was a trend toward reduction in the number of clinical colds, compared with those who were infected and received placebo (59% vs. 86%; $p = 0.0883$) (Sperber SJ et al. 2004).

Barrett (2004) runs an investigation to determine if *Echinacea purpurea* is effective in reducing the duration and/or severity of URI symptoms in children and to assess its safety in this population. The main outcome measures were duration and severity of symptoms and adverse events recorded by parents. There was no difference observed in the duration between URIs treated with Echinacea or placebo ($p = 0.89$). The only difference detected in the study was in the occurrence of rash in which 7.1% of the subjects treated with Echinacea developed rash compared to 2.7% of those treated with placebo ($p = 0.008$). Therefore, the study concluded that Echinacea purpurea was not effective in treating URI symptoms in patients 2 to 11 years old, and its use was associated with an increased risk of rash. The same study was done by Taylor et al. (2003) and found similar results.

A randomized-controlled trial tested a standardized dose of *E. purpurea*, prepared from the aerial portion of the plant, for effectiveness at reducing the severity of symptoms and the duration of the common cold when treatment is started within 24 hours of the onset of cold symptoms. Symptoms (sneezing, nasal discharge, nasal congestion, headache, sore or scratchy throat, hoarseness, muscle aches, and cough) were scored subjectively by the patient and recorded daily in a diary. This study failed to show that Echinacea effectively reduces the symptoms and duration of the common cold. No statistically significant difference was observed between treatment groups for either total symptom scores (p range, 0.29–0.90) or mean individual symptom scores (p range, 0.09–0.93). The time to resolution of symptoms was not statistically different ($p = 0.73$) (Yale and Liu 2004).

The most recent study on Echinacea was done by Turner and colleagues (2005). These investigators performed a randomized prospective study to evaluate the effect of chemically defined extracts from *E. angustifolia* roots on rhinovirus infection. The results of this study indicate that extracts of *E. angustifolia* root, either alone or in

combination, do not have clinically significant effects on infection with a rhinovirus or on the clinical illness that results from it. There were no statistically significant effects of the three Echinacea extracts on rates of infection or severity of symptoms.

The most current systematic review by the Cochrane Database was done to assess the effects of preparations containing extracts of Echinacea in the prevention and treatment of the common cold. Majority of the available studies report positive results. However there is not enough evidence to recommend a specific Echinacea product, or Echinacea preparations for the treatment or prevention of common colds (Melchart et al., 2005). The result from the Cochrane Database Review was supported by other review articles which concluded that Echinacea use cannot be recommended due to a lack of standard product, variability in dose, and variability in outcome measures (Islam and Carter 2005, Fugh-Berman 2003). Fugh-Berman (2003) also concluded that the use of Echinacea to prevent URIs should be discouraged due to occurrence of severe adverse effects such as anaphylaxis, acute asthma, and urticaria/angioedema. Besides that, there is also a risk for hepatotoxicity (Bielory 2004).

Conclusion

Although the use of Echinacea is very common especially among Western populations to treat the common cold, but the evidence exists so far clearly favors the opposite. There is more evidence against than those supporting its use for common cold. Furthermore as reported by the systematic reviews, studies were done using different formulations, different parts of the plants and with different doses. Therefore, the use of Echinacea either to treat or to prevent the common cold cannot be recommended especially by pharmacist until there is clear and conclusive evidence to support its use.

GARLIC

A brief introduction

Garlic, *Allium sativum*, has been consumed as a spice and also as a medicine for thousands of years all over the world. In ancient Egypt, garlic was consumed to treat diarrhea. In ancient Greece, it was consumed to treat intestinal and lung disorders (Sato and Miyata 2000). In Asia, it has been a remedy to treat common cold, fever, and sore throat. Garlic also has claimed to possess antimicrobial, antineoplastic, anticardiovascular, immuno-stimulatory and hypoglycemic properties (Sato and Miyata 2000). Garlic's historic and worldwide medicinal use has made it one of the most extensively studied medicinal herbs. Nevertheless, the actual therapeutic benefits of this member of the Liliaceae family are unclear (O'hara et al., 1998). There is also very little known about the actual safety profile of garlic. Kao et al. (2004) discovered the garlic allergen which contributes to hypersensitivity reactions.

Evidence supporting its use

A double-blind, placebo-controlled survey by Josling (2001) was designed to determine whether a unique garlic supplement that contains only stabilized allicin could prevent colds in healthy volunteers. One hundred forty-six volunteers were randomized to receive a placebo or an allicin-containing garlic supplement, one capsule daily, over a 12-week period. They used a five-point scale to assess their health and recorded any common cold infections and symptoms in a daily diary. The group receiving garlic supplement had significantly fewer colds than the placebo group (24 vs 65, $p < 0.001$) with shorter duration of symptoms (1.52 vs 5.01 days, $p < 0.001$). Consequently, volunteers in the active group were less likely to get a cold and recovered faster if infected. Volunteers taking placebo were much more likely to get more than one cold over the treatment period. The study concluded that an allicin-containing supplement can prevent attack by the common cold virus. However, there is very little known about the actual safety profile of garlic (Kao et al., 2004).

Evidence against its use

No study available

Conclusion

Although garlic has been used for the treatment of a wide range of medical conditions, it is most commonly linked to the prevention and treatment of hyperlipidemia and coronary heart disease (Andrea et al., 2005). There are no studies available to suggest the effectiveness of garlic to treat common cold. Therefore, from available data, we can only suggest the use of commercially-available garlic to prevent common cold but for treatment.

OTHER HERBS

GINSENG

Ginseng is one of the most popular and expensive herbs in the world. At least six million Americans use the root (O'hara et al., 1998). It is derived from the roots of several plants. One of the most commonly used and researched of the ginsengs is *Panax ginseng*, also called Asian or Korean ginseng. The main active components of *Panax ginseng* are ginsenosides, which have been shown to have a variety of beneficial effects, including anti-inflammatory, antioxidant, and anticancer effects. Results of clinical research studies demonstrate that *Panax ginseng* may improve psychologic function, immune function, and conditions associated with diabetes (Kiefer and Pantuso 2003).

Because of the use of combination products and the limitations of some studies on ginseng (e.g., poor methodologic quality, research focusing on healthy volunteers, small sample size, unstandardized ginseng preparations, varying doses), it is difficult to draw

conclusions about some of the clinical effects of ginseng (Kiefer and Pantuso 2003).

GOLDENSEAL

Goldenseal is also known as *Hydrastis Canadensis*. The root of goldenseal is believed to help chronic inflammation of the mucous membranes, such as those lining the throat, sinuses, and lungs.

One clinical trial investigated the antigen-specific in vivo immunomodulatory potential of continuous treatment with Echinacea and goldenseal root extract over a period of six weeks using rats. Results from this study suggest that Echinacea or goldenseal may enhance immune function by increasing antigen-specific immunoglobulin production (Rehmann et al., 1999).

GINGER

Ginger (*Zingiber officinale*) has a long history of medicinal use. It is one of the best-known medicinal herbs in China and Japan, where it has commonly been prescribed for head-aches, nausea and other stomach problems, and colds. The rhizome is the part used for culinary and medicinal purposes. Commercial varieties of ginger are usually described in relation to their geographic origin. Commonly found in Southeast Asia, India, Africa, and the West Indies, this herb can be cultivated in other areas with proper growing conditions (Grant 2000). In laboratory animals, the gingerols have analgesic, sedative, antipyretic, antibacterial, and GI tract motility effects (O'hara et al., 1998).

MA-HUANG

Ma-Huang is a traditional oriental herbal medicine frequently used for the treatment of the common cold in Japan. A study by Takagi et al. (2004) investigated the effects of Ma-Huang administration on influenza in mice. Results from this study showed that Ma-Huang suppresses the proliferation of influenza virus in the lungs and suppresses the discharge of the virus from the upper respiratory tract. From these results, the study concluded that Ma-Huang is effective in controlling the infectious expansion of the influenza virus.

ANDROGRAPHIS PANICULATA

Andrographis paniculata is an annual herbaceous plant, widely found in tropical and subtropical Asia, Southeast Asia, and India. The plant is one of the most important medicinal plants used in traditional Chinese and ayurvedic medicine for the treatment of the common cold, influenza, and other infectious diseases. It has been used extensively in Scandinavia for the past 20 years for the treatment and prevention of the common cold (Andrea et al., 2005).

A double blind, placebo-controlled, parallel-group clinical study was carried out to evaluate the effect of an *Andrographis paniculata* extract in the treatment of acute upper respiratory tract infections, including sinusitis. Temperature, headache, muscle aches, throat symptoms, cough, nasal symptoms, general malaise and eye symptoms were taken as outcome measures with given scores. The study concluded that *Andrographis paniculata* has a positive effect in the treatment of acute upper respiratory tract infections and also relieves the inflammatory symptoms of sinusitis (Gabrielian et al., 2002).

A very recent systematic review was done to assess the efficacy of *Andrographis paniculata* in the symptomatic treatment of uncomplicated upper respiratory tract infection. The review reported a significant difference in effects and in symptom severity score when compared with placebo ($p < 0.0001$ and $p = 0.0002$ respectively). Therefore the review concluded that *Andrographis paniculata* extract may be more effective than placebo and may be an appropriate alternative treatment of uncomplicated acute upper respiratory tract infection (Poolsup et al., 2004).

ASTRAGALUS

In the United States and China, the root of astragalus has been shown to increase nearly every phase of immune-system activity. One study showed that long-term use (35 days) heightened immune-cell activity. Another showed that astragalus increases the production and storage of interferon which stimulates cells to begin their defense in fighting illnesses such as the common cold (Block and Mean 2003).

Conclusion

Ginseng, goldenseal, ginger, Ma-Huang, *Andrographis paniculata*, and astragalus have all been used to treat the symptoms of common cold. Besides these herbs, other herbs such as Anise (*Pimpinella anisum*), Elderberry (*Sambucus nigra*), Licorice (*Glycyrrhiza glabra*), Marsh mallow (*Althaea officinalis*), Mullein (*Verbascum thapsis*), Osha (*Lomatium dissectum*), Pennyroyal (*Hedeoma oblongifolium*), Purslane (*Portulaca oleracea*), Slippery Elm (*Ulmus rubra*), and Stinging nettle (*Urtica dioica*) have also been used (www.herbmed.org). These remedies are claimed to have activities of the expectorants, decongestants, antitussive, and immunomodulators. Like the other herbs, all these herbs have not been studied, specifically in treatment for the common cold. Most of them are being studied for other conditions. Ginger, for example, is very well studied for prevention of cancer and for hypertension. With the current information that we have, there is no reason to support the use of any of these herbal medicines to treat the common cold.

SUMMARY

Herbal medicines are generally considered comparably safe. However, severe side effects and interactions with other herbs or drugs have been reported (Klaus L et al. 2001). Echinacea for example, has been associated with anaphylactic reaction, exacerbation of allergic asthma, and atopic dermatitis. Although some of these herbal remedies have been used for thousands of years, we still do not have the data on how effective and how safe they are. In third world countries including Malaysia, many people still believe that herbs are the answers to many diseases but all that we have been hearing so far are the benefits of those herbs. How about the side effects of those herbs? Have anybody died from it? If yes, then was it ever reported? That is why it is very difficult to study these traditional medicines. People or users tend to relate the use of these herbs only to their effectiveness, but not to their toxicity. Thank to science and emergence of new knowledge in this field, we hopefully will be able to give definite answers to all these questions.

Roles of pharmacists in the use of herbal medicines for common cold

1. Gather adequate knowledge about herbal medicines

Pharmacists should equip themselves with the latest knowledge and information on herbal medicines. In Malaysia, for example, there are training courses available on herbal medicine in which pharmacists can participate to acquire new knowledge in this field. Pharmacists should also be able to identify the sources of information on herbs. Being able to choose the correct source of information is also a key in order to differentiate between facts and personal opinions. For example, knowledge about herbals for common cold are readily available on the internet but pharmacists must be able to choose a reputable website with evidence-based information.

2. Educate patients on the efficacy and safety of herbal medicines

Pharmacists should educate patients or users on the efficacy and safety of herbal medicines. Education can be delivered in a form of verbal counseling, or written information. Counseling can be done for an individual or a group of patients. Pharmacists should be able to provide information on the dosage, correct route of administration, and the duration of use. Potential interactions with other herbs or with other medications should also be emphasized. Opportunities to educate patients on use of these herbs in common cold should not be a problem because the condition is very common.

3. Provide appropriate suggestions or recommendations to public regarding the use of herbal medicines

Recommendations may include not taking any of

the herbal medicines. If the patient insists, then at least precautions have been told. Before making any recommendation for use, pharmacists should know patient's background especially the medication history. This is because some of the herbals may interact or have additive/synergistic effect on other medications the patient is taking or they may worsen the patient's condition. For example, if the patient is on a decongestant for runny nose, then a herb with known antihistaminic properties would not be appropriate. Similarly, if the patient has history of hypertension, pharmacists should not recommend herbs with known antihypertensive activity because the patient might already be on an antihypertensive medication.

4. Control the sales of herbal medicines

Community pharmacists should control the sale of herbal products to public. Pharmacists should only sell herbal products with known evidence to support their use. The National Pharmaceutical Bureau should also play a role in controlling the sales of herbal products. This is because there are now many herbal products with added constituents that can harm the consumers.

5. Participate in or perform studies on herbal medicines

Pharmacists should actively involve in studies on herbal medicines because we are the only professional who receive formal knowledge in the field. Most studies lack the application of pharmacokinetics and pharmacodynamics principles which are vital in studying the effect of xenobiotics. By participating in these types of studies, pharmacists may be able to improve some methodological weaknesses in current studies and provide more convincing results.

Implications of this review to pharmacy practice

This review alerts pharmacists to be more cautious and well-versed when recommending the use of herbal medicines for common cold. At least for now, we know that there is no single herbal product found to be beyond doubt, effective to treat or prevent the common cold. Pharmacists should take this opportunity to educate the public so that they are more well-informed and able to make the correct decisions.

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Anxiety Level, Sleep Quality and Physical Activity among Malaysian University Students in the Klang Valley during COVID-19 Pandemic

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ABSTRACT

Introduction: The movement control order (MCO) imposed by the government during the COVID-19 pandemic has caused several changes for all individuals including the university students. Some of the changes include lifestyle, physical activity and sleep quality that influence mental health especially the anxiety level of university students.

Objective(s): This study aims to assess the association between anxiety level, sleep quality and physical activity among Malaysian university students in the Klang Valley during COVID-19 pandemic.

Methodologies: Data from 367 Malaysian university students were collected using a convenient sampling method in this web-based cross-sectional survey. Anxiety level, sleep quality and physical activity were assessed using the Generalized Anxiety Disorder-7 questionnaire (GAD-7), Pittsburgh Sleep Quality Index (PSQI) and International Physical Activity Questionnaire-Short Form (IPAQ-sf), respectively.

Results: About one-third of the university students have mild anxiety (28.9%) and another 28% reported having moderate anxiety. Slightly more than half (52%) of the students reported poor sleep quality, majority of them (73%) were physically active, and a significant association was found between anxiety and sleep quality ($\chi^2=50.13$, $p<0.05$) of the university students.

Conclusion: The results showed that university students were experiencing some sort of anxiety and have poor sleep quality, nevertheless they were active physically during the movement restriction period due to COVID-19 pandemic. Considering the findings, it is important to introduce activities and programmes that promote mental health and sleep quality among university students so that their overall health status could be improved.

Keywords: COVID-19; MCO; anxiety; sleep quality; physical activity

INTRODUCTION

In Malaysia, COVID-19 was first detected on 25 January 2022 (Shah et al., 2020), and the government has implemented the Movement Control Order (MCO) to reduce the transmission of COVID-19 outbreak. The mandatory closure of universities and social distancing (lockdown) action brought a major impact on the lifestyle and mental health of university students (Mattioli et al., 2020). Anxiety is a normal process in life, but it could impair the life functioning of an individual when it becomes serious, which can be categorised as a disorder or illness (Maideen et al., 2015). Numerous studies have shown that the anxiety level of an individual increased during the COVID-19 pandemic, and it is the main mental health issue affecting university students in Malaysia (Na et al., 2021; Twenge and Joiner, 2020).

The COVID-19 pandemic has changed the daily habits and behavior patterns of many individuals such as the normal life routines including mealtime and physical activity that lead to alterations in circadian rhythm and reduce sleep quality (Altena et al., 2020; Morin et al., 2020). Based on a study by Gupta et al., (2020), lockdown disrupts sleep cycles, resulting in a later start to sleep, shorter nocturnal sleep duration, and more daytime naps. Also, the MCO due to COVID-19 pandemic has contributed to a marked decrease in physical activity level and an increase in sedentary behaviors of many individuals (Ammar et al., 2020; Castañeda et al., 2020).

Unhealthy lifestyles increase the tendency of mental health issues such as depression and anxiety (Boni et al., 2020). According to the Anxiety and Depression Association of America (2021), anxiety and sleep are

associated interactively as anxiety can induce sleep problems and sleep deprivation can cause anxiety disorder. On the other hand, World Health Organization (2020) suggested that regular physical activity can help in reducing depression and anxiety symptoms.

This study aims to assess the anxiety level, sleep quality and physical activity, as well as to determine the association between anxiety, sleep quality and physical activity among Malaysian university students in Klang Valley during the COVID-19 pandemic.

METHODOLOGIES

2.1 Participants and Study Design

This was a cross-sectional study, and the study sample comprised Malaysian university students (aged 18 to 35 years) studying in universities located in the Klang Valley during the COVID-19 pandemic. They were recruited using a convenience sampling method and the survey was conducted between 24 January 2022 and 17 April 2022 using Google Forms. The online questionnaires link and QR code were shared with participants via selected social media (Facebook, Instagram, and LinkedIn) and communication platforms (WhatsApp group and Telegram group). This study has obtained an ethical clearance from the Institutional Ethics Committee, UCSI University (IEC-2022-FAS-011), and informed consent was obtained from participants prior to the start of the study.

2.2 Questionnaires

A set of questionnaires (Google Forms) consisting of four sections were prepared and participants were required to complete them virtually. In the first section, social-demographic information was collected. The second section assessed the anxiety symptom of university students by using the Generalized Anxiety Disorder-7 questionnaire (GAD-7). GAD-7 consists of seven items based on different anxiety-related conditions, each item was given four options including “not at all”, “several days”, “more than half of the days”, “nearly every day”, corresponding to score of “0”, “1”, “2”, and “3”, respectively. The score of the seven items was summed up and categorised into four categories including the “norm” (0 to 4), “mild anxiety” (5 to 9), “moderate anxiety” (10 to 14) and “severe anxiety” (15 to 21), respectively (Spitzer et al., 2006). The third section adopted Pittsburgh Sleep Quality Index (PSQI) to assess the sleep quality and disturbances of the participants (Buysse et al., 1988). PSQI scale consists of a total of 19 questions (five questions that were supposed to be rated by the bed partner or roommate were not included in this study) and can be classified into seven components and yielding a global score range from 0 to 21. A cut-off point of 5 and above on the PSQI was used to determine poor sleep quality. The last section is the physical activity assessment that adopted the International Physical Activity Questionnaire-Short Form (IPAQ-sf), IPAQ-sf consists of seven questions covering

four domains to measure the time spent engaging in physical activity (vigorous, moderate, and walking) and sedentary behavior (sitting). The scoring of IPAQ-sf was based on the official IPAQ scoring protocol (IPAQ Research Committee, 2005).

2.3 Data Analysis

All the data were analysed using Statistical Package for Social Sciences (SPSS) version 20.0. Descriptive statistics were performed to obtain the frequency, percentage, mean, and standard deviation. Chi-square test was performed to assess the association between anxiety and sleep quality, sleep quality and physical activity as well as anxiety and sleep quality. The significance level was set at $p < 0.05$.

RESULTS AND DISCUSSION

3.1 Sociodemographic Characteristics of Participants

Table 1 shows the sociodemographic characteristics of 367 subjects recruited with a mean age of was 21.64 years old. More than half of the subjects were female (58.3%) and Chinese ethnic group (60.8%), respectively. Majority of the subjects (84.5%) were pursuing an undergraduate study programme and more than of the subjects (58.9%) were having their study on-campus (physical mode) as the MCO has been relaxed by the government.

Table 1: Social-demographic characteristics of study subjects (n=367)

Social-demographic characteristics	n (%)
Age (year, mean \pm SD)	21.64 \pm 2.27
Gender	
Male	154 (41.7)
Female	214 (58.3)
Ethnicity	
Malay	107 (29.2)
Chinese	223 (60.8)
Indian	30 (8.2)
Other	7 (1.9)
Current Mode of Study	
Physical	216 (58.9)
Virtual	151 (41.1)
Study Programme	
Pre-University	39 (10.6)
Undergraduate	310 (84.5)
Postgraduate	18 (4.9)

Note: n, number; SD, Standard Deviation.

3.2 Generalized Anxiety Disorder (GAD)

During the COVID-19 pandemic, only about one-quarter of the study subjects (24%) had normal anxiety level whereas the majority of the study subjects (76%) experienced mild to severe anxiety (Figure 1).

Of the study subjects who experienced anxiety, 28.9% experienced mild anxiety, 28% reported to have moderate anxiety followed by about one-fifth (19.1%) had severe anxiety. A study conducted by Hooper et al. (2021) that involved 16 different universities in Malaysia found quite a similar prevalence of anxiety level among university students (30.5% mild, 21.1% moderate and 26.1% severe anxiety). During the COVID-19 pandemic, the university students' anxiety level is exacerbated by abrupt changes to their study environment and a decline in physical social engagement and the feeling of worry about the personal health and health of their loved ones (Lee et al., 2021).

3.3 Sleep Quality

Among the 367 subjects, half (52%) of them had poor sleep quality while 48% had good sleep quality, as shown in Figure 2. Du et al., (2021) and Bosi et al., (2021) also reported that 49.5% of Malaysian and 53.4% of Turkish university students were having poor sleep quality. Kocavska et al. (2020) suggested that lockdown or better known as movement control in the Malaysian context affects sleep quality inconsistently and the effect of COVID-19 on sleep quality may differ critically across participants. Interestingly, the present study reported a lower prevalence of poor sleep quality compared to the studies that were assessing the sleep quality of Malaysian university students before the COVID-19 pandemic, which ranged from 59.6% to 70.6% (Mohd et al., 2018; Nurismadiana and Lee, 2018; Said et al., 2020).

3.4 Physical Activity

Figure 3 shows about three-quarters (73%) of the study subjects were physically active with a high proportion having high physical activity level (40.3%) followed by a moderate physical activity level (32.7%) and a low physical activity level (27%). A similar prevalence of 75% Malaysian adults were physically active as reported by the National Institutes of Health Ministry of Health Malaysia in 2019.

3.5 Association among Anxiety, Sleep Quality and Physical Activity

Table 2 shows the association between GAD level and sleep quality along with the association between GAD level and physical activity. A significant association was found between sleep quality and the level of anxiety ($\chi^2=50.13$, $p<0.05$) among Malaysian university students. A study in Malaysia had reported a similar result, where students with poor sleep quality were more likely to experience anxiety than those with high sleep quality (Mohamad et al., 2021). This study result was supported by Peltz et al., (2016) that found a significant bidirectional relationship

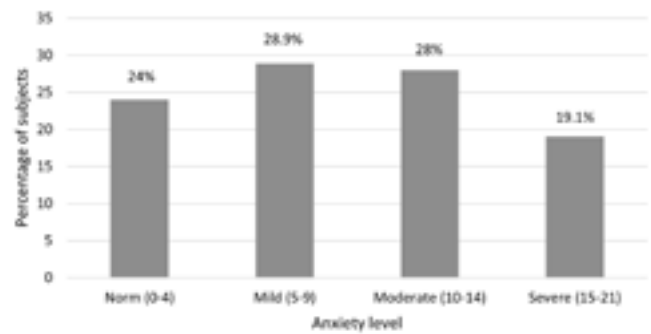


Figure 1: Distribution of anxiety levels based on GAD classifications among the study subjects (n=367)

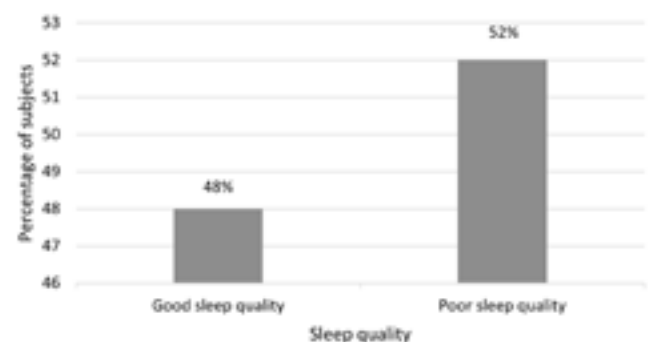


Figure 2: Distribution of sleep quality based on PSQI classification among the study subjects (n=367)

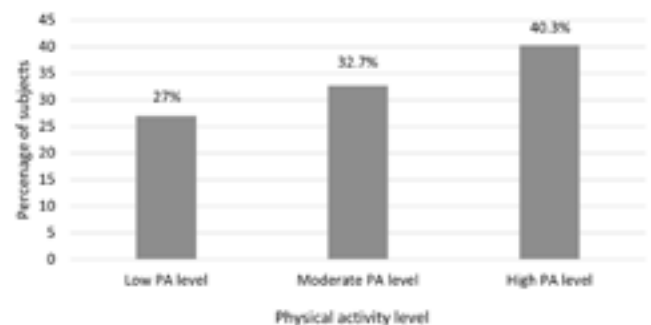


Figure 3: Distribution of physical activity level based on IPAQ scoring protocol among the study subjects (n=367)

between sleep and anxiety symptoms among university students, sleep quality. The anxiety-induced stress may further lead to hormonal, behavioral and autonomic responses that affect sleep quality (Staner, 2022), and on the other hand, poor sleep quality may lead to sleep problems dependent on anxiety (Orsal et al., 2012).

There was no significant association between physical activity level and level of anxiety ($\chi^2=9.43$, $p=0.151$) among Malaysian university students found in this study. A study by Selvakumar et al., (2022) reported a similar result in which physical activity and sedentary behavior

Table 2: Association between anxiety level, sleep quality and physical activity among study subjects

Demographic Data	Anxiety Level				Statistical significance
	Norm (n=88)	Mild (n=106)	Moderate (n=103)	Severe (n=70)	
Sleep quality					
Good sleep quality	68 (38.6)	50 (28.4)	42 (23.9)	16 (9.1)	$\chi^2=50.13$
Poor sleep quality	20 (10.5)	56 (29.3)	61 (31.9)	54 (28.3)	p=0.000*
Physical activity level					
Low	29 (29.3)	17 (17.1)	32 (32.3)	21 (21.2)	$\chi^2=9.43$
Moderate	27 (22.5)	41 (34.2)	31 (25.8)	21 (17.5)	p=0.151
High	32 (21.6)	48 (32.4)	40 (27.0)	28 (18.9)	

Note: n, number. *Chi-square test with significance at $p<0.05$.

Table 3: Association between sleep quality and physical activity (PA) among study subjects.

Variable	Low PA (n=99)	Moderate PA (n=120)	High PA (n=148)	Statistical significance
Sleep quality				
Good sleep quality	52 (52.5)	59 (49.2)	65 (43.9)	$\chi^2=1.865$
Poor sleep quality	47 (47.5)	61 (50.8)	83 (56.1)	$p=0.394$

Note: n, number. Association between variables using Chi-square test, $p<0.05$.

have no significant association with mental health among university students in Malaysia. However, the current finding was incongruent with most studies that reported a significant association between anxiety and physical activity (Chekroud et al., 2018; Ghrouz et al., 2019; Svensson et al., 2021). Multiple mechanisms such as the ability of physical activity to stimulate dopamine contributes to stress resilience and the protective effects of physical activity by reducing inflammation in an individual have been proposed to elucidate the association between anxiety and physical activity (Greenwood, 2019; Svensson et al., 2021). There was mounting evidence that more frequent physical activity was related to improve mental health even though the current research found no significant association between anxiety and physical activity. Hence, the advantages of continuing to remain active should not be disregarded.

3.6 Association among Sleep Quality and Physical Activity

There was no significant association between sleep quality and physical activity level ($\chi^2=1.895$, $p=0.394$) among Malaysian university students (Table 3). Previous study among university students from 23 countries revealed a similar result that no association was observed between vigorous physical activity and sleep quality (Pengpid and Peltzer, 2020). Another study involving 658 young adults by Kakinami et al., (2017) also found that physical activity was not associated with sleep quality or sleep quantity.

CONCLUSION

This study's findings indicated that the university students have some sort of anxiety and poor sleep quality,

but a physically active lifestyle during the MCO. Thus, creative health promotion strategies and interventions that are aligned with the new norms after the pandemic need to be planned and conducted to raise awareness and improve the mental health as well as the sleep quality of university students.

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Emotional Eating, Stress, Food Purchasing and Consumption among Malaysian Undergraduate Students in Klang Valley during the COVID-19 Pandemic

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ABSTRACT

Introduction: The COVID-19 pandemic resulted in the implementation of the Movement Control Order (MCO) in Malaysia since March 2020. This had led to major lifestyle disruptions including university students, influencing the way they perceive stress and their psychological well-being, which in turn prompted a shift in their behaviour towards food.

Objective(s): This study aims to evaluate the association between stress, emotional eating and food consumption among undergraduate students in Klang Valley during the COVID-19 pandemic. Methodologies: An online 4-part questionnaire was used to evaluate the association between emotional eating, stress, food purchasing behaviour and preferences among 335 Malaysian undergraduate students studied at universities located in the Klang Valley.

Results: About half (48.4%) of the undergraduate students were classified under the high stress group. Male emotional eaters (30.3%) were higher than their female (23.6%) counterparts. A significant association between stress and emotional eating ($\chi^2=7.494$, $p=0.006$) was found among undergraduate students in Klang Valley during the COVID-19 pandemic.

Conclusion: The MCO had been found to be associated with the shift in behavioural nutrition among the undergraduate students. This study provides a reference point for further studies on undergraduate health and well-being.

Keywords: COVID-19; MCO; food purchasing; food consumption; emotional eating.

INTRODUCTION

The “Movement Control Order” (MCO) imposed by the government comprising a series of actions and procedures that aimed towards decreasing the spread of COVID-19. The MCO along with border closures contributed to the major disruptions towards the food supply system and resulted a change in behavioural nutrition of many individuals (Janssen et al., 2021). Countless psychological alterations due to the pandemic was having a direct effect on food-related behaviours, including the occurrence of panic buying, reduced food shopping that directly affects the fresh food purchase and decreased in fresh food consumption, increased purchase of highly processed foods and consumption of “comfort foods” as a coping mechanism for psychological distress and emotional eating (EE) were also reported (Devit, 2020; Pak et al., 2021).

Major lifestyle disruption observed in university students was the substitution of face-to-face learning with online teaching, and this change may create stress to the students they are still required to learn and grasp the knowledge within the semester and attend examinations as usual via online mode (Yang et al., 2021). The stressful university life influences how students perceive stress and how it affects their emotions, learning process engagement as well as their psychological well-being that influences their behaviour towards food (Hasan et al, 2020; Song et al., 2020; Janssen et al., 2021).

Emotional eating can be defined as the tendency to over consume food when negative emotions such as depression, anxiety and stress are present (Thayer, 2003). Past study had shown the use of stress-related eating to cope with stressful situations (Bracale and Vaccaro, 2002), hence, the risk of developing EE due to the presence of

negative emotions have since increased. Individuals with higher perceived stress during the pandemic, were shown to have higher EE and demonstrated the mediation of EE towards the association between perceived stress and food choice motives (Shen et al., 2020). Studies have shown that the amount and types of food consumed is affected by stress as individuals with high stress scores tend to consume more calories and hyperpalatable, energy-dense foods that consists high amounts in sugar and fat (Groesz et al., 2012; Kim et al., 2013; Al-Musharaf et al., 2020).

Thus, this study aims to determine the food purchasing behaviours, food consumption along with prevalence of stress and emotional eating as well as the association between stress, emotional eating, and food consumption among undergraduate students in Klang Valley during the COVID-19 pandemic.

METHODOLOGIES

2.1 Participants and Study Design

There were 335 Malaysian undergraduate students (18-24 years) from the Klang Valley participated in this cross-sectional study evaluating the association between emotional eating, stress and food purchasing behaviour and preferences in the Klang Valley during the COVID-19 pandemic. An online Google Forms consisted of socio-demographic profile, food purchasing behaviour and consumption, Perceived Stress Scale (PSS) and the Eating Behaviour Questionnaire was used. The Food Purchasing Behaviour and Consumption questionnaire was adopted from Janssen et al. (2021), whilst the PSS measures the degree to which life has been experienced as “unpredictable”, “uncontrollable”, and “overloaded” for the past month using a 5-point Likert scale (Cohen et al., 1983). Participants who scored ≤ 20 were classified as “low stress” whereas participants with scores ≥ 21 were classified as “high stress” (Cheng and Wong, 2021). The Eating Behaviour Questionnaire was adopted from the Emotional Eating Subscale of the Dutch Eating Behaviour Questionnaire (DEBQ) (van Strien et al., 1986). The Emotional Eating (EE) Subscale consists of 13 items assessing the EE behaviours with a 5-point Likert scale. A cut-off score of >3.25 was used to identify negative EE, those with higher mean subscale scores propose more severe emotional eating symptoms (van Strien et al., 2012). The ethical clearance was obtained from UCSI University Institutional Ethics Committee (Project Code: IEC-2022-FAS-011). Participation was voluntary and informed consent was obtained from the participants through clicking on the “Yes, I agree” option on the information section of the Google Forms.

2.2 Data Collection

The data collection was conducted from January to March 2022 where the Google Forms link was distributed through various social media platforms such as Facebook, Instagram, Twitter, WhatsApp and UCSI Cn. Study

participants were required to answer a series of questions (approximately 15-20 minutes to complete) and were made aware that there were no risks or direct benefits and no incentives given by participating in this study.

2.3 Data Analysis

Statistical Package for Social Sciences (SPSS) version 21.0 was used to analyse all the data. Chi-square test was used to determine the association between stress and emotional eating as well as the association between food consumption and stress among Malaysian undergraduate students in the Klang Valley. The level of statistical significance was set at $p < 0.05$.

RESULTS AND DISCUSSION

3.1 Sociodemographic Characteristics of Participants

Table 1 shows that majority of the participants were females (73.4%), majority of the students were living with their family members during the MCO period (77.6%), and slightly more than half (53.5%) and more than one-third (36.1%) of the participants were from B40 and M40 income households, respectively.

Table 1: Sociodemographic characteristics of participants (n=335)

Socioeconomic Information	n (%)
Gender	
Male	89 (26.6)
Female	246 (73.4)
Ethnicity	
Malay	40 (11.9)
Chinese	275 (82.1)
Indian	16 (4.8)
Other	4 (1.2)
Current Living Arrangement	
With family members	260 (77.6)
With friends	40 (11.9)
Alone	35 (10.4)
Institute	
Public	27 (8.1)
Private	308 (91.9)
Monthly household income*	
Less than RM2500 (B40 (B1))	93 (27.8)
RM2501- RM4849 (B40 (B2-B4))	86 (25.7)
RM4850- RM10959 (M40)	121 (36.1)
RM10960 and above (T20)	35 (10.4)

*The household income range for B40, M40 and T20 is based on the Household Income & Basic Amenities Survey Report 2019 (Department of Statistics Malaysia, 2019).

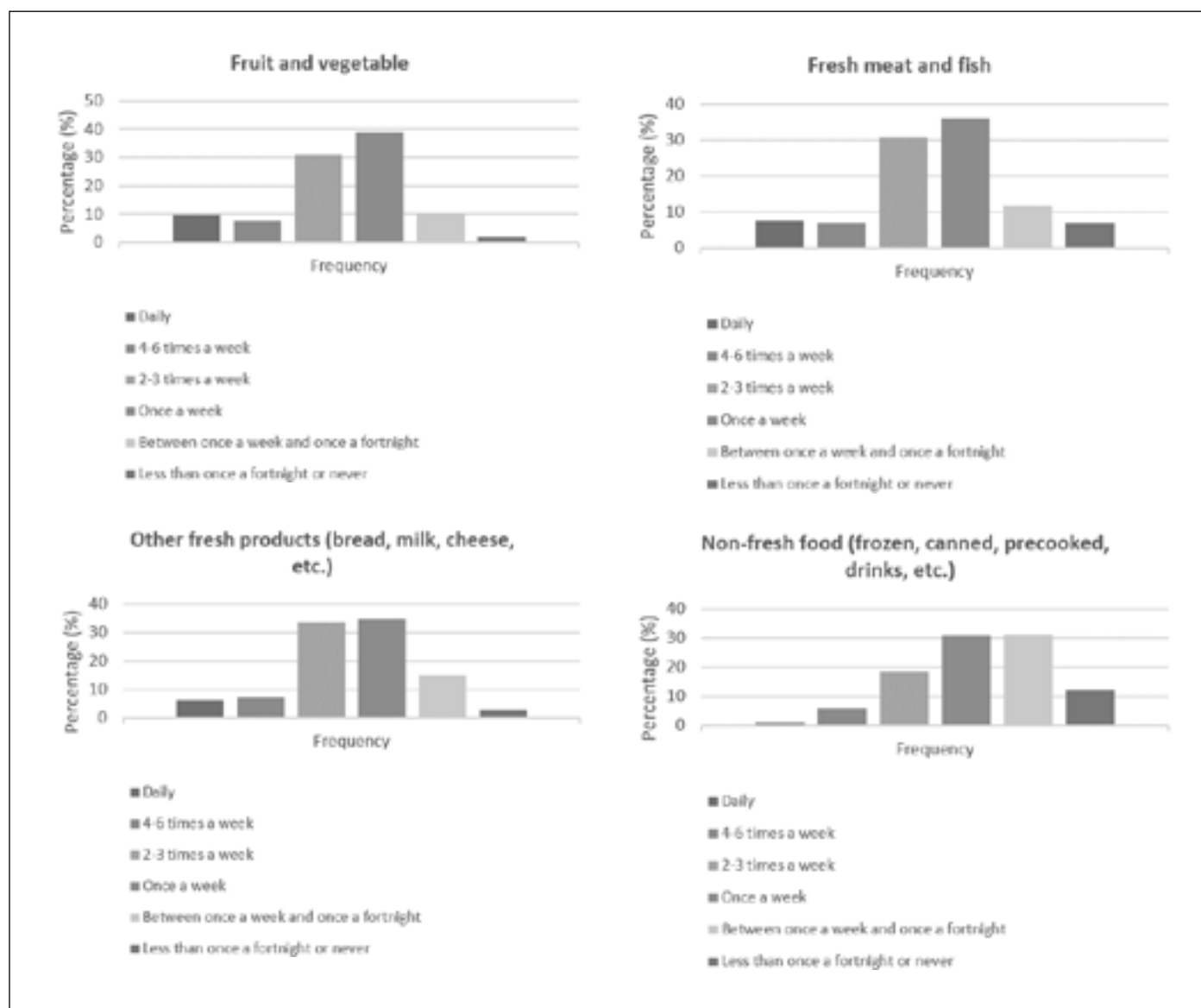


Figure 1: Frequency of food obtained by participants during the pandemic (n=335)

3.2 Food Purchasing and Consumption

During the COVID-19 pandemic, food products, such as fruits and vegetables (39.1%), fresh meat and fish (36.1%) and other fresh food products such as bread, milk, cheese and so forth (34.9%) were purchased once a week, whereas non-fresh foods (31.3%) were purchased between once a week and once a fortnight, as shown in Figure 1. A decrease in shopping frequency and the purchase of fresh food products was observed in this study, similar observation was reported in a Slovenian study where a decrease in shopping frequency of fresh food (42–58%) along with a decrease for non-fresh food (35%) (Janssen et al., 2021). A greater change in food purchasing frequency may be a result of stricter restrictions or MCO implemented in both Malaysia and Slovenia (Teoh 2021; Janssen et al., 2021).

The situation of the pandemic and implementation of MCO has triggered a shift in food-related activities. As shown in Figure 2, majority of study participants

consumed fruits and vegetables (43.0%) along with fresh meat (34.6%) daily, while fresh fish (37.0%), bread (34.6%), dairy products (36.1%), frozen food (40.0%) as well as cake and biscuits (34.6%) were consumed 2-3 times a week. Canned food (27.8%) was consumed once a week, whereas ready-made meals (31.6%), chocolate and candies (26.0%) along with wine, beer and other alcoholic drinks (76.7%) were consumed less than a fortnight or never by the participants. Individual's risk perception of COVID-19 might be a possible cause that led to changes in food consumption and those with higher risk perception of the virus tend to be more concerned and practice a healthier diet with the intention of strengthening their immune system (Rodríguez-Pérez et al., 2020). There is a possibility that students may have a higher risk perception that led to a shift in dietary habits during MCO. The MCO implementation had increased the consumption of ready-made meals and "comfort foods" such as chocolate, candies, and snack food items have been demonstrated elsewhere (Scarmozzino and Visioli, 2020).

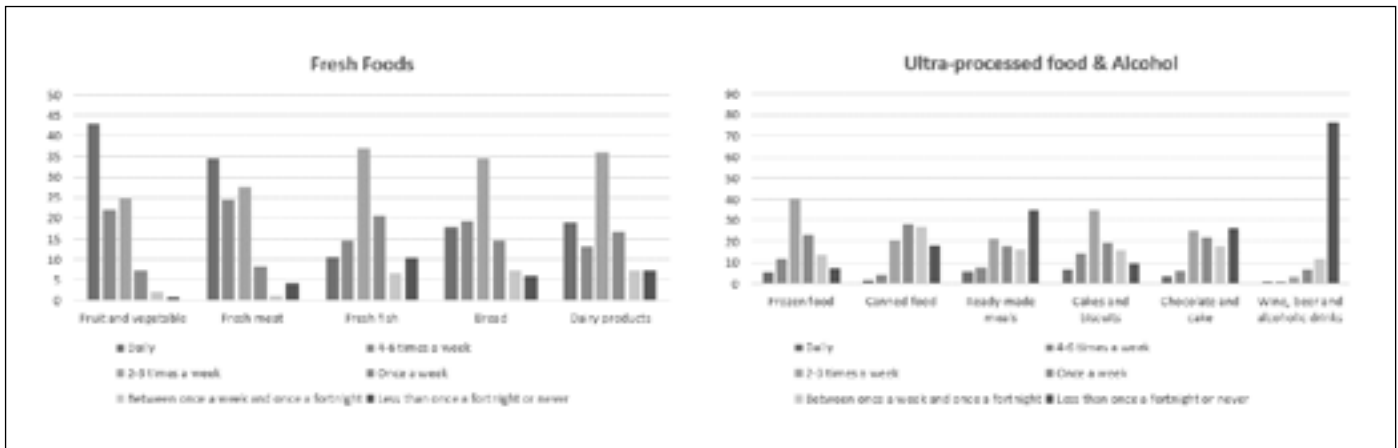


Figure 2: Frequency of food consumed by participants during the pandemic (n=335)

3.3 Stress, Emotional Eating and Its Association

Table 2 shows the stress intensity and emotional eating status of participants according to gender. About half (48.4%) of the participants were classified under the high stress group, and this prevalence was higher than other studies conducted during the first Malaysian MCO where 22% and 40% were moderately to severely stressed as reported by Wan Mohd Yunus (2021) and Cheng and Kamil (2020), respectively. Females were found to have dominated both stress groups in the present study, similar trend was reported by Graves et al. (2021), and majority (74.6%) of them were classified as non-emotional eaters. The prevalence of male emotional eaters (30.3%) was higher than females (23.6%) in this study, similar result was reported in Cheng and Wong (2021) study. It was expected that during MCO many may experience drastic changes in eating behaviours that may lead to overeating (Haddad et al., 2020).

There was a significant association between stress and emotional eating among undergraduate students in Klang Valley during the COVID-19 pandemic ($\chi^2=7.494$, $p<0.05$) with 32.1% experienced high stress and 19.1% low stress levels were emotional eaters, respectively. This finding was supported by past studies that demonstrated eating being used as a stress relief method for those experiencing stress, this was linked to the high levels of cortisol released during stressful situations triggers the activity of eating (Epel et al., 2004; Oliver and Wardle, 1999). Furthermore, the association between EE with stressful life events along with perceived stress were also observed (Klatzkin et al., 2019; Michels et al, 2012).

3.4 Association between Food Consumption and Stress

There was no significant association found between the stress level and type of food consumed in the study (Table 3). Errisuriz et al. (2016) also reported no association was found between stress and the consumption of fruits and vegetables, fresh meat, fresh fish, and dairy products. In addition, no significant association was found between stress level and ultra-processed foods and “comfort foods” in the present study. Positive association was reported

Table 2: Stress level and emotional eating status of participants according to gender and stress level by emotional eating status of participants (n=335)

Variable	Male (n=89) n (%)	Female (n=246) n (%)	χ^2 value
Stress level			$\chi^2=0.066$
Low stress	47 (27.2)	126 (72.8)	p=0.797
High stress	42 (25.9)	120 (74.1)	
Emotional eating status			$\chi^2=1.577$
Non-emotional eaters	62 (69.7)	188 (76.4)	p=0.209
Emotional eaters	27 (30.3)	58 (23.6)	
	Low Stress (n=173) n (%)	High Stress (n=162) n (%)	χ^2 value
Emotional eating status			$\chi^2=7.494$
Non-emotional eaters	140 (80.9)	110 (67.9)	p=0.006*
Emotional eaters	33 (19.1)	52 (32.1)	

*Chi-square test with significance at $p<0.05$.

between chronic stress and the consumption of foods that are highly palatable and lack nutrients along with the activation of the endogenous opioid (reward) system with a reduced hypothalamic-pituitary-adrenal (HPA) axis stress response that alleviates stress (Papier et al., 2015). Among the studies conducted on college students, there was an association between high levels of stress and increased favour towards ultra-processed foods (Errisuriz et al., 2016). The occurrence of the pandemic and MCO have increased perceived stress levels in participants, which in-turn affects healthy eating behaviour and promotes the tendency of “comfort foods” consumption and decrease the consumption of healthy and nutrient-dense foods (Buckland et al., 2021).

Table 3: Association between types of food consumed and stress level (n=335)

Variable	Stress level, n (%)		χ^2 value
	Low stress	High stress	
Fruits and vegetables			$\chi^2=6.741$ p=0.241
Fresh meat			$\chi^2=8.134$ p=0.149
Fresh fish	173 (51.6)	162 (48.4)	$\chi^2=3.439$ p=0.633
Bread			$\chi^2=5.401$ p=0.369
Dairy			$\chi^2=4.930$ p=0.424
Frozen food products			$\chi^2=7.077$ p=0.215
Canned food			$\chi^2=5.403$ p=0.369
Ready-made meals			$\chi^2=11.010$ p=0.051
Cake and biscuit	173 (51.6)	162 (48.4)	$\chi^2=1.626$ p=0.898
Chocolates, candies			$\chi^2=4.981$ p=0.418
Wine, beer and other alcoholic drinks			$\chi^2=1.466$ p=0.917

CONCLUSION

The implementation of MCO due to the COVID-19 pandemic had been found to be associated with the shift in behavioural nutrition among undergraduate students that includes the occurrence of emotional eating, high perceived level of stress, changes in food purchase and consumption. Thus, more studies on the impact of the MCO on human's nutrition, eating habits and psychological aspects are recommended to better understand and monitor the well-being of all individuals in the future.

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Factors Affecting Poor Performance Among First Year Medical Students: A Qualitative Survey

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ABSTRACT

Introduction: First Year MBBS students usually face a difficult time adjusting to the tough medical curriculum even without the pandemic. Recently in the University of Cyberjaya, there has been a dramatic increase in the number of students performing poorly at the recent Year 1 end of course examinations.

Objective(s): The aim of this study is to understand the reasons for poor performance during the end of course examinations among Year 1 MBBS students.

Methodologies: This research utilises a qualitative survey design. All students Year 1 MBBS students with Probation 1 status took part in the survey.

Results: A total of 12 students took part in this study. Almost all students involved agreed that not being able to attend face-to-face teaching and go to campus affected their studies. Analysis showed that the factors for poor performance in this study can be concluded into 4 overarching themes; 1) Personal factors, 2) Environmental factors, 3) Teaching methodology/ faculty factors and 4) Social Factors.

Conclusion: This study confirms that the lockdown imposed to control the pandemic affected students' performance through personal, environmental, teaching methodology/faculty and social challenges. Although the pandemic is now officially over, there is a need for further studies to develop resilience in students to prevent major adverse events to affect their performance in the future.

Keywords: pandemic; medical students; academic performance

INTRODUCTION

The COVID-19 pandemic has affected the world in many aspects essentially with regards to business, education, health and tourism industries (Pragolapathi, 2020). In order to control the spread of the disease, governments across the globe had to implement restrictions including travel bans, social distancing, self-isolations, curfews and lockdowns (Gostin & Wiley, 2020). This has directly or indirectly impacted on the education system at all levels including medical schools. Most universities worldwide had to either postpone their academic activities or transfer them to online based education in order to minimize contact and reduce transmission of the virus. These actions unfortunately has led to many repercussions to both the university and students (Nicola et. al., 2020).

Several issues related to online teaching learning has been studied in various institutions. Whilst students seem to agree with the benefits of online teaching, namely the

ability to learn at their own pace, decreased time spent on commuting and more flexible learning experience, most students still feel that there are more disadvantages to online learning. (Dost et al., 2020). Students reportedly agreed that online teaching learning activities lack in terms of the quality of education, are less engaging, more distractions being at home and technical difficulties. (Dost et al., 2020). Additionally, many studies continue to report on the impact of COVID-19 on the mental health of students (Zis et. al., 2021). Although many studies focused on the challenges related to online teaching learning, very few studied the impact on academic performance of the students.

The COVID-19 pandemic required the medical schools to quickly change and adapt from face-to-face teaching to online (Rose S., 2020). For first year medical students, they usually have a difficult time adjusting to the tough medical curriculum even without the pandemic. Adjusting to online learning on top of going through their

first year as medical students would certainly be an added challenge for them in their studies (Slivkof et. al., 2021). Recently in the University of Cyberjaya, there has been a dramatic increase in the number of students performing poorly at the recent Year 1 end of course examinations. The aim of this study is to understand the reasons for poor performance during the end of course examinations among Year 1 MBBS students and how to remedy the situation.

METHODOLOGIES

Study design

This research utilises a qualitative survey design. This design has been chosen since it is the best method to answer the research question.

Participants

All students Year 1 MBBS students with Probation 1 status took part in the survey.

Data collection

Two focus group discussions (FGD) have been conducted. Each FGD consisted of 5 to 6 students and were held using an online medium. An independent researcher with no affiliation to the university conducted the discussions. Each FGD lasted about 1 to 1.5 hours and were audio recorded. Each recording was then reviewed, and

conversations transcribed verbatim. The transcriptions were then analysed using thematic analysis.

RESULTS AND DISCUSSION

A total of 12 students who performed poorly during their Year 1 End of Course examinations took part in the survey. Among them 4 were male and 8 were female. There were 2 international students and 10 local students.

Impact of the Movement Control Order (MCO) on studies

Almost all students involved agreed that not being able to attend face-to-face teaching and go to campus affected their studies. They reported a number of problems related to the MCO (Figure 1). Hence, when the MCO ended and they were able to attend classes at the campus, these problems were resolved. However, a few students had problems were not related to the MCO such as culture shock and personal problems. These problems continued even after the MCO.

Factors affecting poor performance

Analysis showed that the factors for poor performance in this study can be concluded into 4 overarching themes; 1) Personal factors, 2) Environmental factors, 3) Teaching methodology/ faculty factors and 4) Social Factors. The factors are summarized in the following table (Table 1):

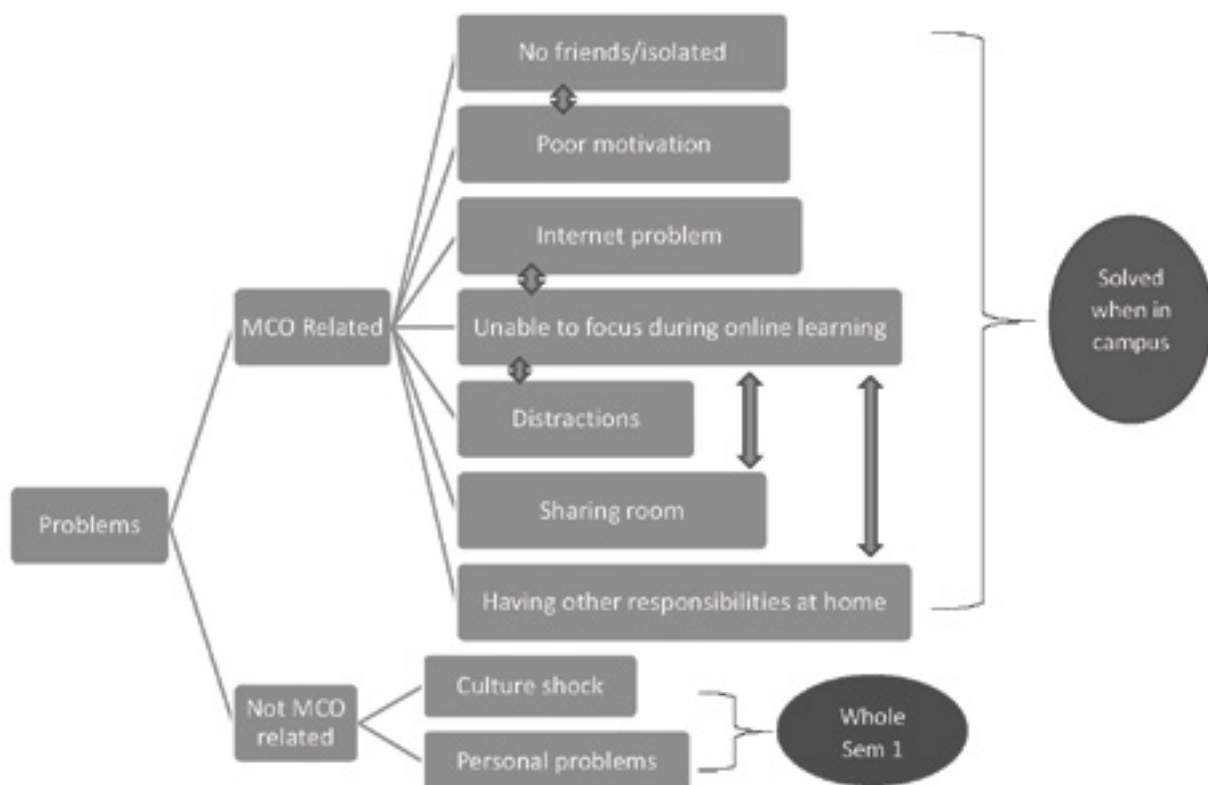


Figure 1: Problems related to studies during the MCO period

Table 1: Factors leading to poor performance

Personal Factors	Environmental Factors	Teaching methodology/ faculty factors	Social Factors
1. Poor study skills <ul style="list-style-type: none"> studies alone, not adapted to student centred learning, poor time management, lack of discipline, does not ask for help, cramming before exams 	1. Internet problems	1. Difficulties with online learning <ul style="list-style-type: none"> Teaching method not effective Examination very anxiety provoking since worry about internet stability, having to switch camera on 	1. Online learning from the start <ul style="list-style-type: none"> were not able to make friends from the same course felt isolated and unmotivated
2. Having personal problems	2. Home environment not conducive for studying <ul style="list-style-type: none"> sharing room, no proper place to study This also leads to stress 	2. Has problem with a specific lecturer in a specific course <ul style="list-style-type: none"> Does not understand the lecturer teaching and when asked for help the lecturer did not respond 	2. Due to lockdown and hence closure of campus, did not meet mentors in person <ul style="list-style-type: none"> felt awkward and uncomfortable to ask for help
3. Poor motivation	3. Distraction in the form of gadgets, people or responsibilities <ul style="list-style-type: none"> Some students had to look after their grandparents since they were at home 		3. Culture shock
	4. Time difference (international students) <ul style="list-style-type: none"> Have to wake up at odd hours for classes 		

The transition to online learning was a challenging change that had to be adapted by students in a short timeframe. Many students are struggling with various of distractions online and at home and having a non-conducive learning environment. Without a specific study space and distracted by other house-hold activities that is interfering with their study habit, so they tend to lose focus and motivation to learn (Donaldson-Pressman et. al., 2014). Other than that poor connectivity has been a major disadvantage in online learning (Naziva 2020; Radu et; al., 2020) as experience by the students in this study too. A study that was conducted by Hassan (2020) on students' perception on online learning revealed that some students were having difficulties adapting to online learning due to lack of appropriate facilities, materials to aid the learning process and lack of support from their lecturer and peers. Not to mentioned that some lectures were too didactic with minimum engagement between the students and lecturers that makes the learning less motivating (Naziva 2020; Radu et; al., 2020).

Several studies had showed that online learning for students during lockdown periods were associated with significantly reduced social interactions and poor motivation. Similar like the findings in this study, where the students are less interacting with their peers and having no friends. Less social interactions as well as personal problems could leads to poor motivation. A regression analyses also revealed that stress and fatigue were significant predictors of poor academic performance

(Radu et. al., 2020). Thus, all these cumulating problems with poor study skills could add up to stress and fatigue as well as to the extent of burnt-out and thereby affecting their studies and academic performance. Nonetheless some of the factors are more towards students' interpersonal skills especially to communicate with their lecturers or mentors and also with their peers as well as adapting to the medical curriculum in University of Cyberjaya.

CONCLUSION

This study confirms that the lockdown imposed to control the pandemic affected students' performance through personal, environmental, teaching methodology/faculty and social challenges. Although the pandemic is now officially over, there is a need for further studies to develop resilience in students to prevent major adverse events to affect their performance in the future.

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Knowledge, Attitudes and Practices towards Dengue Fever and Dengue Hemorrhagic Fever among Pharmacy Students in University of Cyberjaya

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ABSTRACT

Introduction: Dengue is one of the leading public health concerns in Malaysia which could lead to health complications and fatalities. Selangor has had the highest cases of dengue for the past few years. Up until June 2022, Sepang was reported as the district with 5th highest dengue cases in Selangor.

Objective(s): This cross-sectional survey aimed to identify the knowledge, practice and attitude (KAP) on dengue fever among pharmacy students at University of Cyberjaya, Sepang, Selangor.

Methodologies: Questionnaire were distributed to 274 students who have consented to participate in this study.

Results: The study found an overall good knowledge among the students (mean score 11.7 ± 1.25). Most of the respondents (63%) did not get involved in any health promotion activities on dengue. Other than that, 96% of the respondents indicated that they received the information about dengue fever and from the internet. Analysis using one-way ANOVA between respondents from all years of study found that there was a statistically significant difference in knowledge scores ($p < 0.001$). The study also found a statistically significant difference in both knowledge scores ($p < 0.001$) and attitudes ($p=0.039$) between students in clinical and non-clinical years. There was no statistically significant difference between females and males with regards the knowledge and attitude ($p > 0.05$).

Conclusion: This study concluded that the respondents had good knowledge, positive attitude and moderately good practice about dengue fever.

Keywords: Dengue fever; public health; KAP; students

INTRODUCTION

Dengue is a mosquito-borne infection that had become a major public health concern. It is a disease found in most tropical and subtropical areas of the world and had become the most arboviral (arthropod-borne) disease of human (Ibrahim et. Al., 2009). Dengue fever (DF) and dengue haemorrhagic fever (DHF) are viral disease transmitted by Aedes mosquitoes, usually *Aedes aegypti*. Dengue should be suspected when a high fever (40°C) is accompanied by 2 of the following symptoms severe headache, pain behind the eyes, muscle and joint pains, nausea, vomiting, swollen glands or rash (WHO, 2009).

A few studies have shown that the continuous process of urbanization has resulted in increased incidence of

dengue in Malaysia (Hairi et al., 2002). Selangor has recorded the highest number of dengue cases from 29 December 2019 until 27 September 2022, with 25, 448 cases and almost 40 fatalities between 2020-2021 (National Crisis Preparedness and Response Centre (CPRC), Ministry of Health Malaysia (MOH)). A cross-sectional study involving 135 students at International Islamic University Malaysia (IIUM) showed a very good level of KAP towards dengue prevention, symptoms, and transmission, especially among medical students (Zamri et al., 2020). People with knowledge of dengue, has been reported having significantly higher use of prevention measures than people without knowledge of dengue (Bota et al., 2014). This showed that correct knowledge is important to prevent dengue fever. Another cross-sectional study involving staff and students at a public university in Malaysia concluded that dengue preventive

strategies should focus on maintaining good dengue-related preventive practices (Lugova & Wallis, 2017).

METHODOLOGIES

This cross-sectional study was conducted among all pharmacy students (Year 1 to Year 4) studying in University of Cyberjaya (UOC), Cyberjaya, Malaysia. Convenient sampling method was used to select the participants. The minimum required sample size for this study was found to be 191 participants. However, the total number of participants consented to this study was 274. Prior to the actual data collection, a pilot study was conducted in 30 participants. The purpose of this pilot study was to verify the applicability of the data collection form and the validated questionnaire to ensure their comprehensiveness.

The data collection process was carried out during the period of September 2015 until October 2015. The questionnaire divided into 5 parts; Part A until Part E. Part A involves the demographic data for the participants, include gender, race, marital status, current year of study and residents' area of participants. Part B involves the source of information in which they receive regarding DF and DHF. Part C involves the knowledge of DF which included signs and symptoms, transmission, treatment and prevention. Part D involves the attitude of the participants towards DF. Finally, Part E involves the practice of the participants towards DF in the aspect of prevention.

Independent t-test was conducted to compare the mean difference in knowledge and attitude between females and males. It was also used to compare the mean difference in knowledge and attitudes between participants in clinical years (Year 3 & 4) and non-clinical years (Year 1 & 2). The test was also used to compare the mean difference in knowledge and attitude between participants residential area, either hostel or others. One-way ANOVA test was used to compare the mean difference in knowledge and attitudes between the year of study. Post-hoc analysis was conducted accordingly.

Pearson's correlation test was used to identify the correlation between knowledge and attitude scores. Pearson's correlation coefficient, r , is a measure of strength of a relationship and it has a value between -1 (perfect negative correlation) and +1 (perfect positive correlation). Positive correlation means one variable increases as the other increases. On the contrary, negative correlation means one variable increases as the other decreases.

RESULTS

A total of 274 pharmacy students responded and completed the questionnaire. The demographics of the respondents are as shown in Table 1.

Table 1: Demographic characteristic of study population (N = 274)

Demographic variables	Frequency (n = 274)
Current year of study	
Year 1	79 (28%)
Year 2	85 (31%)
Year 3	52 (19%)
Year 4	62 (22%)
Gender	
Male	43 (15.7%)
Female	231 (84.3%)
Ethnicity	
Malay	225 (82%)
Chinese	28 (10%)
Indian	16 (6 %)
Other	5 (2%)
Resident area	
University hostel	184 (67%)
Others	90 (33%)

Majority of the respondents were female students (> 80%). The result is similar to most of studied in which more females are more likely to participate in a survey compared to male (Smith WG, 2008). However, it could also be due to higher distribution of female students studying pharmacy at UOC. This study also found that most of the respondents were single. One of the possible reasons could be the fact that the respondents were concerned about the influence of marriage on their academic performance. A study investigating the academic performance of married women students in Nigerian higher education. It showed that more than 60.0% of single women respondents performed better academically compared to respondents who were married (Potokri, 2012).

This study found that 46% of respondents had high knowledge, 41% had moderate knowledge while 13% had low knowledge on DF and DHF. Majority of students answered correctly on fever as one of the symptoms. Most of the students, however, incorrectly answered pain behind the eyes and rashes as DF presenting symptoms. This could be due to confusion with similar symptoms in other common viral infections like flu and measles. In this study, comparisons on mean knowledge scores among respondents were done between year of study, between clinical and non-clinical years and between genders.

This study showed that there were statistically significant differences in the mean knowledge score between respondents from all years ($p < 0.001$). Post-hoc analyses showed that Year 4 respondents had statistically greater knowledge compared to Year 1 respondents [mean (\pm SD): 14.58 (± 1.12) versus 9.62 (± 1.26), $p < 0.001$, 95% CI

0.83 - 1.91], Year 2 respondents [mean (\pm SD): 14.58 (\pm 1.12) versus 10.12 (\pm 1.20), $p < 0.001$, 95% CI 0.52 - 1.64], Year 3 respondents [mean (\pm SD): 14.58 (\pm 1.12) versus 12.53 (\pm 1.41), $p < 0.001$, 95% CI 0.21 - 1.26]. The mean (\pm SD) DF and DHF knowledge scores for clinical and non-clinical year respondents were 13.55 (\pm 1.27) and 9.87 (\pm 1.23) respectively. The difference in mean knowledge scores between the 2 groups was statistically significant ($p < 0.001$, 95% CI -1.34 to -0.62). One of the reasons could be because clinical year students (Year 3 & 4) have undergone clinical pharmacy courses and joined some educational programs. The mean (\pm SD) knowledge scores on DF and DHF between females and males showed 12.56 (\pm 1.23) and 12.97 (\pm 1.23) respectively. The difference in mean knowledge scores between males and females was not statistically significant ($p > 0.05$, 95% CI -0.31 to -0.57). The result reflected that health care professional play an important role in public health care based on their knowledge regardless of their gender (Matta et. al., 2006).

This study found that respondents from all years of study had an overall positive attitude. Table 2 below shows the distribution of respondents' attitude towards DF and DHF.

Table 2: Distribution of respondents' attitude towards DF and DHF (n =274)

Statement	No. of respondents (%)	
	Agree	Disagree
I am afraid of dengue fever	256 (93.4)*	18 (6.6)
Dengue is serious illness	267 (97.4)*	7 (2.6)
Dengue cannot be prevented	12 (4.4)	262 (95.6)*
I am at risk of getting dengue	156 (56.9)*	118 (43.1)
Fogging is not essential for prevention	220 (80.3)*	54 (19.7)
Elimination of larvae breeding is a complete waste of time	10 (3.7)	264 (96.3)*
Public has important role in dengue control	242 (88.3)	32 (11.7)

*indicates a correct answer

Comparisons on mean attitude scores among respondents were done according to year of study, clinical and non-clinical and females and males. It was found that there were no statistically significant differences in the mean attitude score between respondents from all years and between males and females ($p > 0.05$ for both). However, the difference in mean attitude scores between clinical and non-clinical years respondents were statistically significant ($p = 0.039$).

This study found an overall moderate practice among the respondents, indicated by the total mean attitude scores 23.12 (\pm 5.32). Year 4 respondents have higher positive practice level towards DF and DHF. The mean scores (\pm SD) for Year 1, 2, 3 and 4 respondents were 22.45 (\pm 5.66); 25.61 (\pm 5.78); 21.15 (\pm 4.45); 23.25 (\pm 4.95), respectively. Table 3 shows the distribution of respondents' practice towards DF and DHF.

Table 3: Distribution of respondents' practice towards DF and DHF (n =274)

Statement	No. of respondents (%)				
	VNC	NC	MC	C	VC
I can change the water in the plant pot tray every week.	12(4.1)	22(8.0)	158 (57.7)	69(25.2)	13(5.0)
I can clean the drain from blockage every week	12(4.1)	48(17.5)	139 (50.7)	58(21.1)	17(6.6)
I can always cover tightly all water containers	7(2.6)	26(9.5)	45(16.4)	153 (55.8)	43(15.7)
I can convince my family/ friends to always put all garbage into closed bin	31(11.3)	98(35.8)	95(34.6)	32(11.7)	18(6.6)
I can change water container under the fridge every week	29(10.6)	53(19.3)	167 (60.9)	15(5.5)	10(3.7)
I can allow health authority to fog and inspect my house at anytime	127 (46.3)	67(24.4)	39(14.2)	30(10.9)	11(4.2)
I can always put larvacide in all water container at my house	23(8.3)	45(16.4)	86(31.4)	98(35.7)	22(8.2)

Note: VNC = Not confident at all; NC = Not confident; MC= moderately confident; C= Confident; VC= Very confident

Pearson's correlation test showed statistically significant positive correlation between knowledge and attitude among all respondents ($r = 0.135$, $p = 0.048$). This means that respondents with the higher knowledge will display more positive attitudes towards DF and DHF.

This study showed that 63.0% of the students did not involve in any health promotion activities on dengue. The

remaining percentage of students who did get involve in the health promotion activities, indicated that they joined public lectures and public awareness programs such as health promotion campaigns and public awareness program.

This study found that among 96% of respondents who have received information regarding DF and DHF, almost 50% of them received the information from the internet. Other sources of DF and DHF information obtained by the respondents include television and radio (21.3%), public announcement (9.8%) and printed media (6.8%).

CONCLUSION

This study has showed that pharmacy student at UOC had overall good knowledge about DF and DHF. However, there was a lack of concern about the importance of dengue control and the impact of dengue outbreak in the community. It is shown by their poor practice on dengue prevention. More practical health education programmes should be organized. It will give more benefits and exposure about the effect of good practice towards DF prevention. The knowledge is crucial for these future pharmacists to prepare them in facing the real practice or work.

According to The American Society of Health-System Pharmacists (ASHP), pharmacist's role is expanding beyond the traditional product-oriented functions of dispensing and distributing medicines and health supplies. The pharmacist's services of today include more patient-oriented, administrative and public health functions. Knowledge and attitude of a pharmacist can significantly influence the effectiveness of the care or service given to the public.

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Effectiveness of Good Storage Practices Implementation in IMARET Warehouse

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ABSTRACT

Introduction: Good storage practice (GSP) is one of the guidelines that needs to be implemented in a pharmaceutical-based warehouse to ensure the safety, efficacy and quality of pharmaceutical products stored as well as inventory movement. Globally, World Health Organisation (WHO) had established their Annex 9 World Health Organisation Guide to Good Storage Practices for Pharmaceutical Products to be adopted and adapted by local authority of each country. In Malaysia, National Pharmaceutical Regulatory Agency (NPRA) is the local authority under Ministry of Health Malaysia has established local Good Distribution Practice Guidelines that includes the GSP elements based on the guideline from the WHO guideline.

Objective(s): The effectiveness of implementation of GSP in Islamic Medical Association of Malaysia (IMAM) Response and Relief Team (IMARET) warehouse was assessed to indicate the warehouse performance.

Methodologies: The study was done by collecting data from IMARET warehouse and mobile clinics. All the cost incurred was calculated based on the master invoice provided by pharmaceutical products suppliers and national medication essential list Ministry of Health Malaysia.

Results: The total amount of procurement and expenditure of pharmaceutical products was increased while the total wastage of pharmaceutical products reduced in 2017 indicating that even though the demand for pharmaceutical products increase, the warehouse manage to control the inventory and stock movement to reduce the pharmaceutical products wastage.

Conclusion: However, the study is unable to provide enough reflection to the IMARET warehouse performance as this study only cover the mobile clinics for Rohingyas. Further study needs to be conducted to reflect total performance of IMARET warehouse.

Keywords: Good storage practice; GSP; pharmaceutical products; warehouse

INTRODUCTION

Good storage practice (GSP) has been implemented within healthcare supply chain (Mustaffa & Potter, 2009) in order to ensure the safety, efficacy and quality of pharmaceutical products at any point of storage by protecting them from extreme condition such as high temperature, high humidity and direct sunlight exposure (Elhassan et al., 2014; Pedroso & Nakano, 2009; Kumar & Jha, 2015). Establishment of GSP also is to control the inventory movement of pharmaceutical products from the warehouse to the designated receiver such as patients and healthcare centre (Rachmania & Basri, 2013). These were done to ensure that patients received intact pharmaceutical products in term of safety, efficacy and quality of the pharmaceutical products (Kumar & Jha, 2015) as well as good control of inventory movement for

the pharmaceutical warehouse in term of cost incurred for the pharmaceutical products management (Rachmania & Basri, 2013).

Islamic Medical Association of Malaysia (IMAM) Response and Relief Team (IMARET) is a medical based non-profit non-government organisation (NGO) that response to natural or man-made disaster by providing healthcare support alongside with other NGOs. On top of that, IMARET also provides free health care to the marginalised people such as refugees and Orang Asli via setting up of mobile clinics. Currently, IMARET actively send their teams to remote Orang Asli villages and set up three mobile clinics located at Selayang, Seri Kembangan and Cheras for the Rohingyas to provide basic health care (IMARET, 2015).

It is an obligation for IMARET to have a well control pharmaceutical warehouse in order to make their pure intention become a successful plan. In 2016, IMARET warehouse management was not under supervision of qualified personnel such as pharmacist. The staffs who manage the warehouse have no pharmacy background. The warehouse also did not practise GSP thoroughly where there was no proper recording of the warehouse activities such as stock receiving and pharmaceutical products movement. The pharmaceutical procurement also did not correspond to the current warehouse inventory to fulfil the IMARET charity works demand which will further cause wastage and underutilise pharmaceutical products. Hospitals also sometimes faced these kind of problem (Rachmania & Basri, 2013). This caused underutilisation and wastage of pharmaceutical products due to expiration and deterioration. The location of the warehouse which situated in housing areas is also exposed to the risk of thievery.

In 2017, involvement of pharmacist to supervise the warehouse activity helps IMARET to manage their warehouse more efficiently. They also hired staffs that have medical background to help the pharmacist to execute the tasks. IMARET has transferred their warehouse to a new location situated at Bandar Sri Permaisuri, Cheras, Selangor. They had implemented GSP under supervision of a pharmacist such as First In/First Out (FIFO) and First Expired/First Out (FEFO) principles, systematic physical pharmaceutical product recordings coupled with computerised data recording system and standard operating procedures (SOP) to enhance their warehouse management and capability to response to the increasing demands in providing sufficient logistics support to their charity works.

There was no data or study done to report the effectiveness of the improvement done by IMARET as their warehouse performance benchmark. Thus, this study was done to assess the effectiveness of the steps taken by IMARET to improve their warehouse management. Generally, GSP can be divided into two parts which are the storage conditions and inventory management. This study focusses on the inventory management in term of procurement, expenditure and wastage of pharmaceutical products as the baseline data for 2016 was done by the previous researcher. This study can help IMARET in determining their warehouse performance and take further steps in improving their warehouse management correspond to their charity works in the future.

METHODOLOGIES

The research was conducted at the Islamic Medical Association of Malaysia (IMAM) Response and Relief Team (IMARET) warehouse located at Bandar Sri Permaisuri, Cheras, Selangor. IMAM Response and Relief Team (IMARET) administrative had improvised the

management of the warehouse by implementing some strategies. First, they had implemented a computerised system to track all of the product's movement in and out of the warehouse and also to track the dispensed medicines to patients.

Blanket sampling was done in this study. All pharmaceutical products have been included in the study according to inclusion and exclusion criteria. For data in 2016, there was no record for the warehouse activities. A complete list of donated and purchased pharmaceutical products was obtained from the IMARET administration to assist in differentiating all of the pharmaceutical products available in the warehouse according to the inclusion and exclusion criteria.

All pharmaceutical products that were purchased by IMARET were included in the study. Dosage forms other than parenteral usage were also been included in this study. Donated pharmaceutical products and pharmaceutical products that had been expired before year 2016 were excluded from this study.

Cross sectional study was implemented in this study where the duration of this study started from March 2017 until October 2017. Comparison of pharmaceutical products procurement, expenditure, and wastage between year 2016 and 2017 was conducted. Quantitative study was done where the expenditure and wastage of the pharmaceutical products were estimated by calculating the cost with the current market price (2017). The costs for the pharmaceutical products were referred from the master invoice provided by the suppliers to IMARET and national essential medication list from Ministry of Health Malaysia.

RESULTS AND DISCUSSION

A total of 1017 prescriptions was analysed starting from February until October 2017 compared to 1402 prescriptions starting from October 2015 until November 2016 (Table 1).

Table 1: Total number of prescriptions

Year	Total number of prescriptions
October 2015 – November 2016	1402
February – October 2017	1017

The total pharmaceutical products prescribed in 2016 was 2976 and 5774 pharmaceutical products was prescribed in 2017. The comparison of total pharmaceutical products prescribed for 2016 and 2017 shows an increase of 94% of the total pharmaceutical products prescribed recorded in one year period (Table 2).

Table 2: Comparison of Total Pharmaceutical Products Prescribed in year 2016 and 2017

Year	Total Pharmaceutical Products Prescribed	Percentage Change (%)
October 2015 – November 2016	2976	94%
February – October 2017	5774	

The total expenditure of pharmaceutical products for 2016 was RM 7749.25 and in 2017 the total expenditure of pharmaceutical products was RM 9846.45. The comparison of total expenditure of pharmaceutical products prescribed for 2016 and 2017 shows an increase of 27.1% of the total pharmaceutical products prescribed recorded in one year period (Table 3).

Table 3: Comparison of Total Expenditure Pharmaceutical Products Prescribed in year 2016 and 2017

Year	Total Expenditure of Pharmaceutical Product (RM)	Percentage Change (%)
October 2015 – November 2016	RM 7749.25	27.1%
February – October 2017	RM 9846.45	

The total pharmaceutical products wastage in 2016 was RM 2721.32 while in 2017 the total pharmaceutical products wastage was reduced to RM 594.55. A 78.2% of total pharmaceutical products wastage was recorded within one year period (Table 4).

Table 4: Percentage change of pharmaceutical products wastage between year 2016 and 2017

Year	Total Wastage (RM)	Percentage Change (%)
2016	RM 2721.32	78.2%
2017	RM 594.55	

In total, there were 1017 prescriptions were analysed starting from January until October 2017 compared to 1402 prescriptions were analysed starting from October 2015 until October 2016. Selayang mobile clinic site maintained the most mobile clinic site visited by the Rohingya community for both 2016 and 2017.

The total number of prescribed pharmaceutical products in 2017 was 5774 while in 2016 the total number of prescribed pharmaceutical products was 2976. Total expenditure reported was RM 7749.25 and RM 9846.45 for 2016 and 2017 respectively. Out of the total pharmaceutical

product prescribed, analgesic/anti-inflammatory agents' group was the most prescribed pharmaceutical product in both 2016 and 2017 and they also cost the highest expenditure for IMARET in both years. However, increase in total expenditure was not directly proportional to the total prescribed pharmaceutical products or total number of patients visiting the mobile clinics as they had implemented GSP and certain SOP that affects the IMARET expenses. Hence, continuous studies need to be done to study on IMARET warehouse performance.

The total wastage of pharmaceutical products was reduced by 78.2% within one year resulting in reduction from RM 2721.32 in 2016 to RM 594.55 in 2017. The decrease in total wastage was paralleled with other studies that stated the implementation of GSP result in reduction of pharmaceutical products wastage.

IMARET for Rohingya is one of the established missions conducted by IMARET to provide free health care service assess for the Rohingyas community in Malaysia through the set-up of mobile clinics. Previously, starting from December 2015 until October 2016, 1402 prescriptions from IMARET mobile clinics based in Cheras, Selayang and Seri Kembangan had been studied. A total of 1017 prescriptions were analysed starting from February until October 2017. The mobile clinics in 2017 were set up at Selayang, Seri Kembangan and Ampang.

The mobile clinics site was set-up based on the migration pattern of the Rohingya refugees from rural to urban areas. Majority of the Rohingya refugees have migrated from rural areas to urban city in order to obtain a better living condition and services such as health care service access and education. There are significant pull factors for the refugees such as better work opportunities, education, health care service access and better livelihoods in the cities especially in developing countries (Amara et. al., 2014). Malaysia is one of the successful developing countries and has a lot of opportunities in urban cities (Ragayah, 2014).

Pharmaceutical products cause major expenditure for an organisation that if the total expenditure was well controlled, this can give significant cost saving effect to the organisation (Rachmania & Basri, 2013). Thus, it is important to monitor the expenses throughout the period of operation so that the expenditure can be well controlled.

The total expenditure for 2016 was RM 7749.25 and in 2017 the total expenditure was RM 9846.45. There was an increase of 27.1% in total expenditure within one year. It was expected that the pharmaceutical products expenditure to increase annually as the system govern this component becoming more complex and it plays a large portion to healthcare service (Pedroso & Nakano, 2009; (Rachmania & Basri, 2013); WHO, 2010). Even though the

expenditure increases in year 2017, it does not indicate any significant changes because total expenditure is indirectly proportional to the total number of patients visiting the mobile clinics. This is because in year 2016, most of the pharmaceutical products were donated by other entities. Whereas in year 2017, IMARET started to buy pharmaceutical products and received less donation in term of pharmaceutical products.

Organisations that deal with healthcare services tends to have a large amount of pharmaceutical products in their possession to coup with the emergency needs hence, this leads to high operational cost and accumulation of expired pharmaceutical product (Rachmania & Basri, 2013). Thus in 2017, IMARET administration restructured their warehouse management to improve their warehouse performance and capability. These significant steps were implemented to enable them to adapt with the increasing demand to conduct more charity works such as mobile clinics for Rohingya, Orang Asli outreach and disaster relief missions. The main aim in improving their warehouse management is to achieve the lowest cost possible without denying the patients' right to reach a quality, efficacious, and safe pharmaceutical products (Rachmania & Basri, 2013).

The improvement step taken was system reengineering where the organisation structure was reviewed and improvised (Rachmania & Basri, 2013). The first taken was by hiring qualified personnel to lead the warehouse management. At this stage, they appointed an IMARET EXCO who is a pharmacist to play a major roles and responsibilities in managing a pharmaceutical-based warehouse (Kumar & Jha, 2015; Shafaat et. al., 2013). Involvement of pharmacist in IMARET warehouse witnessed a great transformation in the warehouse management where many improvements were introduced for the betterment of the warehouse performance and capability. IMARET also hires two staffs with medical field background to help the pharmacist to execute the tasks. Pharmaceutical products inventory management need to be at the best performance as it affects the whole operation of the organisation (Rachmania & Basri, 2013).

Based on the study conducted, it was reported that the total wastage of pharmaceutical products in year 2016 cost IMARET a value of RM 2721.32 and RM 594.55 in 2017. 78.2% reduction of pharmaceutical products wastage was recorded within one year, reducing the total wastage by RM 2126.77. Implementation of GSP can result in reduction of pharmaceutical products wastage (Elhassan et. al., 2014; UNHCR, 2006). Increase in effectiveness of pharmaceutical products supply chain can cause a marked reduction of cost of healthcare expenditure (Rachmania & Basri, 2013).

Back in year 2016, there was no proper recording for the movement of the warehouse activities. The current

inventory status for year 2016 was undetected and leads to over purchased and wastage. GSP for pharmaceutical warehouse was not practised thoroughly that may lead to loss due to expiration, deterioration and thievery, compromising the pharmaceutical products quality that reach the patients, lack of accurate inventory records, stock movement information and break in continuous supply (UNHCR, 2006).

Due to these problems, in year 2017 IMARET had implemented a thorough GSP under pharmacist supervision and a systematic physical inventory records coupled with computerised inventory records for greater magnitude of warehouse management. These significant steps are known as reengineering of system. Reengineering system is not just implementing an automatic monitoring system. It has a greater scope where reengineering system is about reviewing and improvising the current system and implementing new recording and monitoring system such as computerised inventory records (Rachmania & Basri, 2013). However, computerised inventory records are not meant to replace the physical inventory records totally (NPCB, 2013). By implementing these steps, it eases the recording of the warehouse activities, better expiry date monitoring and stock minimum alert. It also helps in saving the pharmaceutical products related costs (Rachmania & Basri, 2013).

Implementation of First Expired/First Out (FEFO) and First In/First Out (FIFO) principles also help in eliminating these problems. FEFO by definition means any pharmaceutical product that will expired soon in three months period need to be distribute or utilize first (WHO, 2010; NPCB, 2013). Implementation of FEFO will prevent accumulation of near expiry date pharmaceutical products in warehouse. In the other hand, FIFO means any pharmaceutical products receive first need to be distributed or utilised first to ensure that the older stock are not stagnant in the warehouse (WHO, 2010).

Another improvement step taken by IMARET was implementing a standard operating procedure in receiving donation from other entities. Starting from year 2017, IMARET encourages the donors to donate in the form of financial funds for them to manage the warehouse better as they can utilise the financial funds for the general purposes of the warehouse.

For the donors who want to donate pharmaceutical products to the warehouse, they are still able to donate but with some strict conditions that they need to comply with. First of all, they need to submit complete list of all the pharmaceutical products to be donated to IMARET including type of the pharmaceutical products, quantity, brand name, dosage form, and expiry date of each batch of the pharmaceutical product. Next, the list is screened by the pharmacist. The pharmacist would

shortlist the accepted pharmaceutical products that meet the IMARET warehouse qualifications and needs. Then, IMARET produces the accepted pharmaceutical products to the donors for the acknowledgement and to prepare the pharmaceutical products for transportation. Transportation can be done by either two manners which are IMARET pick up the pharmaceutical products from the donors or the donors can send the pharmaceutical products to IMARET warehouse (IMARET, 2015).

Finally, IMARET also provides a list of the current available inventory for each mobile clinic conducted. The purpose is to acknowledge the physicians about pharmaceutical availability (Pedroso & Nakano, 2009) and ease them to select the available pharmaceutical products suitable for the diagnosis. The inventory list will be updated for every mobile clinic conducted. The content of the list includes generic name of the pharmaceutical products, product strength and quantity available. This can significantly increase the utilisation of the pharmaceutical products and avoid untreated condition of the patient. The inventory list is designed not to violate the physicians' freedom in pharmaceutical products selection but is to increase access to the available pharmaceutical products. Physicians can request to the IMARET's pharmacy department to add new pharmaceutical products into the list by providing relevant justification (UNHCR, 2013). The requested pharmaceutical products reviewed by the pharmacist for approval.

CONCLUSION

The total number of prescribed pharmaceutical products in 2017 was 5774 while in 2016 the total number of prescribed pharmaceutical products was 2976. Out of the total pharmaceutical product prescribed, analgesic/anti-inflammatory agents' group was the most prescribed pharmaceutical product in both 2016 and 2017 and they also cost the highest expenditure for IMARET in both years. However, increase in total expenditure was not directly proportional to the total prescribed pharmaceutical products or total number of patients visiting the mobile clinics as they had implemented GSP and certain SOP that affects the IMARET expenses. Hence, continuous studies need to be done to study on IMARET warehouse performance.

The total wastage of pharmaceutical products was reduced by 78.2% within one year resulting in reduction from RM 2721.32 in 2016 to RM 594.55 in 2017. The decrease in total wastage was paralleled with other studies that stated the implementation of GSP result in reduction of pharmaceutical products wastage.

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Qualitative study on medication delivery services (MDS): perspective of pharmacists and caregivers

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ABSTRACT

Introduction: Face to face communication between pharmacist and patient in a pharmacy is the best optimum and safest way of dispensing and delivering medications by a licensed pharmacist to a patient. Increasingly more common due to technological advances and the Covid-19 pandemic, medication delivery services are carried out at hospitals and community pharmacies as one of the value-added services (VAS) provided for patients' medicines supply.

Objective(s): The aim of the study was to explore opinions regarding medication delivery services (MDS) from the perspective of the pharmacist and caregivers and to identify issues in providing MDS.

Methodologies: This purposive sampled qualitative study involved interviewing pharmacists and caregivers who have participated in medication delivery service (MDS). Interviews were audio recorded and transcribed verbatim.

Results: Three themes emerged, namely factors influencing accessibility in MDS, favorable clinical outcomes and issues arising in MDS. The subthemes of factors influencing accessibility in MDS were distance, ability to travel, convenience, time, money and medication preference. The subthemes of beneficial clinical outcome were improved compliance and better continuity of medicine supply. The subthemes of issues emerged were increased resources, delay, technological barriers and new workflow.

Conclusion: Medication delivery service (MDS) provides many benefits to patients and health care providers. There were only a few issues that emerged from the health care providers but those were minimal and manageable.

Keywords: Medication delivery service (MDS); value-added service; pharmacist; innovation; technology

INTRODUCTION

Patients with chronic illnesses requiring long term medical therapy are often provided with repeat prescriptions by outpatient clinics, to be dispensed on a monthly basis at pharmacies (Andersson et al., 2005). This highly centralised traditional counter services (TCSs) had consistently resulted in long waiting time among the local hospital pharmacies (Chan et al., 2015). The Pharmaceutical Services Programme (PSP), Ministry of Health introduced innovative ways for patients to refill their repeat prescriptions. Based on a study in a Malaysian Public Hospital, postal delivery of medicines gained popularity during the COVID-19 lockdown implemented in March 2020 nationwide because patients do not need to travel and physically present at the pharmacy, hence reducing social contact (Shin et al., 2021). Less is known on medication delivery service (MDS) carried out at in the private hospitals and community pharmacies. "Guidelines for delivery service of medications for patient by Type A Licensed Holder" was launched in February 2021 by the

Pharmaceutical Services Program, Ministry of Health Malaysia. The aim of the study was to explore opinions regarding medication delivery services (MDS) from the perspective of pharmacists and caregivers and to identify issues in providing MDS.

METHODOLOGIES

Several stakeholders comprising of hospital pharmacists, community pharmacists and caregivers were recruited through purposive snowball sampling. Inclusion criteria included hospitals pharmacists and community pharmacists who had participated in medication delivery service for a minimum of 3 months and caregivers of patients who were able to speak and read English and had purchased medication via medication delivery service at least 3 times. Approval for the study was granted by Cyberjaya Research Ethics Review Committee [Ref UoC/CRERC/ER/382]. In-depth semi-structured interview were conducted after getting verbal and written consent of all participants. Interviews were conducted virtually using

online platform and phone calls. Interview guides were used for all participants. Study's results showed that across 16 tests using various approaches to saturation, the sample size for saturation ranged between 5 and 24 interviews (Hennink & Kaiser, 2022). Data collection ceased when data saturation was achieved.

The interviews ran between 15 minutes to 35 minutes per participant. Interviews were audio recorded and was transcribed verbatim transcription and stored electronically as Word files. Analysis was conducted by researcher and the team comprising two senior academicians on identifying the codes. Codes were compared and differences of opinion were discussed until consensus was reached on a coding tree and themes identified. Repeating themes were identified and findings subsequently summarized.

RESULTS AND DISCUSSION

Demographic details of participants are presented in Table 1.

Table 1: Demographic details of participants

No	Group	Participant	Gender	Years of experience/ age
1	A	Hospital pharmacist	M	10 years
2	B	Hospital pharmacist	F	5 years
3	C	Hospital pharmacist	F	12 years
4	D	Community pharmacist	F	12 years
5	E	Community pharmacist	F	10 years
6	F	Caregiver	M	50
7	G	Caregiver	M	55

Three themes emerged in this study which include factors influencing accessibility in MDS, favourable clinical outcome/pharmacotherapy benefit and issues in MDSThe subthemes of factors influencing accessibility in MDS were distance, ability to travel, convenience, remote area, save time and save money. The subthemes of favourable clinical outcome were improved compliance, continuous supply and preference. The subthemes of issues emerged were increase resources, delay, technological barrier and new workflow.

3.2. Theme 1: Factors influencing accessibility in MDS

3.2.1. Subtheme 1: Distance and remote area

When the hospital pharmacists started promoting medication delivery service (MDS) to patients, patients welcomed the service of MDS. Patients have told pharmacists that MDS is a good service because with the availability of MDS service, patients do not have to travel to the hospital to pick up their medicines. Besides that, in hospitals some patients are who those who stay far distance from the hospital

or in remote areas appreciates the MDS service because the service covers sending to far and remote areas.

Actually, 1 or 2 months even before MCO they actually welcome the idea. They said "Oh. This is good. I don't have to purposely come to the hospital to pick up my medicines". So, this is a bit of distance from the hospital itself with I think the furthest that I have ever sent before was someone staying in Batu Pahat because he is an oncology patient. So, usually he would like to see the resident oncologist as a ritual thing. But actually, he appreciated that the service can be extended all the way up to Batu Pahat [...]. [Hospital pharmacist, male, 10 years' experience]

For hospital point of view, we are able to provide services to more patients who are stay maybe in more remote area. [Hospital pharmacist, female, 5 years' experience]

Let's say the patient is staying very nearby to the hospital, usually they won't opt for medication delivery. They are still wanted to come and take the medication in the hospital. They prefer to come back to our hospital and collect the medication that's one. And then for those who are stay far means some distance away from the hospital, they are quite happy with it [...]. [Hospital pharmacist, female, 12 years' experience]

Those patients staying a bit far from our pharmacy, they prefer delivery. [Community pharmacist, female, 10 years' experience]

Well...delivery service of medication, I would say it benefits people who stay far away from hospitals. So, the delivery service helped. She doesn't have to travel maybe 300 km just to collect her medicines. [Caregiver, male, 55 years old]

3.2.2. Subtheme 2: Ability to travel

Some patients may not be able to travel. For these patients, MDS will be beneficial and because they will not have to travel just to collect the medicines every month. They will only need to go the hospital during their check-ups.

Not every patient can travel to go and get the medicines. So, I think this delivery service should keep on going [...] unless the hospital calls or you know the pharmacists call and say that 'You need to come for next check-up and all that'. Then, you know you have to go [...] but the delivery service of medicine. I think it should keep on going because people staying few hundred kilometres away and some are, you know they can't even walk properly and then just to take a medicine, you need to travel all the way. [Caregiver, male, 55 years old]

3.2.3. Subtheme 3: Convenience

Most patients have been open to MDS because MDS

is convenient for them. This is because MDS reduces patient's burden and hassle of coming to the hospital every month. For example, some patients need to use multiple modes of transportation to reach the hospital. Some patients depend on family members to collect the medicine from the hospital. Their family member who have to go to work feel MDS is convenient.

Most of them are very open and very responsive to this service. Because it actually reduces their burden and also the hassle of coming to the hospital. [Hospital pharmacist, female, 5 years' experience]

And then to provide the convenience to the patient because during the pandemic, Covid time, patient couldn't come to collect the medication. They were quarantined right. They do not need to travel back to the hospital, get the parking and get the medicine. So, they are actually quite happy with the medication delivery services. [Hospital pharmacist, female, 12 years' experience]

Delivery service actually, my mother you know she gets medicine from hospital. So, she need to travel from Kuantan by bus to KL, take a teksi and go to the hospital to collect her medicine. So, she asks them whether they can deliver this medicines in monthly basis to the house. So, they said yes. So, from there on, you know, it was very efficient. I mean it helps the patient. So, the patient don't have to depend on others to go and get the medicines for them. So, it's very very beneficial. [Caregiver, male, 55 years old]

I have to go to work. So, medicine delivery is helpful because medicines get delivered to my home. It is convenient for me. Otherwise, I have to drive all the way to the hospital just to get the medicines. When there is medication delivery, it is easier for me. [Caregiver, male, 50 years old]

3.2.4. Subtheme 4: Save time

MDS can save time because patient do not have to travel to collect the medicine from the hospital or community pharmacy.

Also, save time for them. [Hospital pharmacist, female, 5 years' experience]

So, some customers might be interested because it saves their time. [Community pharmacist, female, 10 years' experience]

Well. I think delivery service for medicine should keep on going [...]it saves a lot of time you know. [Caregiver, male, 55 years' old]

3.2.5. Subtheme 5: Save money

By using MDS, patients get to save their money because they only have to pay for the delivery fee

which is cheaper compared to transportation charges of travelling.

Because she don't have to spend money you know. So, it saves. But I think you pay a very little amount [...], just pay a certain amount for the delivery only. But it's much much cheaper medicines delivered to you instead of you going and buying. [Caretaker, male, 55 years' old]

3.2.6. Subtheme 7: Preference

One patient preferred to get their medicines from their regular hospital. The patient did not prefer buying the same medicine from the nearby community pharmacy. This is possibly due to patients' preference. Besides, the caregiver finds it confusing when community pharmacy offered them the same medicine but in different brand. The caregiver feels MDS is better provided the medicine comes from the regular hospital they go.

Because certain medicines you can buy from pharmacy but certain medicines you cannot get from pharmacy. So, that is the difference [...]. So, sometimes we go to pharmacy and buy because in today's world there's a lot of imitation. So, people like my mother all, I told her 'Hey. These medicines, I can buy for you even in pharmacy'. She said 'Oh. No. I want my medicines from my hospital'. So, what we can do? Unless one of us go to the hospital with the prescription, take it from the pharmacy. I think medicine also you need to take the correct type of medicine you know. You go to pharmacy, they say 'This brand and this brand is the same. Only the brand differs but the medicine is the same'. See a lot of confusion. So, I think delivery service is the best. If it's coming from the clinic itself. [Caregiver, male, 55 years old]

3.3. Theme 2: Favourable clinical outcome

3.3.1. Subtheme 1: Improve compliance

MDS helps patients to be more compliant to their medicine regime because with MDS pharmacists can ensure patients have access to their medicines. Especially during the movement control order (MCO) when patients could not go directly to the hospital to collect their medicine, pharmacists sent patients' medicines using MDS. This ensured continuation of care for their patients.

We also helping patients to be comply with the medicine because we are sending constantly and regularly to the patient as mentioned just then, I think if there are any changes whether it's in the dosage or changes in the brands or changes in the regime is also as part of our duty of care to also notify to the patients. So, that's one thing [...]. And I think particularly during the pandemic especially with the 2 major MCO that was occurring at that point of time. So, we were bringing rather than waiting for the patient to just come directly to our hospital, why not we bring the hospital service directly back to the patient themselves. So,

we are not incurring any losses in the sense of reputation or in terms of continuation of care. [Hospital pharmacist, male, 10 years' experience]

Also to improve compliance because they don't need to make their way here. [Hospital pharmacist, female, 5 years' experience]

The benefits would be to help the patients to be comply towards their medication so they would not comply because they do not have their medications. [Community pharmacist, female, 12 years' experience]

3.3.2. Subtheme 2: Continuous supply

Pharmacist can ensure patients can get continuous supply of their medicine by using MDS.

So, the main objective why we do this service is so that we can ensure the continuous supply of prescribed medication to patients. [Community pharmacist, female, 12 years' experience]

So, it's easier for them to get their medication regularly on time. [Hospital pharmacist, female, 5 years' experience]

First, is the benefit [...] is to ensure the patient continue taking their medication. [Hospital pharmacist, female, 12 years' experience]

3.4. Theme 3: Issues emerged

3.4.1. Subtheme 1: Increase resources

In the implementation of MDS, there are a few issues that are emerged. There has been increase in operational expenses in MDS. However, the costs for operational expenses are manageable. Some hospitals bound the delivery costs of MDS to promote the service. Besides, more manpower needed to be allocated because it was a new service started.

I mean the risk is very minimal. Those are just, you know [...], just the operational expenses like things like, we probably have to expense out on, like our consumables like you know envelopes, parcels all those things but I think in terms of manpower managements I mean in terms of resources for manpower or even like consumables. Those are manageable. [Hospital pharmacist, male, 10 years' experience]

Maybe slightly of the negative impact actually it also increases costs because a lot of delivery costs are bound by hospital. In order to promote this, we actually offer like free delivery at our own expenses. Other than that, also because it's a new service right. You need to allocate more manpower and more resources into making this work. Maybe you need like a extra dispatch team which we have [...]. [Hospital pharmacist, female, 5 years' experience]

Definitely, we will need to appoint a third party vendor

to do the delivery [...]. If it is out of the coverage area. So, there will be costs involvement for this case right. So, for hospital management, usually we will need to cover the costs [...]. [Hospital pharmacist, female, 12 years' experience]

3.4.2. Subtheme 2: Delay

Lead time of medication delivery is important. This is to ensure patients get their medication on time. Sometimes, there can be delay in delivery due to courier delays, bad weather or delivery partner unable to reach Felda area.

Because unlike parcels, the lead time of medication delivery is crucial. If let's say, the medication received in delay, the patient may not be able to take the medications on time. So, when we first started medication delivery, 2 of the major concern would be number 1 lead time of the delivery. [Community pharmacist, female, 12 years' experience]

There has been delays. For example, courier delays. So, it may not reach the patient within the expected time frame. And also, some patients may need to start on their medication almost immediately. For example, antibiotics. So, if we are doing delivery service, there's actually a significant delay in terms of getting their medication on time. Because you don't come to the counter and get your medication immediately right. So, that sought of delay and also sometimes when we have bad weather like for example, during the flood. So, you can't continue with your delivery as per schedule. [Hospital pharmacist, female, 5 years' experience]

For example, if the patient is staying in the Felda area. There are some delivery partners, they couldn't reach to the place. So, it may delay the delivery time [...]. That would be our challenges. [Hospital pharmacist, female, 12 years' experience]

3.4.3. Subtheme 3: Technological barrier

Most MDS users are elderly members. Elderly members might not be very familiar with using technological devices like using apps, operating smart phone, online banking or writing emails. This may be a barrier for elderly members to use MDS.

When we say about medications delivery most of the users for medication delivery are silver care members meaning to say that they are elder and it also means that probably and more likely they are not so well versed with the technology. They may not have applications or they may have a smart phone but they do not know how to actually operate the smartphone. So, this creates a barrier for the patients when it comes to medication delivery. [Community pharmacist, female, 12 years' experience]

And then talking about that one also, a lot of patients maybe elderly and technological barriers are problem for them because they may not be very well versed in online banking and writing emails. [Hospital pharmacist, female, 5 years' experience]

3.4.4. Subtheme 4: New workflow

In some hospitals and community pharmacies MDS is done online. When MDS is newly started, pharmacists need a new workflow. Pharmacists are also busier because they must cater to the patients in the physical pharmacy and also need to take care and follow up the patients that they deliver medicines using MDS.

So, you need a totally new workflow to make this work because everything is done online. So, it's a new workflow through instead of through counters and staff face to face, you need emails, you need like webpage or telephone calls. [Hospital pharmacist, female, 5 years' experience]

We are now worse off and I would say busier because not only that we need to cater our customers or patients in the pharmacy. We also need to take care and to follow up the patients that we deliver our medications to. [Community pharmacist, female, 12 years' experience]

MDS brings beneficial clinical outcomes to patients as it improves patients' medicine compliance, improve adherence to treatment and enhanced communication between staff and patients (Mash et al., 2022, Al-Zaidan et al., 2021, Chaomuang et al., 2022). Patients with transportation or walking difficulties greatly benefit from this delivery service (Tan & Gan, 2016). Longer term home care can prevent time away from work and loss of earnings to collect medication (Louw et al., 2020). This can improve house hold income and food security (Mash et al., 2022). Convenience and reducing burden of patients and family travelling to hospital were factors that influence accessibility in MDS. MDS greatly helps patients who stay in remote areas. Through telehealth, patients living in remote areas can get the care they need from home (Elbeddini & Yeats, 2020). From the perspective of hospital pharmacists and community pharmacists, the issues of resources emerged. One issue is the increase in resources. Operational expenses include consumables like envelopes, parcels and extra resources for manpower. Operational expenses are minimal and manageable. Some delivery costs are bound by hospital. Another issue is delay in delivery. This is because lead time is crucial in medication delivery. Technological barrier is also an issue in MDS because elderly member might not be well versed with using technological devices. New workflow is also an issue when MDS is done online. Instead of through counters, pharmacists

need to use webpages, emails and telephone calls to conduct the MDS.

CONCLUSION

Face to face communication between pharmacist and patient in a pharmacy premise is an optimum and safe way of dispensing and delivering medications by a licensed pharmacist to patient. However, medication delivery services can be more convenient for patients to get their medicine supply. MDS is a value-added service and provides many benefits to patients and health care providers. There are a few issues that emerged in providing MDS from the perspective of health care providers but those are minimal and can be managed. Factors influencing accessibility in MDS, favourable clinical outcome and issues emerged are related to MDS. Caretakers in this study welcomed the idea of MDS and found the service convenient. Hence, pharmacists in various health care settings should promote and explain regarding the process of MDS to their patients so that patients get to know about MDS and can benefit from the service.

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Characterization of Coronary Artery Disease Patients Managed in an Outpatient Facility in Selangor

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ABSTRACT

Introduction: Coronary Artery Disease (CAD) remains a major disease in the world. As CAD often presents suddenly with little warning, identification of early cardiac disease could allow intervention that may be effective in slowing the progression. To this end, characterization of patients would be useful to aid healthcare practitioners to plan the best care needed by individual patients.

Objective(s): The aim of this study is to characterize the patients treated at an outpatient facility in Selangor by focusing on the trends of HbA1c and serum lipid profile.

Methodologies: Sample data were taken from 119 CAD patients at An-Nur Specialist Clinic, Bangi. Patient demographic data such as age, sex and BMI was collected through the hospital records. Lipid profile and HbA1c results was obtained from hospital records. All patient's data were collected retrospectively from records obtained in the year 2014. IBM SPSS was used as the tool for statistical analysis. Total cholesterol (TC), Triglyceride (TG), High density lipoprotein (HDL), low density lipoprotein (LDL) and glycated haemoglobin (HbA1c) were analysed according to gender, age and BMI.

Results: Result show that TG and HDL in this study does not show a significant as a strong indicator for CAD risk factor. LDL and HbA1c show promising positive result to be useful as a parameter to monitor CAD.

Conclusion: LDL and HbA1c show positive indication to be used in further characterizing CAD patients in Selangor and the prevalent risk factor for this population include LDL level and diabetes.

Keywords: Coronary artery disease; diabetes; HbA1c; LDL; HDL

INTRODUCTION

Coronary artery disease (CAD) is one of the leading causes of death globally. In Malaysia, CAD is one of the main causes of morbidity and mortality (National Heart Association of Malaysia, 2018). CAD is on the rise in Asian-Pacific countries that are currently undergoing rapid urbanization, industrialization, and lifestyle changes; in parallel with increasing life expectancies (Lu et al., 2014). A Malaysian study shown by Rissam, Kishore & Trehan (2001), Indians have 15 times higher rate of CAD than Chinese and 10 times higher rate than Malays < 40 years. Besides that, research by Gijsberts et al., (2015) stated that South Asians have repeatedly been described as a high-risk group for early onset and severe CAD.

Cardiovascular health was defined by American Heart Association to be characterised by components that covers health behaviours and health factors that include blood cholesterol, body mass index (BMI), blood pressure

and blood glucose (Tsao et al., 2022). Risk factors of CAD are divided into non-modifiable factors that include age, gender, and family history and also the modifiable risk factors such as hypertension, smoking, physical inactivity, obesity, diet, diabetes mellitus and dyslipidaemia (Yahagi et al., 2015).

CAD often presents suddenly with little warning (Knopp et al., 2002). Therefore, prevention of CAD should start with global risk assessment and proceed to suitable treatment of correctable risk factors. If the blood lipid profile is abnormal, this should be corrected thus the indications for drug therapy in CAD prevention are increasingly well defined (Assman et al., 1999). Vasan et al. (2001) noted that several epidemiologic studies have demonstrated that systolic and diastolic blood pressures have an association with CVD outcomes. Franklin & Wong (2013) described that Framingham Heart Study show that diastolic blood pressure <70mm Hg with systolic blood pressure ≥120 mm Hg was associated with increased CAD risk.

Diabetes mellitus is one of the most important diseases in the modern society and represents not only a medical but also a social problem (Silva et al, 2018). Diabetes and its predominant form, type 2 diabetes mellitus (T2DM), has distinctive association with CAD and have two-to-five-fold higher risk in developing coronary disease (Ali et al.,2010). Besides that, in the Framingham study, the incidence of cardiovascular disease among diabetic men was twice that among nondiabetic men and similarly was three times more elevated in diabetic women compared to nondiabetic women (Chiha et al., 2012). In Malaysia, the National Health and Morbidity Survey 2019 showed that the prevalence of diabetes for adults aged >30 years old was 9.4%, increased by 11.2% within 8 years from 2011 to 2019. Also 6th Clinical Practice Guideline of Diabetes Mellitus (2020) showed the prevalence of T2DM is the highest among Indian ethnic at 31.4%, followed by Malays and Chinese at 22.6% and 15.1% respectively.

The HbA1c test is an indicator of average blood glucose concentrations over the preceding three months, and it is a well-established biomarker of long-term glucose control (Matheka et al., 2013). Studies show that HbA1c is more useful than fasting plasma glucose levels for assessing CAD risk and mortality (Selim et al., 2010). HbA1c in the range of 5.5% to 6.5% poses considerably high risk of morbidity and mortality due to CAD (Syed & Khan, 2011). Based on Cai et al., (2014) observational study, they found out that in non-diabetic population HbA1c level was associated with the severity of CAD. This further supports the notion that HbA1c may be a useful and independent indicator for CAD risk evaluation. High levels of cholesterol increase the risk of formation of plaques and atherosclerosis, thus increase risk of CAD. Serum lipid profile is measured for cardiovascular risk prediction and has now become almost routine test. The test includes four basic parameters: total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides (Nigam, 2010). Raised total cholesterol, low density lipoprotein-cholesterol (LDL-c) and reduced high density lipoprotein-cholesterol (HDL-c) level have been shown to be strong independent risk factors for CAD in numerous cross sectional, prospective and intervention trials (Cromwell et al., 2007). Karalis (2009), also noted that high concentration of LDL-C is a major risk factor for CAD. Furthermore, by monitoring dietary intake it is proved that lowering serum cholesterol level will effectively decrease atherosclerotic disease (Dawber et al., 1982).

METHODOLOGIES

STUDY DESIGN

This was a retrospective study which involved patients of Specialist Clinic An-Nur in 2014.

DATA COLLECTION

The tool for data collection in this study was a case record form.

Study site

Study was conducted at Specialist Clinic An-Nur, Bangi.

Inclusion Criteria

Patients >18 years old diagnosed with CVD with co-morbidity of T2DM, HTN or Hyperlipidemia.

Exclusion Criteria

Patients with incomplete medical profile.

Data Analysis

All data was analysed using Statistical Package for Social Sciences (SPSS) version 22.0. All continuous data was checked for the normality. Parametric test such as T-test, Pearson correlation test were used. Pearson chi square analysis was utilised to determine association between variables.

RESULTS AND DISCUSSION

Total of 119 patients from Specialist Clinic An-Nur from 2014 were included in the study. Demographic data of patients are shown in Table 1.

Table 1: Demographic data

	Characteristics	Frequency	Percentage (%)
Gender	Male	71	59.7
	Female	48	40.3
Age	≤45 years	55	46.2
	46-65 year	50	42
	≥66 years	14	11.8
BMI	Underweight, <18	3	2.5
	Normal, 18.5-22.9	13	10.9
	Pre-Obese, 23-27.4	27	22.7
	Obese 1, 27.5-34.9	57	47.9
	Obese 2, 35-39.9	14	11.8
	Obese 3, >40	5	4.2

There were 71 (59.66%) males and 48 (40.34%) were females. Among middle-aged people, CAD is 2 to 5 times more common in men than in women (Jousilahti et al., 1999). Although this shows men are more affected by CAD, it remains as a major concern for both sexes. In women the risk of death from cardiovascular disease shows a significant increase when reaching 60 years of age (Mikkola et al., 2013). It is generally accepted that as age increases, they are more likely to develop

CAD. Furthermore, aging is associated with increased vulnerability to endothelial injury and decreased endothelial repair (Torella et al., 2004). However, in this study it shows that patients in group of 45 years below have the highest number diagnosed with CAD. This shows a transition of population of those having CAD as it may be seen even at the middle age.

The mean total BMI in patients in this study was 29.14 kg/m². Obesity is one of the risk factors for CAD and earlier onset of metabolic diseases such as diabetes mellitus and hypertension (Ritchie & Connell, 2006). There was no significant difference in mean of male BMI (29.47 kg/m²) and mean of female BMI (28.65 kg/m²), $P=0.466$.

Data for serum lipid level was only available for 112 patients. Analysis of the mean total cholesterol of patients showed value of 5.12 mmol/L, which is within the normal limit of 5.2 mmol/L. There was no significant difference in mean cholesterol of male (5.09 mmol/L) and the mean of cholesterol of female (5.17 mmol/L), $P=0.812$. This reflects the high level of medication adherence among the patients surveyed. Besides that, dietary intakes also play a major role in controlling cholesterol level. In a further analysis, patients were divided into 2 groups based on their cholesterol level: group 1 the normal group (<5.2 mmol/L) and group 2 the higher-level group (>5.2 mmol/L). It was found that 57 (48.8%) CAD patients (34 males and 23 females) are classified under normal group whereas 55 (46.2%) CAD patients (33 males and 22 females) result to have higher cholesterol level. The distribution of cholesterol level in different age group shows that CAD patients who have higher cholesterol are those aged less than 45 years old followed by group 46-65 years and more than 66 years. This shows that the younger generation already experienced an abnormal cholesterol level which then progress to atherosclerosis thus increasing the risk of CAD at an early age. This observation may be linked to the about high prevalence of CAD patients among patients who are less than 45 years old (Nadeem et al., 2013). The contribution to the trend may be due to the lifestyle of consuming a high lipid diet as well as smoking habits among young adults.

Association between obesity with cholesterol level was investigated. The positive relationship between level of cholesterol with BMI was not seen in this study as there were no significant difference in the cholesterol levels between different BMI classes, $P=0.26$. Mean total triglyceride (TG) of CAD patients in this study was 1.29mmol/L. There was no significant difference in mean TG of males (1.23mmol/L) and females (1.38 mmol/L), $P=0.927$. The mean TG is >1.68mmol/L. TG as a risk indicator for CAD is still being debated. Evidence state that the role of TG as biomarker has been inconclusive and treatments aimed at lowering TG level have not yet succeeded in reducing disease risk (Do et al., 2013).

The mean total HDL cholesterol level of patients was 1.29 mmol/L. The results show that patients HDL level is in the normal range (>1.03 mmol/L). There was no significant difference in mean cholesterol of male (1.38 mmol/L) and the mean of cholesterol of female (1.23 mmol/L), $P=0.927$. Patients were divided into 2 groups based on their HDL level: group 1 the normal group (>1.03) and group 2 the lower-level group (<1.03). It was found that the normal group was the majority with 99 (83%) patients (57 males and 42 females). Low serum levels of HDL are commonly encountered in patients with CAD (Toth, 2004). As a result, HDL-C is gaining increasing interest as a therapeutic target (Natarajan et al., 2010). In this study, it was observed that the mean of total HDL cholesterol was 1.29 mmol/L (1.23 males and 1.38 females) which fall between the desired range.

The mean total LDL cholesterol level of patients was 3.12 mmol/L. There was no significant difference in mean cholesterol of male (3.12 mmol/L) and the mean of cholesterol of female (3.08 mmol/L), $P=0.887$. Majority of patients (87 patients, 73%) in this study have higher level of LDL level than the normal range (<2.58 mmol/L). Disorders LDL metabolism is associated with accelerated atherosclerosis (Grundy et al., 2004). The age group with highest LDL level are those <45 years old. Diet high in saturated fat leads to high LDL cholesterol and has been associated with increased risk of CAD (Siri-Tarino et al., 2010). Raised LDL level has been shown to be strong independent risk factor for CAD in numerous cross sectional, prospective and intervention trials (Cromwell et al., 2007). Analysis of the association of LDL level with BMI observed that the number of patients in all BMI classifications are higher in the group having abnormal reading of LDL level. This may be due to the established correlation between LDL level and CAD risk (Cromwell et al., 2007). This reinforced the hypothesis that LDL level is an independent risk factor as it has no association with BMI.

Data for HbA1c was available for 49 patients. Diabetes mellitus (DM) is one of the major public health problems worldwide, affecting approximately 24 million individuals in the US alone (Cowie et al., 2009). DM patients face 2- to 4-fold increased risk of death due to cardiovascular problems and are also regarded to have worse CAD prognosis (Aronson & Edelman, 2014). More than 70% of patients with type 2 diabetes die from cardiovascular causes (Moss et al., 1991). Plus, individuals with HbA1c $\geq 6.5\%$ had 10-fold increase CAD risk (Cahill et al., 2015). Mean HbA1c level of patients was 7.37%, with majority having readings within the range of 6.5%-7.5%. It was found that there was no significant difference in mean HbA1c of male (7.17 %) and the mean of HbA1c of female (7.45 %), $P=0.220$. Current study results show that patients HbA1c level is high (7.37 %). This may indicate uncontrolled diabetes although medication has been prescribed. National Health and Morbidity Survey 2019

revealed that 1.7 million Malaysians (8.1%) have the three major risk factors for CAD which are diabetes, HTN and high cholesterol levels. A concerning 5% of young Malaysians aged 18-29 are already diabetic (6th Clinical Practice Guideline for Management of Type II Diabetes, 2020). In this study, patients with diabetes are mostly aged between 46-65 years old. As diabetes is also a strong indicator for CAD, monitoring of HbA1c level in this age group should be considered. However, careful glycaemic control does not contribute to better outcomes as it leads to higher incidence of hypoglycaemia but has no effect on mortality (Aronson & Edelman, 2015). Study by Nura et al., (2021) revealed that uncontrolled DM was associated with anxiety and depression among CAD patients. Thus, this may suggest HbA1c is a parameter that needs to be emphasized when monitoring CAD, but the therapy should be holistic to include mental health as well.

CONCLUSION

A total of 119 patients were characterised and cholesterol level results most of patients have an undesired level of LDL level. Based on result of HbA1c level, majority of patients have >6.5% HbA1c level. The results confirmed an expected connection between CAD and non-modifiable risk factors such as gender and BMI. Results of current research can be used to promote public health awareness that will ultimately reduce heart disease in CAD patients in Malaysia, positively change public policy health laws and implementations, and contribute to social change by providing insight into the need for public policy that encourages a competent health care system.

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Fall Among Geriatric Patients: Prevalence, Risk Factors and Clinical Outcomes

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ABSTRACT

Introduction: Fall among geriatric patients has become a great concern that leads to public health problem, including in Malaysia. To date, there is lack of local published studies on the prevalence of fall among geriatric patients and its associated clinical outcomes.

Objective(s): This cross-sectional study was conducted to determine the prevalence, risk factors and clinical outcomes of falls among geriatric patients.

Methodologies: Convenient sampling method was used to select patient admitted to Hospital Tengku Ampuan Rahimah (HTAR), Klang in 2016 and 2017. Morse Fall Scale (MFS) was used to classify the risk of falls. Regression analysis was used to measure the association between demographic factors and clinical characteristic with falls. Independent T-test was used to measure the difference in mean number of comorbidities and length of stay in hospital between fallers.

Results: A total of 132 patients were included in this study. This study found that the prevalence of fall was 30 cases among geriatrics. Majority of fallers (73.3%) were classified with high risk of falling. There was a statistically significant association between kidney impairment and falls (OR= 3.14; p=0.018). There was a statistically significant difference in the mean length of stay in hospital between fallers with ≤ 1 comorbidity and those with ≥ 2 comorbidities.

Conclusion: Fall is prevalent among geriatric patients and more effective prevention methods are important especially for patients with kidney impairment and multiple comorbidities.

Keywords: Geriatric, fall, prevalence, risk factors, outcomes

INTRODUCTION

A study conducted among 69 geriatrics in Australia found that the incidences of falls are increasing due to population ageing that leads to accidental injuries and injury-related deaths (Bird et al., 2010). Previous studies have reported that individuals with history of previous falls have risk doubles or triples in the presence of cognitive impairment (Aama, 2017; Ambrose et al., 2013). The prevalence of falls has also been reported to increase with increasing comorbidities. Geriatric with underlying neurological diseases such as stroke, Alzheimer's disease and Parkinson's disease will experience more fall incidences compared with healthy older adults (Bao et al., 2017). Apart from these factors, environmental factors can also lead to increased incidence of falls. A study among 1520 geriatrics found that the most common place where elderly experience falls is their own homes (64%) and followed by the falls on streets (26%). The study also found that the incidence of falls mostly happens in bedroom and bathroom, and this can be prevented by

using non-slippery flooring material, adequate lighting, and absence of rugs (Rodrigues et al., 2014).

Patient who experiences falls suffers high costs, increase length of stay in hospital and liability (Bouldin et. al., 2013). The hospital stays with an average of 6-12 day or more will cause higher costs among patients with serious injuries. Increased length of hospital stay may cause other complications such as increased risk of nosocomial infection among elderly patients (Dunne et. al., 2014).

There is lack of published studies conducted on Malaysian geriatric population related to fall and its clinical outcomes. This cross-sectional study was conducted to investigate the risk factors and clinical outcomes of falls in elderly population.

METHODOLOGIES

This retrospective cross-sectional study was conducted at geriatric and medical wards at HTAR, Klang. All geriatric

patients admitted in 2016 and 2017 were sampled conveniently, screened and selected based on the pre-set inclusion and exclusion criteria. Data was collected using a data collection form which contains 3 sections namely Section 1 (demographic data), Section 2 (fall episodes) and Section 3 (other geriatric syndromes). Morse Fall Scale (MFS) was used to classify the fall risk among patients. Regression analysis was used to measure the association between demographic factors and clinical characteristic with falls. Independent T-test was used to measure the difference in mean number of comorbidities and length of stay in hospital between fallers. All characteristics of the study and related protocols were reviewed and authorized by National Medical Research Register (NMRR Malaysia), Clinical Research Centre (CRC Malaysia) and Medical Research and Ethics Committee (MREC Malaysia). The study protocol and data collection form used in this study were submitted to NMRR for evaluation and registration. Ethical approval to conduct the study was endorsed by MREC [NMRR-18-780-40357].

RESULTS

A total of 132 geriatric patients were included for final analyses. Majority of the patients were below 80 years old, females and of Malay ethnicity. The patients' demographics are as shown in Table 1.

Table 1: Demographic characteristic of study population (N = 132)

Variables		n (%)
Age range (in years)	60-79	105 (79.5)
	80 and above	27 (20.5)
Gender	Male	23 (17.4)
	Female	109 (82.6)
Ethnicity	Malay	49 (37.1)
	Chinese	36 (27.3)
	Indian	42 (31.8)
	Others	5 (3.8)

Of the 132 patients, 72.7% were found to have ≥ 2 comorbidities. The distribution of comorbidity categories is as shown in Figure 1.

This study found that among the endocrine diseases, majority of the cases (69.2%) were type 2 diabetes mellitus (T2DM). This finding is consistent with previous local studies that found, among 2764 geriatrics in Malaysia, the prevalence of T2DM was higher among geriatrics with 34.4% compared with 20.8% for population aged 30 and above (Ho et al., 2014). Another study reported that T2DM could be associated with chronological age where both reductions in insulin sensitivity and muscle mitochondrial dysfunction were commonly observed phenomena among geriatric patients (Teh et al., 2014).

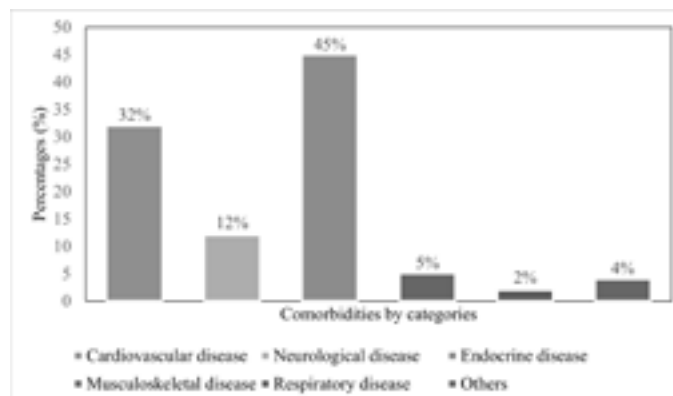


Figure 1: Comorbidity cases among patients (N = 286)

Fall prevalence

This study found that the overall prevalence of fall was 30, giving an overall fall rate of 22.7%. Majority of patients have experienced at least 1 fall episode in a year. The mean number of falls experienced by 30 fallers was 1.43 (± 0.73). Figure 2 shows the frequency of falls among the 30 patients who have previous fall.

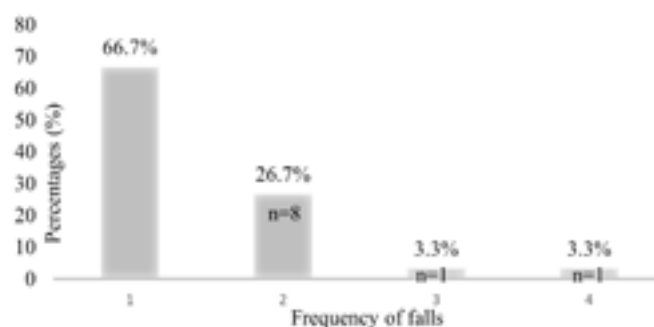


Figure 2: Frequency of fall episodes among fallers (N = 30)

Fall risk factors

Results from univariate analyses showed that only kidney impairment ($P=0.018$, $OR=3.14$ [1.22-8.09]) was statistically significantly associated with falls. Patients with kidney impairment were 3.14 times more likely to experience falls than were patients with no issue of kidney impairment. The finding from this study is consistent with the results published in 2007. In a study involving 489 geriatric patients, it was reported that decreased renal function was associated with falls. The potential mechanism was the creatinine clearance (CrCL) associated with declined vitamin D receptors (VDR) in muscle. Hence, this could lead to decrease of muscle strength and predispose more in incidence of falls (Gallagher et. Al., 2007). A meta-analysis of 39 high-quality evidence published in 2020 highlighted that the risk of fractures increased when kidney function worsened, with the highest risks in the patients with stage 5 CKD or dialysis (Goto et. Al., 2020). The relationship between demographic and clinical factors among fallers and non-fallers is as summarized in Table 2.

Table 2: Demographic factors and clinical characteristics between fallers and non-fallers.

Variables	Non-fallers (n=102) n (%)	Fallers (n=30) n (%)	OR* (95%)	P value
Age range (in years)				
60-79	81 (77.1)	24 (22.9)	0.96 (0.35-2.67)	0.964
80 and above	21 (77.8)	6 (22.2)		
Gender				
Male	17 (73.9)	6 (26.1)	1.25 (0.44-3.51)	0.673
Female	85 (78.0)	24 (22.0)		
Cardiovascular disease				
Hypertension	62 (73.8)	22 (26.2)	1.78 (0.72-4.37)	0.213
Heart Failure	5 (62.5)	3 (37.5)	2.16 (0.48-9.60)	0.310
Respiratory disorder				
Asthma	6 (85.7)	1 (14.3)	0.55 (0.06-4.77)	0.589
Musculoskeletal Disorder				
Osteoarthritis	8 (61.5)	5 (38.5)	2.30 (0.71-7.81)	0.613
Neurological Disease				
Stroke	16 (76.2)	5 (23.8)	1.07 (0.36-3.22)	0.897
Epilepsy	3 (75.0)	1 (25.0)	1.14 (0.11-11.36)	0.912
Alzheimer's disease	7 (87.5)	1 (12.5)	0.47 (0.06-4.00)	0.500
Endocrine disease				
Type 2 DM	71 (78.9)	19 (21.1)	0.75 (0.32-1.78)	0.517
Kidney Impairment	14 (58.3)	10 (41.7)	3.14 (1.22-8.09)	0.018
Dyslipidemia	15 (93.8)	1 (6.2)	0.20 (0.03-1.58)	0.127
Others				
Cancer	5 (62.5)	3 (37.5)	2.16 (0.48-9.60)	0.484

Fall sites and clinical outcomes

In this study, most falls took place in bathrooms and only 16.7% occurred outdoors. This finding is consistent with another study that reported the bathroom as the most hazardous place compared to outdoor locations. Increasing time amount spent indoors was one of the reasons. In this study, the major extrinsic factor of falls was slippery bathroom floor (Sebestina et. al., 2008). In this study, most of geriatric patients who experience the fall episodes reported to have suffered some kind of injury (80.0%). The most common injuries were scrapes, bruises or blisters and fractures. The findings were similar to another study among 389 geriatrics in Brazil and found that scratches, abrasions and bruises were the main consequences of falls (Ferretti et. al., 2013). This study also found that there was a statistically significant difference in the mean length of hospital stay between fallers with ≤ 1 comorbidity and those with ≥ 2

comorbidities. The summary of fall incidences among the patients is as shown in Table 3.

Table 3: Details of incidence of falls (n=30).

Variables	n (%)
Type of injuries	No injury
	6 (20.0)
	Fractures
	6 (20.0)
	Concussion/Brain injury
Site of injuries	3 (10.0)
	Scrapes, bruises, or blisters
	11(36.7)
Place of Falls	Lacerations
	4 (13.3)
	No injury
	6 (20.0)
Site of injuries	Hip
	5 (16.7)
	Head (include facial bones)
Place of Falls	14 (46.7)
	Knee and lower leg
	5 (16.7)
	Bathroom
Place of Falls	11 (36.7)
	Living room
	7 (23.3)
Place of Falls	Ward (bedside)
	6 (20.0)
Place of Falls	Others
	5 (16.7)

CONCLUSION

This study has showed that fall is common among the geriatric populations. Majority of the fall cases occurred indoor and resulted in some degrees of injuries. Patients with comorbidities, especially those with chronic kidney diseases, was shown to have higher odds to fall. This study concludes that fall among the elderly can lead to more severe clinical outcomes and that appropriate preventative strategies should be taken by the patients and healthcare professionals.

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Optimization of Polymer/Salt Aqueous Biphasic System (ABS) for Direct Recovery of Recombinant *Bacillus Subtilis* Protease

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ABSTRACT

Introduction: The growing market demand for protease in various industries has sparked the interest among researchers to develop a simple, cost-effective and high yield method for the downstream recovery of proteases.

Objective(s): In this study, the partitioning behavior of recombinant *Bacillus subtilis* protease and different parameters are investigated using polymer/salt aqueous biphasic system (ABS).

Methodologies: Response surface methodology (RSM) and Box-Behnken design (BBD), the multivariate statistical methodology, were employed to optimize the specific parameters including composition of polymer, composition of salt and pH of the biphasic system in order to achieve optimal partition coefficient and recovery yield of protease.

Results: The optimized ABS was exhibited at 17.50%(w/w) of polyethylene glycol (PEG) 1000 and 20.34%(w/w) of potassium phosphate, 20%(w/w) of crude feedstock, at pH 8.2, room temperature and without addition of sodium chloride (NaCl). Proteases preferentially partitioned to the PEG rich top phase with high partition coefficient of 5.387 and relatively high recovery yield of 84.82% were obtained although there are technical errors existed in the partition coefficient model analysis.

Conclusion: The results achieved with the optimized system held great promise on ABS, the single-step operation capable of surpassing conventional downstream processing methods and applying in the large-scale production of protease.

Keywords: Protease; Aqueous biphasic system; Response surface methodology; Box-Behnken design; Polyethylene glycol

INTRODUCTION

Proteases are the proteins capable of breaking down peptide bonds with their catalytic function and found abundantly in nature as they are playing important roles in various physiological and biochemical functions of living organisms (Gimenes et al. 2019). Proteases are very important in diverse industrial sectors, major utilized in detergents, food and beverage processing, feather processing, silk gumming, pharmaceuticals, biosynthesis, biotransformation and bioremediation (Shine et al. 2016, Rawaliya et al. 2022). Conventional methods to be used to recover protease are specific, time consuming, expensive, difficult to scale-up in large-scale production and have low recovery yield which is insufficient to meet the increasing market demands on

enzyme production (Golunski et al. 2011, Iqbal et al. 2016, Gimenes et al. 2019). Therefore, it is necessary to develop of a simple, low-cost, environmentally-friendly and efficient downstream processing method for large-scale recovery of protease.

Aqueous biphasic system (ABS) is a liquid-liquid fractionation technique that recovers a wide variety of products such as proteins, enzymes, cell organelles, antibodies and other biological products by forming two immiscible liquids (Iqbal et al. 2016, Teixeira et al. 2017). The ABS method has attracted the interest of many researchers because of its potential to extract, separate and isolate various products also to study the partitioning behaviour. The comparative advantages of ABS include single-step process, easy operation, cost-effective,

environmental friendly, reduced risk of destroying targeted biological products and their enzymatic activity (Ratanapongleka 2010, Iqbal et al. 2016). Polymer/salt ABS is applied in this study due to cost-effective, short phase separation time, low toxicity and low volatility (Rosa et al. 2010, Raja et al. 2011, Iqbal et al. 2016).

The bacterial strain used in this study is *Bacillus subtilis* PT5 also known as recombinant *B. subtilis* where the novel keratinase KerP within the bacteria were isolated from *B. polyfermenticus* B4 obtained from soil feather compost (Dong et al. 2017). *B. subtilis* strain is commonly used in enzyme production for several advantages such as generally recognized as safe (GRAS) status, able to produce numerous native or heterologous proteins efficiently, fast growth with short fermentation period, easy to cultivate on affordable substrates and changing environment which simplifies the downstream processing and reduces processing cost (Earl et al. 2008, Aslankoochi et al. 2015, Chen et al. 2016, Dong et al. 2017, Contesini et al. 2018, Su et al. 2020). With the GRAS status of *B. subtilis*, microbial proteases are applied in various food and beverages processing like food waste treatment, beer brewing process, meat tenderization, milk coagulation and casein hydrolysate preparation in cheese production (Patel et al. 2019, Su et al. 2020).

Various parameters that affect the partitioning behaviour of protease in polymer/salt ABS significantly: polymer phase composition, salt phase composition and pH were studied to determine the optimal conditions of polymer/salt ABS on the recovery of recombinant *B. subtilis* protease. In order to optimize the direct recovery of protease in ABS effectively, the response surface methodology (RSM) is applied to obtain the optimal conditions for experimental design and validate them with actual experiments. Box-Behnken design (BBD) with three-factor design, consisting of 15 experimental runs according to the three most significant factors mentioned is used to determine the ideal Box-Behnken model for the optimum partition coefficient and recovery yield of recombinant *B. subtilis* protease in polymer/salt ABS in this study.

METHODOLOGIES

Fermentation of *Bacillus subtilis* for production of protease

25 g/L of Luria-bertani (LB) broth, pH 7 was prepared by adding appropriate amount of LB broth powder into distilled water for fermentation. A total of 90 mL of the LB broth were added into clean 250 mL conical flasks respectively. All conical flasks together with their contents were sterilized by using an autoclave machine at 121°C for 20 minutes. The recombinant *B. subtilis* was revived in the LB broth with inoculum size of 10%(v/v) and incubated at 37°C in an orbital shaker with speed of 150 rpm for 24 hours. The 10%(v/v) of inoculum

from the culture medium was transferred into 90mL of LB medium and incubated at 37°C in an orbital shaker with speed of 200 rpm for another 24 hours to produce protease. The fermented broth was centrifuged at 4000 rpm for 30 minutes to isolate extracellular protease from the fermentation medium. The supernatant collected was sealed and stored at 4°C in the chiller for future use (Dong et al. 2017).

Stock solutions preparation

The 50%(w/w) PEG1000 stock solution was prepared by adding appropriate amount of PEG and distilled water in a 100-mL beaker and mixed well. The 10mM Tris-HCl buffer solution of pH 9 was prepared by weighing appropriate amount of Tris-HCl and added into distilled water to mix well. 1M sodium hydroxide solution was prepared to adjust the desired pH of Tris-HCl buffer solution. The 0.4M TCA solution was prepared by weighing appropriate amount of TCA and added into distilled water to mix well. The stock solutions were stored in Schott bottles or centrifuge tubes of appropriate sizes.

Box-Behnken design (BBD) configuration

The 3 selected independent parameters (concentration of PEG1000, concentration of potassium phosphate and pH of ABS) were undergoing the screening step, applying BBD matrix at the two factor levels so that significant variables can be studied using statistical software, MiniTab®. The parameters selected along with 15 experimental runs were performed so that predicted equations for both partition coefficient and recovery yield of protease could be formed.

ABS partitioning experiments using Box-Behnken design (BBD)

ABS of 5g was prepared by adding a known amount of PEG1000 stock solution and potassium phosphate into a 15mL centrifuge tube. The desired pH of the ABS system and concentration of potassium phosphate were prepared by different combinations of dipotassium hydrogen phosphate (K₂HPO₄) and potassium dihydrogen phosphate (KH₂PO₄). Then, 20% (w/w) crude protease was added. Distilled water was added to make up the ABS system to a total weight of 5g. The system was mixed thoroughly using a vortex mixer and centrifuged at 4000 rpm for 10 minutes for phase separation to take place completely. The volumes of top and bottom phases of the system were recorded. Samples from both top and bottom phases were collected respectively for sample analysis to determine protease enzyme activity.

Sample analysis using protease activity assay

The method of this assay was adopted and modified from Jin et al. (2019) using casein as the substrate. 0.25%(w/v) casein was added into an appropriate amount of 10mM Tris-HCl buffer solution, pH 9. 250 µL of the samples from top and bottom phases were pipetted into 2 mL microcentrifuge tubes, followed by the addition of 250

μL of preheated mixture of 0.25%(w/v) casein and 10mM Tris-HCl buffer (pH 9.0). The mixture was gently mixed with vortex mixer and incubated at 40°C for 10 minutes. 500 μL of 0.4M TCA solution was added in order to stop the enzymatic reaction. The mixtures were centrifuged at 10,000 rpm for 10 minutes. The absorbance of the supernatant was measured and recorded at the wavelength of 280 nm using a spectrophotometer for tyrosine concentration determination. Protease enzyme activity was expressed as $\mu\text{g}/\text{mL}$ based on the tyrosine standard curve. One unit of protease enzymatic activity was defined as the increase of 0.01 absorbance unit at 280nm per minute under the described assay conditions.

Optimization of protease extraction and validation of predicted extraction equations

Optimization was done with Analysis of Response Surface Design tool and Response Optimizer tool in MiniTab® to plot out predicted optimum extraction equations, response surface design analysis, surface and contour plots for protease extraction in this study. Validation experiments were performed to verify the optimal partition coefficient and recovery yield of proteases using the predicted equations, and both results were recorded. The random equations and validation experiments were conducted with the similar procedures.

Determination of partition coefficient, recovery yield and percentage similarity

Partition coefficient (K_E) of protease was calculated using Equation 1 (Amid et al. 2012).

$$\text{Partition coefficient } (K_E) = \frac{\text{protease enzyme activity at top phase } (A_T)}{\text{protease enzyme activity at the bottom phase } (A_B)}$$

Recovery yield (Y) of protease was represented in percentage (%) and calculated using Equation 2 (Amid et al. 2012).

$$\text{Recovery yield } (\%Y) = \frac{100}{1 + \frac{1}{[\text{volume ratio of top and bottom phases } (V_R) * K_E]}}$$

The percentage similarity between experimental values and theoretical values by MiniTab® (% Similarity) were measured with Equation 3 (Aziz et al. 2017).

$$\% \text{ Similarity} = 100\% - \left(\frac{\text{Theoretical value} - \text{Experimental value}}{\text{Theoretical value}} \right) \times 100\%$$

RESULTS AND DISCUSSION

Optimization of response surface model

Table 1 summarised the Analysis of variance (ANOVA) for both partition coefficient and recovery yield regression models. The significance of the model terms was identified by its p-value similar to significance of the model, with p-value < 0.05 was significant and p-value

> 0.05 was statistically insignificant (Garai and Kumar 2013). From Table 1, the p-value (0.037) for recovery yield model indicated that this model was significant with good reliability and high F-value (5.54), but not for the partition coefficient model with p-value (0.537) and low F-value (0.99) (Polat and Sayan 2019). The lack of fit p-values for partition coefficient model (0.063) and recovery yield model (0.508) implied that these models were insignificant relative to pure error ($P > 0.05$) and appropriate (Garai and Kumar 2013, Aziz et al. 2017, Zhu and Zhang 2019).

Model determination coefficient (R^2) value is closer to 100% indicates that the higher accuracy of the model. Correction determination coefficient (adjusted R^2) provides variability in test data that can be explained by equation models based on the obtained values (Zhu and Zhang 2019). Adjusted R^2 value should theoretically be close to R^2 value because the model may contain too many extraneous terms if there is too large difference (Garai and Kumar 2013). The results above proved that the recovery yield model was fitting well, statistically significant model and its regression equation was able to precisely forecast the actual situations with R^2 value of 90.9% and adjusted R^2 of 74.5%. In contrast, partition coefficient model was not suitable for further analysis due to statistically insignificant results with R^2 value of 64.0% and adjusted R^2 of 0%, leading to poor fitted model and weak correlation between measured and predicted responses (Polat and Sayan 2019). Both quadratic and interaction terms were significant with p-values of 0.048 and 0.032 respectively in the recovery yield model as shown in Table 1.

Table 2 presented the regression coefficients for partition coefficient and recovery yield regression models. The terms in Table 2 were expressed as concentration of PEG1000 (A), concentration of potassium phosphate (B) and pH (C). The independent parameters involved in this study of concentration of potassium phosphate (B), second-order effect of concentration of potassium phosphate (B^2) and interaction effect of concentration of potassium phosphate and pH (BC) were significant parameters for the recovery yield model with p-values < 0.05 based on Table 2. The interaction effect found in the recovery yield model was further analysed by plotting response surface plot and contour plot using Minitab®. These plots provide useful information on the fittings of the model and estimated responses but may not represent the true behaviour of the system (Baş and Boyacı, 2007).

Figure 1 showed the effect of interaction between pH and concentration of potassium phosphate (BC) on recovery yield of protease in the form of a response surface plot. It is observed that a higher recovery yield presents when the pH is increased and the potassium phosphate concentration increased. This phenomenon may occur due to the electrochemical interactions and salting-out effect of protease. Proteases partitioned to

Table 1: ANOVA for the regression models for partition coefficient (K_p) and recovery yield (Y) of protease

Source	Sum of square	Degree of freedom	Mean square	F-value	p-value Prob > F
Partition Coefficient					
Regression	237.930	9	26.437	0.99	0.537
Linear	91.771	3	30.590	1.14	0.417
Square	12.248	3	4.083	0.15	0.924
Interaction	133.911	3	44.637	1.66	0.288
Residual error	134.069	5	26.814		
Lack of fit	128.338	3	42.779	14.93	0.063
Pure error	5.731	2	2.866		
Total	371.999	14			
Recovery Yield					
Regression	862.58	9	95.84	5.54	0.037
Linear	222.70	3	74.23	4.29	0.075
Square	285.86	3	95.29	5.51	0.048
Interaction	354.01	3	118.00	6.83	0.032
Residual error	86.43	5	17.29		
Lack of fit	53.85	3	17.95	1.10	0.508
Pure error	32.58	2	16.29		
Total	949.00	14			

Table 2: Estimated regression coefficients for partition coefficient (K_p) and recovery yield (Y) of protease

Term	Coefficient	Standard error coefficient	p-value Prob > F
Partition Coefficient			
Constant	7.62000	2.990	0.051
A	-2.81875	1.831	0.184
B	-1.71375	1.831	0.392
C	-0.76750	1.831	0.692
A ²	-0.89875	2.695	0.752
B ²	-1.63875	2.695	0.570
C ²	-0.00625	2.695	0.998
AB	-1.97250	2.589	0.481
AC	-2.89500	2.589	0.314
BC	4.60500	2.589	0.135
Recovery Yield			
Constant	89.777	2.400	0.000
A	-2.126	1.470	0.208
B	-4.107	1.470	0.038
C	-2.539	1.470	0.145
A ²	3.744	2.164	0.144
B ²	-6.603	2.164	0.028
C ²	-4.136	2.164	0.114
AB	-4.897	2.079	0.065
AC	-4.215	2.079	0.098
BC	6.838	2.079	0.022

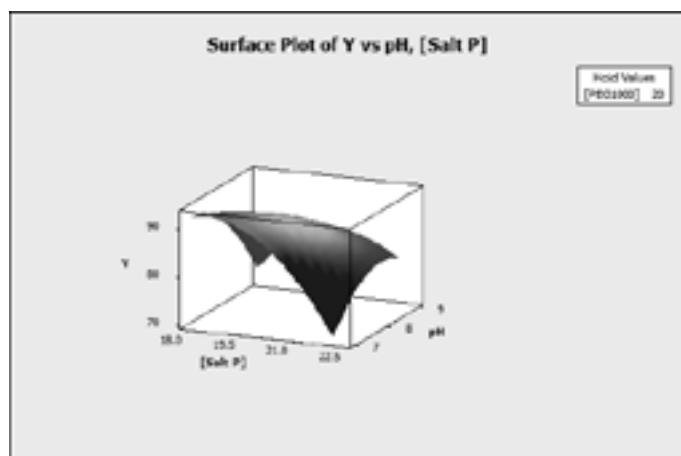


Figure 1: Response surface plot displaying interaction effect between pH and concentration of potassium phosphate variables on the recovery yield of protease. The curve shown is a concave curve; it clearly shows that when potassium phosphate concentration was at the range of 19.5 – 21.0 and pH was at the range of 7 – 8, high recovery yield can be achieved.

PEG rich phase due to salting-out effect in the salt-rich phase where the higher salt concentrations (high ionic strength) in polymer/salt ABS causes a decrease in the solubility of proteins in the salt-rich phase, forcing them to migrate towards the PEG rich phase where they are more soluble, hence improve the enzyme partition to top phase (Hasmann et al. 2008). It is also observed high concentration of potassium phosphate minimize the recovery yield of protease.

Besides, the pH range more than 7 is applied in PEG/phosphate system due to the compatibility of biomolecule distribution (Goja et al. 2013). Negatively charged proteins are preferable for extraction from the polymer-rich phase because they repelled from the salt-rich bottom phase and increase the partition coefficient (Hatti-Kaul 2000, Ng et al. 2021, Ketnawa et al. 2017). Using the pH above the pI of the protein may result in an increase of electrostatic interactions between the protein and polymer molecules, lead to additional affinity towards the polymer-rich phase. However, extreme pH environments can affect protease recovery yield, as high alkaline pH can lead to protein denaturation and possible loss of enzyme stability as shown in Figure 1 (Benavides et al. 2000, Goja et al. 2013).

Figure 2 illustrated the contour plot of the effect on recovery yield with the interaction between concentration of potassium phosphate and pH (BC). The higher intensity of the colour in the plot shows the increases of recovery yield percentage. The middle of the contour plot showed the significant interaction between these two independent variables since there is a cascading effect in the curve. The peak and intensity of colour in the plot also showed a good interaction between pH and concentration

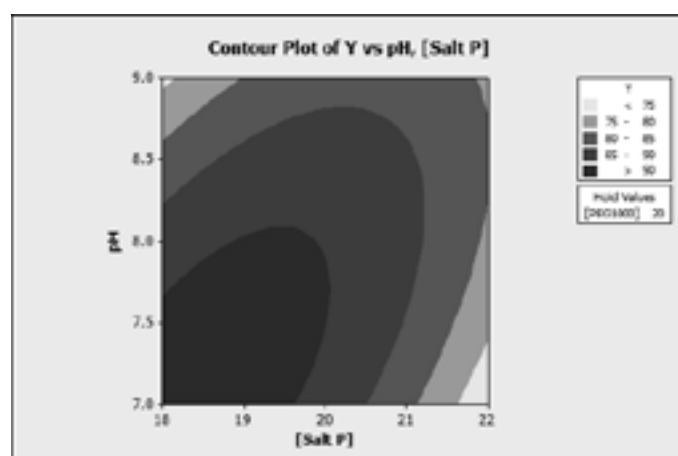


Figure 2: Contour plot displaying interaction effect between pH and concentration of potassium phosphate variables on the recovery yield of protease. Contour plot demonstrated a significant interaction in the system where the area that can be having a high recovery yield values are within the potassium phosphate concentration range of 18%(w/w) -21%(w/w) and the pH range of 7 – 8.5.

of potassium phosphate on the effects of recovery yield of protease.

Experimental validation of model predicted values

The optimum condition on the selected parameters of the polynomial equation model for recovery yield was predicted using the response optimizer function in Minitab® software. Table 3 presented the results of optimal validation experiment performed on the recovery yield model. Using the conditions given by the software, the maximum predicted protease recovery yield of 96.00% could be achieved at pH 8.2, 17.50%(w/w) of PEG1000 concentration and 20.34%(w/w) potassium phosphate concentration in the ABS. Experimental values obtained were recorded and further calculated towards the differences between the predicted and experimental values in percentages for recovery yield of protease using the Equation 3. High percentage in similarity and small difference values show that the optimized recovery yield equation model is valid and appropriate for protease extraction.

Table 3: Optimal validation of experimental and predicted values of the partition recovery yield (Y) of protease

Recovery yield (Y)		Experimental Mean	Difference	% Similarity
Predicted	Experimental			
96.00 %	1) 87.24 %	84.82 %	11.18	88.35 %
	2) 85.55 %			
	3) 81.66 %			

CONCLUSION

ABS was successfully demonstrated in the optimization of proteases recovery from crude feedstock in polymer/salt ABS. Experimental data showed that pH of ABS and concentration of potassium phosphate had possessed a significant impact on the recovery yield of protease in polymer/salt ABS. The highest predicted recovery according to the optimized polynomial predicted response model using ABS was 96.00%, with the optimal condition at pH 8.2, 17.50%(w/w) of PEG1000, 20.34%(w/w) of potassium phosphate, room temperature, constant crude load of 20%(w/w) and without the addition of NaCl. The validation data of recovery yield obtained from the actual experiment was 84.82% with a similarity percentage of 88.35%. Hence, this result proved that the optimization of the recovery yield model for protease extraction was valid for use and approved. In connection with this study, polymer/salt ABS are continue to be proposed as one of the potential approaches for downstream processes of protease from the fermentation of various microorganisms at industrial scale.

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Preliminary Evaluation of *Halal* Status in Respiratory, Immunological Products and Vaccines in Malaysia

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ABSTRACT

Introduction: Muslim consumers and patients are showing a growing interest on the *halal* (permissible) status of pharmaceuticals. This descriptive study was done to explore the *halal* status of selected respiratory and immunological products, and vaccines available in 2 government hospitals in Malaysia.

Methodologies: The *halal* status of products was determined based on the sources of their active pharmaceutical ingredients (API) and excipients. Information regarding sources of active ingredients and excipients was obtained from product leaflets, feedback from manufacturers and standard references such as US Pharmacopeia, British Pharmacopeia and Merck Index. These products were categorized as *halal*, *mushbooh* (dubious) or *haram* (prohibited) based on their contents.

Results: There were 123 medications included in this study (91 were respiratory products while 32 were immunological products and vaccines). Out of 91 respiratory products, 56% were *halal*, whereas 44% were *mushbooh*. Out of the 32 immunological products and vaccines, 96.9% were *mushbooh* and one product was *haram*. No *halal* product was found under immunological products and vaccines in this study. There was 49 API in respiratory products and 79.6% were considered *halal* and 20.4% were *mushbooh*. From 124 excipients used, 83.1% were *halal* and 16.9% were *mushbooh*. Under the immunological products and vaccines, from 32 products analysed, 96.9% were *mushbooh* and 3.1% were *haram*. As of the 42 APIs under this product category, 100% were *mushbooh*. From the 52 excipients, 57.7% were *halal*, 40.4% *mushbooh* and 1.9% *haram*. Lactose, magnesium stearate, ethanol, polysorbate 80 and amino acids are the most common *mushbooh* ingredients. *Haram* ingredients were of porcine origin.

Conclusion: This study concluded that although most excipients are *halal*, but the status of medicines becomes *mushbooh* due to the presence of certain excipients which may actually be replaced with *halal* alternatives.

Keywords: *Halal* pharmaceuticals, active pharmaceutical ingredients, excipients

INTRODUCTION

Products which comply with the *halal* concept are widely accepted by communities as they are considered safe, of high quality and prepared with hygienic procedures (Azmi & Hadeer Akram, 2013). *Halal* pharmaceutical products should not only be free from *haram* (non-*halal*) constituents, but they should also be *thoyyib*, a term given to goods and products which meet certain quality standard and are considered as clean according to Shariah Law (Waarden & Dalen 2010). A previous study has shown that 26% of the 50 Muslim patients in a UK primary care

setting would take a medicine even if they were unsure as to whether it was *halal* or not, 42% of patients stated that they would not take the medications if they were not sure it were *halal*, and 58% of them stated that they would stop taking the medication if they found out it was *haram* (Bashir et. al., 2001). Hence this indicate that *halal* status of medicines is as important as *halal* status of food.

The term *halal* refers to 'lawful or permitted' under the Shariah Law (Islamic rules). *Haram* is the opposite of *halal* which means unlawful or forbidden. However, there is one category that falls between *halal* and *haram*

which is referred to as *mushbooh*. *Mushbooh* means doubtful or suspicious. Products categorized as *mushbooh* are questionable because the origin of some or their constituents may be unknown, possibly containing products from unacceptable animal sources such as porcine (Jusmaliani & Nasution, 2009). The consumption of pharmaceutical products which result in hazardous effects to the patient is also not allowed in Islam. The balance between benefit and harm to treatment modalities should be considered (Kasule, 2002).

Respiratory medications are defined as the prescription drugs for conditions and diseases relating to the lungs or breathing. Usually powder or solution is used together with special device designed to carry the drugs to the target site effectively (Abdul Aziz et. al., 2014). The immune system and immunological products play a critical role in defending the human body against pathogenic organisms (Marcos et. al., 2003). Vaccines are preparations of antigenic materials that are given with the object of inducing in the recipient active immunity to specific infecting agents or toxins. They may contain living or killed micro-organisms, bacterial toxoids, or antigenic materials from particular parts of the infecting organism, which may be derived from the organism or produced by recombinant DNA technology (Martindale, 5th edition).

Religious and moral objections to vaccination are the key in understanding vaccine refusal today. Opposition to immunization programs of selected Muslim communities was detected during the poliovirus immunization programs in Nigeria, Pakistan and Afghanistan in 2003 (Warraich, 2009). Ultimately it falls upon Muslims in the pharmaceutical profession to carry out research into this issue and come up with *halal* alternatives for active ingredients or excipients, so that the question of the dubious nature of medicinal ingredients does not arise. Responsibility also falls on the rest of the society to lobby for the use of *halal* ingredients in medicinal preparations (Gambles, 2010).

This study was carried out to assess the *halal* status of respiratory products, immunological products and vaccines available with regard to their APIs and excipients where sources of APIs and excipients were identified and classified into *halal*, *mushbooh* or *haram*. Also, to identify common types of ingredients that are categorized as *haram* and *mushbooh*.

METHODOLOGIES

This descriptive exploratory study was done in two government hospitals located in Klang Valley. After getting approval from the hospitals, the hospital

formulary was obtained, and products screened and sorted out according to the selected therapeutic areas of the study. Data were collected from product information leaflets and packages which are available at the pharmacy store, and the in-patient and out-patient pharmacy. The collected data such as generic name, brand name, dosage form, strength, APIs, excipients and manufacturer were filled into developed Data Collection Form.

There were two approaches used to obtain details about the products. The first was through enquiry letters and response forms sent to respective manufacturers to be completed with the details regarding the products. They were also required to provide *halal* certificates to prove the ingredients used were *halal*. The feedback received from the manufacturers about the source of ingredients was included in the data collection form as the first priority. If the manufacturers did not respond within the research period, the analysis was performed using the second approach.

Through the second method, the source of each active ingredient and excipient was determined by using the standard pharmaceutical references such as British Pharmacopeia, *Halal* Index, Merck, Martindale, Excipient Handbook, Remington and US Pharmacopeia. Sources of ingredients were classified into eight main categories, namely plant, animal, synthetic, semi-synthetic, natural chemical, mineral, microorganism and Genetically Modified Organism (GMO). They were then classified into *halal*, *mushbooh* or *haram* following guidelines and definition in MS2424:2012, *Halal* Pharmaceuticals-General Guideline.

The *halal* status of pharmaceutical products would depend on *halal* nature of active ingredients and excipients. If both APIs and excipients were *halal*, the product would be categorized as *halal*. If APIs or excipients consist of *mushbooh* then the product would be categorized as *mushbooh*. If any of these is of *haram* origin, the product would be classified as *haram*. The same product found in both hospitals was regarded as one product. The data collected were analysed using Microsoft Office Excel and Google document where descriptive analysis involving frequencies and percentages were generated to present the results of the analysis.

RESULTS AND DISCUSSIONS

There were 123 medications considered in this study; 91 respiratory products, and 32 immunological products and vaccines. For the respiratory products, 56% (N=51) were considered *halal* and 44% (N=40) *mushbooh*. There was no *haram* product reported. With regard to 49 APIs contained in the 91 products, 79.6% (N=39) were reported as *halal*

while 20.4% (N=10) *mushbooh*. On the other hand, of the 124 excipients analysed, 83.1% (N=103) were found to be *halal* and 16.9% (N=21) *mushbooh*.

Of the 32 immunological products and vaccines, 96.9% (N=31) were reported as *mushbooh* and 3.1% (N=1) *haram*. There was not a single *halal* product in this product category. On the 42 APIs of the 32 products, 100% were *mushbooh*, i.e., there were no *halal* or *haram* APIs reported. However, from 52 excipients studied, 57.7% (N=30) were reported as *halal*, 40.4% (N=21) *mushbooh* and 1.9% (N=1) *haram*. Table 1 summarizes the *halal* status of the respiratory products, immunological products and vaccines.

Table 1: Summary of *halal* status of the respiratory products, immunological products and vaccines

Status	Halal	Mushbooh	Haram
Respiratory products (N = 91)	56%	44%	0%
API respiratory (N = 49)	79.6%	20.4%	-
Excipients (N = 124)	83.1%	16.9%	-
Immunological products and vaccines (N = 32)	-	96.9%	3.1%
API respiratory (N = 42)	-	100%	-
Excipients (N = 52)	57.7%	40.4%	1.9%

This study showed that generally most of the respiratory products were *halal* followed by *mushbooh*. No *haram* products were indicated under the respiratory product group. However, there was no *halal* option among immunological products and vaccines. The majority of immunological products and vaccines were *mushbooh*, while one product was *haram*.

Halal and *haram* are clearly stated and defined in the Quran (Azmi & Hadeer, 2013). Even though respiratory pharmaceutical products or medications are among the most commonly used products in the community and hospital settings, Muslims are required to avoid any food or medication that originates from doubtful sources. Products which contain questionable or unknown sources of ingredients are classified as *mushbooh* depending on the nature of the product and how it is made. For instance, lactose was found to be the major substance that contributed to the assertion of *mushbooh* category in this study. According to a previous study, lactose is a *halal* substance but because some of the preparation processes involve the use of bones or bone related substances, it is categorized as *mushbooh* (Waarden & Dalen, 2010). In this study, only three companies clarified that lactose used in their products were derived from *halal* sources which were Noripharma Sdn. Bhd., Malaysian Pharmaceutical Industries Sdn. Bhd. and UPHA Pharmaceutical (CCM) Sdn. Bhd.

Another example of *mushbooh* substance found in this study was magnesium stearate. Magnesium is one of the most widely used lubricants in the tablet production of pharmaceutical products (Bashir et al., 2001). It can be obtained either from plant or animal, or both sources. Due to the uncertainty of its origin, the *halal* status of magnesium stearate has become controversial. Other than that, products containing alcohol as excipients are also categorized as *mushbooh*. It is known that ethanol can be derived from two processes, either synthetically produced from the laboratory or naturally from winemaking processes. Alcohols obtained from the winemaking industry are forbidden in Islam while alcohols which are purely synthesized from laboratory are considered permissible (Jusmaliani & Nasution, 2009).

Also, gelatine is widely used as a binding agent for tablets, pastilles, micro-encapsulation and sugar-coated pills in the pharmaceutical industry (Kasulse, 2002). The most widely used gelatines originate from porcine and bovine sources. Since gelatine is derived from animal bones, skin and tendons, it is likely to be *haram* unless it is from animals or birds that are allowed to be eaten by Muslims, and which have been slaughtered in a *halal* way (Abdul Aziz et al., 2014). However, there are some alternatives available that can be used to replace the animal-based gelatine such as plant-based gelling substances which include Carrageenans (carrageenins), agar-agar (seaweed), pectin or modified forms of starch and cellulose. Another alternative is to use Hypromellose (HPMC; E-Number: E464) isolated from natural sources such as plant materials or bacterial cell cultures (Gambles, 2010).

CONCLUSION

This study indicated that most excipients were *halal*, but medicines became *mushbooh* due to the presence of certain excipients which could have been replaced with *halal* alternatives. This insight should encourage pharmaceutical manufacturers to go for *halal* certification to meet the demand for *halal* medications. This study also provides additional information from existing research regarding *halal* pharmaceutical products available in Malaysia. It may also serve as a platform for future researchers to explore other aspects that were not covered in this study such as *halal* compliance during manufacturing and preparation processes, and the potential harmfulness of the pharmaceutical products.

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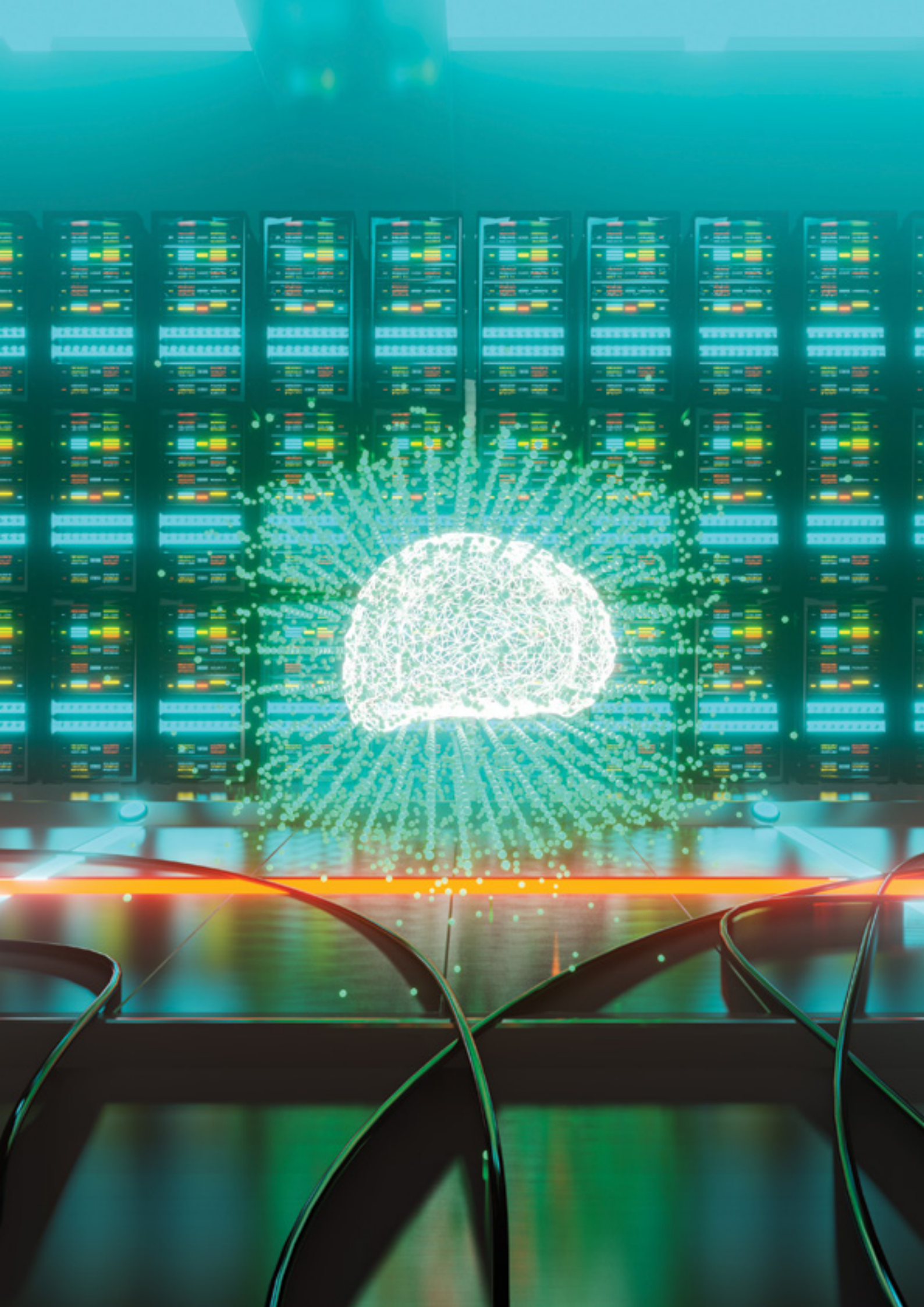
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