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The main objectives of this journal are to;

- nurture the Allied Health Sciences Professionals in their research dissemination/article writing.
- provide a chance and to review/share knowledge in the related research and professional interest.
- facilitate academics and researchers to elevate their intellectual level interacting through this journal.

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This journal will provide an avenue for academics to enhance their intellectual level by reviewing and submitting research articles. This journal broadly covers disciplines namely Nutrition and dietetics, Medical Imaging, Biomedical Sciences, Physiotherapy, Speech and audiology, and Optometry. Furthermore, it covers the sub-disciplines within Nutrition and dietetics (Anthropometric, Biochemical and clinical Nutritional Status Assessments, etc.), in Medical Imaging (Radiographic Techniques, Body, Breast, Musculoskeletal, Cardiovascular, and Paediatrics Imaging), Biomedical Sciences (Biochemistry, Bioinformatics, Immunology, Biomedical Engineering, Biophysics, Biotechnology, Cell Biology, Embryology, Endocrinology, Genetics, Medicinal/Pharmaceutical Chemistry, Microbiology, Parasitology, Pharmacology, Physiology, and Toxicology, etc) Physiotherapy (Rehabilitation, Physical Therapy, and Physiotherapy, etc), Speech & Audiology(Clinical Audiology, Educational Speech-Language Pathology, and Speech Therapy, etc) and Optometry (Clinical, Industrial Optometry and issues on Optometry, etc).

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International Journal of Allied Health Sciences

Volume 8, Issue Number 1, 2024

# TABLE OF CONTENTS

# Childhood picky eating behaviour and its impact on the growth of young children: A scoping review

**Nurshazwani Ahmad Nazri, BSc.**
Department of Nutrition Sciences,
Kulliyyah of Allied Health Sciences,
International Islamic University Malaysia,
Jalan Sultan Ahmad Shah,
Bandar Indera Mahkota,
25200 Kuantan, Pahang
nurshazwani.nazri@live.iium.edu.my

***Nurul Hazirah Jaafar, PhD**
[1]Food Security and Public Health Nutrition Research Group (FOSTER),
[2]Department of Nutrition Sciences,
Kulliyyah of Allied Health Sciences,
International Islamic University Malaysia,
Jalan Sultan Ahmad Shah,
Bandar Indera Mahkota,
25200 Kuantan, Pahang
hazirahjaafar@iium.edu.my

**Suriati Zakaria, BSc.**
Unit Pemakanan, Pejabat Kesihatan Daerah Kuantan, Jalan Tengku Muhammad, Alor Akar, 25050 Kuantan, Pahang, Malaysia.
suriati_z@moh.gov.my

**Wan Azdie Mohd Abu Bakar, PhD**
[1]Food Security and Public Health Nutrition Research Group (FOSTER),
[2]Department of Nutrition Sciences,
Kulliyyah of Allied Health Sciences,
International Islamic University Malaysia,
Jalan Sultan Ahmad Shah,
Bandar Indera Mahkota,
25200 Kuantan, Pahang
wazdie@iium.edu.my

**Nuraniza Azahari, PhD**
[1]Food Security and Public Health Nutrition Research Group (FOSTER),
[2]Department of Nutrition Sciences,
Kulliyyah of Allied Health Sciences,
International Islamic University Malaysia,
Jalan Sultan Ahmad Shah,
Bandar Indera Mahkota,
25200 Kuantan, Pahang
nuraniza@iium.edu.my

**Syifak Izhar Hisham, PhD**
Faculty of Computing, Universiti Malaysia Pahang, 26600 Pekan, Pahang, Malaysia.
syifakizhar@ump.edu.my

**Siti Sabariah Buhari, PhD**
Centre of Nutrition and Dietetics,
Faculty of Health Sciences,
Universiti Teknologi Mara (UiTM),
Cawangan Selangor,
Kampus Puncak Alam,
42300 Puncak Alam, Selangor
sabariah6204@uitm.edu.my

**Corresponding author:* Nurul Hazirah Jaafar,
hazirahjaafar@iium.edu.my

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## Abstract:

**Background:** Malnutrition occurs due to inadequate food intake and low daily energy intake, often associated with picky eating behaviour (PEB). Picky eaters have limited food choices and poor dietary diversity, leading to malnutrition. Therefore, this article aims to explore the impact of childhood eating behaviour on a young child's growth. **Method:** Articles were identified through six electronic search engines using 12 keywords. Articles were included if they met the following criteria: (1) sample of study involved

young children (below six years old); (2) study outcome focusing on the impact of eating behaviour on the growth of the children (3) published in English. Studies were excluded if they were review articles, qualitative studies, and involved children with clinical health problems. **Result:** A total of 413 articles were screened, and 8 full-text articles were evaluated. The prevalence rates of selective eaters varied greatly from 25% in India to 77% in Iraq. The screening tools used for identifying PEB varied, with the Children's Eating Behaviour Questionnaire (CEBQ) being the most commonly used tool. Short-term implications of PEB on children include the risk of poor diet intake and limited consumption of a variety of food groups, which can lead to adverse health outcomes. Meanwhile, long-term implications include the development of eating disorders in adulthood. **Conclusion:** Our findings reveal that PEB has had a significant impact on the growth of young children. Despite the increasing concern about the implications of PEB, there is a lack of sufficient research studies on the effects of this behaviour on the nutritional status of young children.

**Keywords:** eating behaviour; picky eaters; nutritional status; growth; young children

## Introduction:

Proper nutrition is essential throughout the different stages of life. In the case of infants, exclusive breastfeeding is recommended for the first six months, followed by the introduction of complementary feeding up to two years of age (World Health Organization (WHO), 2021; National Coordinating Committee on Food and Nutrition, 2010). The age group of 0-5 years is particularly critical for ensuring optimal nutrition to support growth and good health in children. However, global efforts to improve nutrition quality and prevent undernutrition in young children are still challenging. The double burden of malnutrition, encompassing underweight, stunting, wasting, and obesity (WHO, 2016), contributes to nearly half of all deaths in children under 5 worldwide (United Nations Children's Fund (UNICEF), 2022).

Undernutrition often arises due to insufficient food intake and low daily energy intake (WHO, 2016; Norliza et al., 2021; Mok et al., 2022), and picky eating behaviour (PEB) may play a role in this context. Individuals with PEB exhibit restricted food selection and limited dietary variety, which can lead to malnutrition (Hikmah & Nur Islami, 2022; Mok et al., 2022). Food neophobia and picky eating are common behaviours observed during children's growth and development. Food neophobia refers to the rejection of new foods, while PEB involves inadequate consumption of both familiar and unfamiliar foods (Dovey et al., 2008). While picky eating is not a medical term and encompasses a wide range of behaviours, it can negatively impact a child's diet quality and restrict the consumption of diverse food groups, leading to adverse health outcomes. It is crucial to review how researchers define picky eating, determine the prevalence of picky eaters, and identify potential effect modifiers that could impact the association between eating behaviours and weight status. These modifiers include the types of foods offered to the child, parenting styles, breastfeeding, and complementary feeding. Such a review will help shed light on the topic and provide valuable insights. Therefore, this review aims to explore the effects of childhood eating behaviour on a child's growth.

## Methodology:

The protocol of this scoping review was chosen due to emerging evidence on childhood PEB and its impact on the growth of young children, whilst still ensuring a rigorous and transparent method for mapping (Arksey & O'Malley, 2005). The reporting adheres to the five-stage framework by Arksey & O'Malley (2005), incorporating the checklist from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) extension for scoping reviews (Tricco et al., 2018).

### Stage 1: Identify the Research Questions

The research questions used to guide the search strategy include: 1) What tools or methods have been used to identify young children with picky eating? and 2) What is the impact of eating behaviour towards nutritional status among young children? The studies were then further evaluated by referring to the guided research questions and eligibility criteria.

### Stage 2: Identifying Relevant Studies

Various databases such as PubMed, Science Direct, EBSCO (Medline), Scopus, Google Scholars, and ProQuest were searched to select studies from 2017 to February 2023. There were no restrictions imposed on the study design and publication status. In total, 8

articles were critically reviewed. The search terms used were "Picky" (picky, fuss*, choosy, selective) AND "Growth" (body weight, nutrition*, nutritional status) AND "Child" (child*, young child*, paediat*, pediat*, todd*).

**Stage 3: Study Selection**

Research articles were evaluated using the PICOS (Population, Intervention, Comparators, Outcome, and Study Design) model (Table 1) (Liberati et al., 2009). The following studies were included if they met the following criteria: (1) sample of study involved young children (below six years old); (2) study outcome focusing on the impact of eating behaviour on the growth of the children (3) published in English. Studies were excluded if they were review articles, qualitative studies and involved children with clinical health problems such as autism, down syndrome, dyslexia, global development delay (GDD) or health problem interfering with eating habits.

Figure 1 shows the modified PRISMA flow diagram that provides an overview of the process for selecting articles. Initially, 413 records were screened and 131 duplicates were removed. Out of the remaining 282 articles, only ten were relevant to the study topic. Two reports lacked full articles and were excluded. Therefore, eight publications were included that focused on the association between eating behaviour and nutritional status in young children.

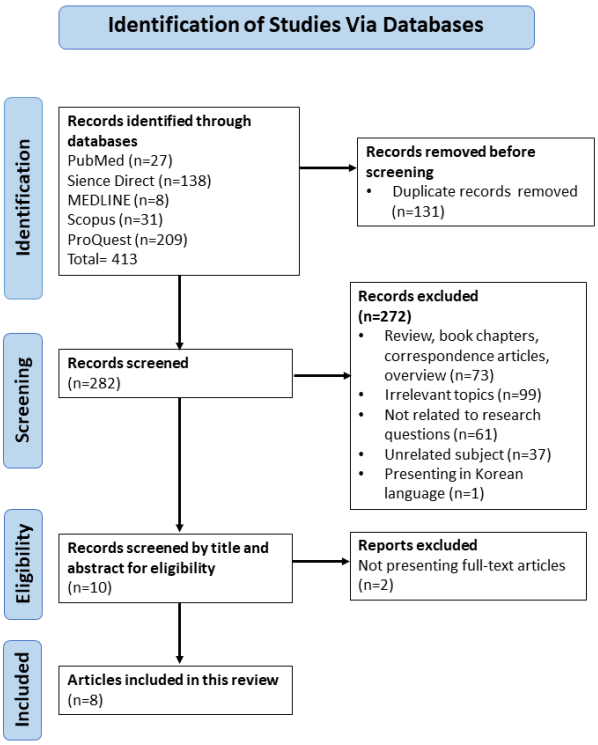


Figure 1: PRISMA Flow Diagram

Table 1: PICOS criteria for inclusion and exclusion of studies

| Category | Inclusion | Exclusion |
|---|---|---|
| Participants | Children aged 0–6 years old. | Children with chronic illnesses or special nutritional needs that will impact their dietary diversity. |
| Intervention | None | None |
| Comparator | Prevalence of PEB. Screening tools. Association between PEB and young children's nutritional status. | None |
| Outcomes | Determination of PEB. Nutrition-related outcomes such as anthropometric measurements (body mass index, waist circumference), dietary intakes, or dietary diversity score. | None |
| Study design | Cross-sectionals, mixed-method, randomized controlled trials, pre-post design quasi-experimental studies. | Review articles. Qualitative studies. |

**Stage 4: Charting the Data**

The main author conducted a thorough search, screening the articles for both quality and relevance based on the established criteria and research question. Meanwhile, the other reviewers independently analyzed each paper and recorded key

details such as the author, year of publication, location of the study, study design, study population, study size, screening tools used to identify picky eating, and the outcomes/findings of child behaviours associated with picky eating.

**Stage 5: Collating, Summarising and Reporting Results**

After screening several studies, eight of them were deemed relevant and selected for further analysis. The authors reviewed these eight publications and extracted the data into a spreadsheet (Table 2). The findings were then independently analyzed by all authors, who identified the factors associated with PEB and its impact on nutritional status. These factors were characterized to help develop successful interventions, and the results were presented in a supplementary table. Finally, the authors discussed the findings, and a consensus was reached.

## Results:

**Study Characteristics**

The selected studies had various characteristics, as shown in the Supplementary table. This review includes seven cross-sectional studies (mentioned in the seven citations) and one cohort research (Derks et al., 2018). The participants' ages ranged from 12 months (Kwon et al., 2017; Shettiwar & Wade, 2019; Kumar et al., 2018) to 6 years old (Kumar et al., 2018; Hikmah & Nur Islami, 2022; Derks et al., 2018), and the sample sizes ranged from 192 (Hikmah & Nur Islami, 2022) to 3,331 children (Derks et al., 2018). In total, these eight articles had 7,196 participants.

Most studies on eating behaviour (87.5%; n=7) were found in Asia, specifically Malaysia, Iraq, India, Taiwan, Vietnam, and Singapore. While only a small portion of the study (12.5%, n=1) was completed in the Netherlands.

**Prevalence of Picky Eating Behaviour**

The prevalence of picky eaters varied across different studies, as presented in Table 1. Reported prevalence rates ranged from 25% in India (Shettiwar & Wade, 2019) to 77% in Iraq (Yaqob Qazaryan & Kazim Karim, 2019). Additionally, Kumar et al. (2018) reported age-specific prevalence, revealing an increase in PEB from 32% to 69% as age increased. However, two articles (Derks et al., 2018; Tan et al., 2022) did not provide data on the prevalence of picky eaters. Instead, they focused on examining the association between picky eating behaviour and nutritional status outcomes in their respective study populations.

**Screening tools for PEB**

The identification of picky eaters in the studies involved the use of various screening tools. In total, nine studies employed four different tools and utilized a total of 14 scales, as summarized in Table 2. The CEBQ by Wardle et al. (2001) was the most used tool, accounting for 75% (n=6) of the studies (Hikmah & Nur Islami, 2022; Yaqob Qazaryan & Kazim Karim, 2019; Chao, 2018; Tan et al., 2022; Derks et al., 2018; Shettiwar & Wade, 2019).

The remaining 25% (n=2) of the studies employed different screening tools, including self-administered surveys (Kwon et al., 2017), a modified version of the United Kingdom Department of Health Survey of the Diets of British School Children (UKSQ) (Chao, 2018), and Stanford Feeding Questionnaire (SFQ) on Child-Parent Feeding Behavior (Kumar et al., 2018). Despite the variation in tools used, all eight studies relied on parental reports regarding their children's picky eating behaviour.

**Association of Eating Behaviour and Nutritional Status Among Young Children**

As shown in the Supplementary Table, all eight articles indicated a significant association ($p<0.05$) between PEB and the nutritional status of young children. These associations were observed in various parameters, including weight-for-age (WAZ), height-for-age (HAZ), and body mass index (BMI)-for-age (BAZ). Specifically, the studies consistently demonstrated that picky eaters had significantly lower z-scores in WAZ, HAZ, and BAZ compared to non-picky eaters ($p<0.05$) (Hikmah & Nur Islami, 2022; Tan et al., 2022; Yaqob Qazaryan & Kazim Karim, 2019; Derks et al., 2018; Shettiwar & Wade, 2019; Chao, 2018; Kumar et al., 2018; Kwon et al., 2017). Overall, the studies revealed that the picky eater group had lower z-score values below the median (z-score 0) for WAZ, HAZ, and BAZ compared to the WHO Child Growth Standards (2016).

## Discussion:

**Prevalence of Picky Eating Behaviour**

The key findings of this scoping review pertain to the prevalence of picky eating, the diverse screening tools employed to identify picky eaters, and the association between eating behaviour and nutritional status in

Table 2: Instruments and scales used in determining PEB

| Author (year) | Screening Tools | n (%) |
|---|---|---|
| ***1. Food responsiveness/ length of time for each meal and eating activities*** | | |
| Hikmah & Nur Islami (2022), Yaqob Qazaryan & Kazim Karim (2019), Chao (2018), Tan et al. (2022), Derks et al (2018), and Shettiwar & Wade (2019) | CEBQ | 6 (75.0) |
| ***2. Emotional overeating*** | | |
| Hikmah & Nur Islami (2022), Yaqob Qazaryan & Kazim Karim (2019), Chao (2018), Tan et al. (2022), Derks et al (2018), and Shettiwar & Wade (2019) | CEBQ | 6 (75.0) |
| ***3. Food preferences/ high selective intake*** | | |
| Hikmah & Nur Islami (2022), Yaqob Qazaryan & Kazim Karim (2019), Chao (2018), Tan et al. (2022), Derks et al (2018), and Shettiwar & Wade (2019) | CEBQ | 7 (87.5) |
| Chao (2018) | Modified version of UKSQ | |
| Kumar et al. (2018) | SFQ | |
| ***4. Desire to drink*** | | |
| Hikmah & Nur Islami (2022), Yaqob Qazaryan & Kazim Karim (2019), Chao (2018), Tan et al. (2022), and Shettiwar & Wade (2019) | CEBQ | 4 (50.0) |
| ***5. Satiety responsiveness*** | | |
| Hikmah & Nur Islami (2022), Yaqob Qazaryan & Kazim Karim (2019), Tan et al. (2022), Derks et al (2018), and Shettiwar & Wade (2019) | CEBQ | 5 (62.5) |
| ***6. Slowness in eating*** | | |
| Hikmah & Nur Islami (2022), Yaqob Qazaryan & Kazim Karim (2019), Tan et al. (2022), and Shettiwar & Wade (2019) | CEBQ | 4 (50.0) |
| ***7. Emotional undereating*** | | |
| Hikmah & Nur Islami (2022), Yaqob Qazaryan & Kazim Karim (2019), Tan et al. (2022), and Shettiwar & Wade (2019) | CEBQ | 4 (50.0) |
| ***8. Food fussiness/ refusal of specific food groups*** | | |
| Hikmah & Nur Islami (2022), Yaqob Qazaryan & Kazim Karim (2019), Tan et al. (2022), and Shettiwar & Wade (2019) | CEBQ | 5 (62.5) |

| | | |
|---|---|---|
| Kwon et al. (2017) | Self-administered survey | |
| ***9. Specific food preparation methods*** | | |
| Kwon et al. (2017) | Self-administered survey | 1 (12.5) |
| ***10. Eating a small amount/ number of meals, diversity and amount of food consumed per day*** | | |
| Kwon (2017) | Self-administered survey | 2 (25.0) |
| ***11. Emotional or behaviors/ eating behaviors*** | | |
| Chao (2018) | Modified version of UKSQ | 2 (25.0) |
| ***12. Neophobic behavior/Fear of feeding*** | | |
| Kwon et al. (2017) | Self-administered survey | 2 (25.0) |
| Kumar et al. (2018) | SFQ | |
| ***13. Enjoyment of food*** | | |
| Hikmah & Nur Islami (2022), Yaqob Qazaryan & Kazim Karim (2019), Chao (2018), Tan et al. (2022), Derks et al (2018), and Shettiwar & Wade (2019) | CEBQ | 6 (75.0) |
| ***14. Parental misperception*** | | |
| Kumar et al. (2018) | SFQ | 1 (12.5) |

young children. Currently, there is no standardized definition of picky eating, nor is there a universally accepted and well-defined assessment method (Taylor & Emmett, 2019). The prevalence of picky eaters varied widely across studies and can be attributed to differences in study designs, assessment tools, and sociocultural factors employed in various studies. Additionally, this review identified that the age at which children develop persistent picky eating behaviour may vary. Yaqob Qazaryan & Kazim Karim (2019) observed the highest prevalence of picky eaters emerging at 36 months of age. These findings align with a previous systematic review by Fitriana et al. (2019) and Taylor & Emmett (2019), which indicated that the peak prevalence of picky eating occurs at about age 3 years and remains stable with increasing age. At this age, the children were picky as they were reflecting on the parental feeding styles in response to increased child autonomy (Taylor & Emmett, 2019).

**Screening tools**

Similarly, we found a varying screening tool used to identify picky eaters among the respondents. However, despite the differences, all the screening tools were answered based on parental reports about their children's eating behaviour. Several of these tools have been validated. Examples include CEBQ, a self-administered questionnaire by Kwon et al. (2017), the UKSQ, and SFQ.

Most of the studies reported on the scoring of the assessment tools used to assess eating style in children. For the CEBQ, a self-administered questionnaire by Kwon et al. (2017), eating style is assessed based on the level of scoring. Meanwhile, Chao (2018) has not reported on the clinical practicability and scoring implications for the Modified version of UKSQ. Thus, even though PEB has been considered a complex behaviour, the accurate definition, assessment, and standardized method to identify PEB is not yet established.

**Association of Eating Behaviour and Nutritional Status Among Young Children**

Children can exhibit picky eating behaviour due to various factors, including food and drink colour preferences (Kumar et al., 2018), taste perception (Keller et al., 2002; Petty et al., 2020), food texture (Kumar et al., 2018), refusal of specific food groups (Yaqob Qazaryan & Kazim Karim, 2019; Shettiwar & Wade, 2019), and preferences for certain food preparation methods (Kwon et al., 2017; Kumar et al., 2018; Shettiwar & Wade, 2019). PEB affects their dietary patterns by limiting the variety of foods consumed, which can lead to a lower quality diet in terms of certain micronutrients and overall energy intake (Norliza, 2021; Mok et al., 2022). Furthermore, pickiness among young children may have negative consequences on developmental quality, physical

activity levels, and general health status (Taylor & Emmett, 2019).

## Limitation:

As the selection was restricted to articles in English, relevant publications in other languages may have been missed. Besides, the determinants of picky eaters were varying as different studies used different definitions for picky eating, resulting in a wide range of picky eater prevalence and making it unclear whether this finding would hold true for everyone.

## Conclusion:

In this review, we provide insights into the prevalence of picky eaters among young children and its impact on their growth. The identification of picky eaters in the studies involved the use of various screening tools as different researchers may define PEB differently. The evidence gathered from various studies consistently demonstrated that PEB had significantly impacted the growth of young children for all growth indicators. In conclusion, the findings from this review emphasize the importance of addressing PEB in children and taking immediate action to manage them. Interventions such as nutritional education or guidance for parents should be developed by researchers and relevant organizations, including the Ministry of Health, to improve the nutritional status of children globally. Further research is warranted to explore effective strategies for addressing picky eating and its long-term implications on health outcomes.

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# APPENDIX

**Supplementary table: Characteristics of the studies.**

| Author (year) | Study Sample | Study Design | Screening tools for PEB | Prevalence of Picky Eater | Outcome/ Findings |
|---|---|---|---|---|---|
| Hikmah & Nur Islami (2022) | 192 children aged 4-5 years. | Cross-sectional | Children's Eating Behavior Questionnaire (CEBQ). | 31.8% | **Behavior assessment:**<br>1. A lower degree of food responsiveness, enjoyment of food and emotional overeating combined with higher degree of food fussiness and slowness in eating were prevalent among picky eaters ($p<0.05$).<br><br>**Association PEB and nutritional status:**<br>1. PEB has significant association ($p<0.05$) with WAZ, HAZ and BAZ.<br>2. More picky eaters were underweight/stunted/wasted while more non-picky eaters were overweight/obese. |
| Kwon et al. (2017) | 184 children aged 1-5 years. | Cross-sectional | Self-administered survey of 21 items | None | **Behavior assessment:**<br>1. The proportion of participants with the behavior: "eating small amounts" (29.9%); "limited variety" (66.9%); "preference for a specific food-preparation method" (49.5%); "refusal to eat specific food groups" (44.0%); and "neophobic behavior" (32.6%). |

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| | | | | | 2. Older children aged 4 to 5 years showed higher rates of "neophobic behavior" (47.5%, p = 0.0032).<br><br>**Association PEB and nutritional status:**<br><br>1. Picky eaters "eating small amounts" aged 4 to 5 years had significantly lower z-scores for all three growth indices.<br><br>2. Picky eaters with "refusal of specific food groups" were related with lower HAZ in this age group. |
| Yaqob Qazaryan & Kazim Karim (2019) | 800 children aged 2-4 years. | Cross-sectional | Eating behavior questionnaires inspired by CEBQ. | 77% | **Behavior assessment:**<br><br>1. Picky eaters were commonly:<br><br>Eating sweets or snacks instead of meals (52.6%); refusing food, particularly fruits and vegetables (37.8%); reluctant to eat regular meals (27.6%); do not like to try new food (neophobia, 23.3%); ingestion of specific kinds of food (16%); and excessive drinking of milk (14.2%).<br><br>**Association PEB and nutritional status:**<br><br>1. Picky eaters had significantly lower average weight-for-age, height-for-age, and BMI-for-age percentiles. |
| Chao (2018) | 300 children aged 2-4 years | Cross-sectional | Modified version of United Kingdom Department of Health | 54% | **Behavior assessment:** |

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| | | | Survey of the Diets of British School Children Questionnaire (UKSQ) (preferences for food and food types) and CEBQ. | | 1. The picky eater group behavior included: being unwilling to eat regular meals (18.5%); refusing food, particularly fruit and vegetables (16.7%); eating sweets or snacks instead of meals (14.8%); being unwilling to try new foods (14.2%); excessive drinking of milk (14.2%) and accepting only a few types of food (13.6%).<br><br>2. Picky eaters did not like to eat meat (37.1%); vegetables (38.9%); fruit (22.2%) and specific kinds of vegetables or fruit (21.6%).<br><br>3. Significant lower number of accepted foods and lower score in food preference were found in picky group (15.1 ± 3.7 vs. 26.7 ± 4.1, P < 0.001; 3.0 ± 1.3 vs. 3.6 ± 1.1, P < 0.001).<br><br>**Association PEB and nutritional status:**<br><br>1. Compared with non-picky eaters, WAZ, HAZ, and BAZ in picky eaters was 0.91, 0.73, and 0.44 SD lower, respectively.<br><br>2. There were significant differences of rates in the weight-for-age, height-for-age, and BMI-for-age percentiles <15, between picky and non-picky eaters (P= 0.04, 0.023, and 0.005, respectively). |
| Tan et al. (2022) | 500 children aged 24–59 months | Cross-sectional | CEBQ | None | **Behavior assessment:**<br><br>1. “Food approach” eating behaviour were positively correlated as each scale independently. |

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| | | | | | 2. Meanwhile, the "food avoidant" eating behaviour demonstrated positive inter-correlations between each scale independently.<br><br>**Association PEB and nutritional status:**<br><br>1. There were significant positive association between food responsiveness, emotional overeating, enjoyment of food with BAZ ($p<0.05$; unstandardized regression coefficient: 0.17 to 0.38).<br><br>2. There were significant negative association between satiety responsiveness, slowness of eating, food fussiness with BAZ ($p<0.01$; unstandardized degression coefficient: −0.35 to −0.36). |
| Derks et al. (2018) | 7294 children recruited at birth but only 3331 children at age 4 years completed the study to the end at 10 years old. | Cross-sectional | CEBQ | None | **Behavior assessment:**<br><br>1. Non-picky eaters scores higher to food approaching behavior, namely: emotional overeating, food responsiveness and enjoyment of food, as well as the subscale satiety responsiveness.<br><br>**Association PEB and nutritional status:**<br><br>1. Cross-lagged models at both directions showed that a higher BMI at the age of 4 years predicted more food responsiveness and enjoyment of food and less satiety responsiveness at 10 years (e.g. satiety responsiveness: $\beta = -0.10$, 95% CI = −0.14, −0.07). |

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| Shettiwar & Wade (2019) | 200 parents of children between 1 to 5 years age | Prospective cohort | CEBQ | 25 % | **Behavior assessment:**<br>1. Maximum age of PEB was 49 to 60 months (38%).<br><br>**Association PEB and nutritional status:**<br>1. 26% of subjects with PEB had HAZ < -3SD (severely stunted).<br>2. 38% of subjects with PEB had weight-for-height z-score (WHZ) < -3SD (severely wasted) as compared to only 4% in non-picky eaters. |
| Kumar et al. (2018) | 1652 parents of children between 1-6 years age | Cross-sectional | Stanford Feeding Questionnaire (SFQ) on Child- Parent Feeding Behavior | 32.2% at 1 year of age to 69.2 % at 6 years of age | **Behavior assessment:**<br>1. Two or more criteria were met to determine picky eater, characterized by eating a limited variety of foods (94%) with strong likes (93%) and dislikes (100%), not accepting new foods readily (0%) and strong opinions about the preparation of food (68%).<br><br>**Association PEB and nutritional status:**<br>1. The mean weight and height of the children is lower in picky eaters than the non-picky eaters. |

# A comparison of noncontact and ultrasound A-scan in the measurement of axial length in myopic subjects

**Nur Syakirah Mardhiah Samsul Bahari, B. Optom**
Optometry and Vision Science Program,
Faculty of Health Sciences,
Universiti Kebangsaan Malaysia,
Jalan Raja Muda Abdul Aziz,
50300 Kuala Lumpur
A163607@siswa.ukm.edu.my

***Bariah Mohd-Ali, PhD**
Optometry and Vision Science Program,
Faculty of Health Sciences,
Universiti Kebangsaan Malaysia,
Jalan Raja Muda Abdul Aziz,
50300 Kuala Lumpur
bariah@ukm.edu.my

**Mizhanim Mohamad Shahimin, PhD**
Optometry and Vision Science Program,
Faculty of Health Sciences,
Universiti Kebangsaan Malaysia,
Jalan Raja Muda Abdul Aziz,
50300 Kuala Lumpur
mizhanim@ukm.edu.my

**Norlaili Arif, MOptom**
Optometry and Vision Science Program,
Faculty of Health Sciences,
Universiti Kebangsaan Malaysia,
Jalan Raja Muda Abdul Aziz,
50300 Kuala Lumpur
norlailiarif@ukm.edu.my

***Corresponding author:** Bariah Mohd-Ali,
bariah@ukm.edu.my

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## Abstract:

**Introduction:** Myopia is a common type of refractive error seen globally. As myopia increases, the axial length (AL) elongates and brings risks of vision impairment in later life. Therefore, AL measurement is an important indicator for myopia management and must be measured accurately. In this study, we compared the difference between AL measurements from two instruments available at the University Kebangsaan Malaysia (UKM) Optometry clinic for reference purposes. **Methodology:** A total of 90 healthy myopic subjects (14 males and 76 females) with a mean age of 22.03 ± 1.14 years were enrolled in this cross-sectional study. Clinical investigations that included visual acuity (VA), refraction and axial length measurement using optical and ultrasound biometry were carried out. **Results:** The mean spherical equivalent refractive error (SE), and axial length measured by optical biometry and ultrasound were found to be -3.04 ± 1.61 D, 24.74 ± 0.90 mm and 24.50 ± 0.86 mm respectively. Paired sample t-test showed that subjects' axial lengths measured by ultrasound A-scan were significantly lower than optical biometry ($p < 0.05$). Negative and strong correlations were found between the degree of myopia and axial length ($r_s = -0.609$, $p < 0.001$). Regression showed that axial length measurement accounted for a significant 33.5% of the degree of myopia, $R^2 = 0.335$, adjusted $R^2 = 0.328$, $F = (1, 88) = 44.38$, $p < 0.01$. **Conclusion:** This study concludes that AL measured using ultrasound is shorter than optical biometry. Measurements of AL should be done consistently with the same instrument to avoid any discrepancies during myopia management.

**Keywords:** myopia, axial length, refraction, ultrasound biometry, optical biometry

## Introduction:

Myopia is a common refractive error that affects the majority of the population. Myopia, as defined qualitatively by Flincroft et al. (2019), is a refractive error in which, when ocular accommodation is relaxed, light rays entering the eye parallel to the optic axis are focused in front of the retina. This typically happens when the eyeball is too long from front to back, although it can also be brought on by an overly curved cornea or a lens with a higher optical power. By quantitative definition, myopia is a condition in which, when ocular accommodation is relaxed, an eye's spherical equivalent refractive error is ≤ -0.50 D. For many, visual disability of myopia is easily remedied with corrective devices (such as contact lenses or spectacles) but the risks of uncorrected visual impairment rise with increasing myopia. For some, during adulthood, myopia can result in permanent visual disability due to co-morbid conditions such as myopic macular degeneration, retinal detachment and glaucoma (Chen et al 2012; William et al 2015). Data from Japan and Taiwan suggest that myopic macular degeneration is already a major cause of blindness in both countries (Hsu et al 2004; Iwase et al 2006).

According to Holden et al. (2016), the prevalence of myopia and high myopia will rise globally by 2050, affecting almost 5 billion and 1 billion individuals, respectively. Myopia is associated with the elongation of the eyeball or AL. Axial length is defined as the distance from the corneal surface to the retinal pigment epithelial layer and is an important indicator of the refractive state of the eye. It is well established that AL elongates with myopia progression and provides a coordinated estimation of the overall ocular structure and changes in that structure in myopia and high myopia (Wang et al. 2016).

Two types of A-scan biometry are based on different working principles, namely optical biometry and ultrasound biometry. Optical biometry such as the Lenstar LS 900™ (Haag-Streit, Germany) is a non-contact, fast, precise and easy-to-use measurement device. Lenstar™, which uses the principle of Optical Low-Coherence Reflectometry (OLCR), can provide a lot of information about ocular parameters like central corneal thickness (CCT), lens thickness (LT), anterior chamber depth (ACD), axial length (AL), keratometry values, and corneal diameter in a single measurement. Ultrasound biometry, on the other hand, is an instrument that utilizes 10-MHz ultrasonic waves to get measurements of ocular characteristics such as the axial length of the eyeball (AL), lens thickness (LT), and the depth of the anterior chamber (ACD) (Wang et al. 2016). A study from Wang et al. (2016) also found that a contactless A-scan was able to measure the AL at a higher value when compared to measurements made with an ultrasound A-scan, as well as what has been reported in several other reports (Nakhli, 2014, Atwa et al. 2019, Goyal et al. 2003, Gopi et al. 2017). This is because ultrasound biometry requires placing the probe directly on the corneal surface, which might cause the corneal surface to be indented, resulting in lower and variable measurement findings compared to contactless biometry.

The Optometry Clinic, Faculty of Health Sciences, UKM recently purchased the Lenstar LS 900 ™ non-contact optical biometry for clinical use. Previously, ultrasound biometry was used to measure the AL for myopia management. The clinicians need to identify if there are any discrepancies in AL measurements between both instruments. Therefore, this study aimed to compare the AL measurements taken using optical biometry and ultrasound biometry in the clinic.

## Methodology:

This study was conducted over a period of 9 months, starting from October 2021 until July 2022 among undergraduate students at the Universiti Kebangsaan Malaysia Kuala Lumpur campus. The inclusion criteria for the subjects were myope with a spherical equivalent of ≤ -0.50 D, aged between 19 to 25 years old with no ocular pathology, amblyopia and antimetropia. Only data on the right eye was presented in this study. This study was approved by the Universiti Kebangsaan Malaysia Research Ethics Committee UKM PPI/111/8/JEP-2022-125 and was conducted after acquiring subjects' written and informed consent.

This study was conducted at the UKM Optometry Clinic, Faculty of Health Sciences, Universiti Kebangsaan Malaysia, Kuala Lumpur. Subjects' history was taken including their previous ocular and systemic diseases, ocular trauma and history of contact lens wear. All subjects underwent a comprehensive eye examination which included visual acquity (VA) at distant and near using Snellen and near chart, retinoscopy, subjective refraction, measurement of AL using optical biometry (Lenstar LS 900™, Haag-Streit AG) and ultrasound A-scan

(VuPad Ultrasound™, Sonomed Escalon). To avoid corneal abrasion due to corneal indentation from A-scan probe, optical biometry was always done first followed by applanation ultrasound.

For optical biometry (Lenstar, LS 900™) the subjects were instructed to fix their gaze directly on the alignment beam to ensure that all measurements were obtained along the visual axis. Three consecutive measurements were taken on the right eye. For applanation ultrasound, the subjects were instilled with 0.5% proparacaine hydrochloride drops in the right eye. They were asked to look straight ahead, and the probe was placed at the center of the cornea perpendicularly without indenting it. Three consecutive measurements were taken on the right eye with a standard deviation of less than 0.1 mm for each subject.

The statistical analysis was performed using the IBM Statistical Package for the Social Sciences (SPSS) Statistics 21. The results were presented in mean ± standard deviation. The data normality assumption was tested with the Shapiro-Wilk test. The mean and standard deviation (SD) values for the AL were analyzed using descriptive tests. A paired sample t-test was used to analyze the value of the AL of the eyeball obtained by both methods. Spearman rho test was used to determine the relationship between the length of the eyeball and the degree of myopia in spherical equivalent refractive error. Regression analysis was performed to predict the degree of myopia from the AL measurement. All p values were 2-sided and a probability level of less than 0.05 was taken as statistically significant.

## Results:

A total of 90 subjects (90 eyes) from 14 (15.6%) males and 76 (84.4%) females were included in the study with a mean age of 22.03 ± 1.14 years old. The mean spherical equivalent refractive error value for the right eye was -3.04 ± 1.61 D ranging from -0.50 DS to -6.75 DS.

The Shapiro-Wilk normality test for axial length measured by Lenstar and ultrasound A-scan showed the data were normally distributed since the significant values for both were more than 0.05. Statistical analysis showed that the mean AL measured using ultrasound A-scan was 0.24 mm less than the one measured using the optical biometer, 95% CI 0.17, 0.31]. This difference was statistically significant, $t(89) = 7.09$, $p < 0.001$. Table 2 summarizes the AL measurements obtained using optical biometry and ultrasound methods.

Table 1: Demographical data of the subjects

| Variable | Frequency (Percent) | Mean ± SD |
|---|---|---|
| Gender<br>Male<br>Female | <br>14 (15.6%)<br>76 (84.4%) | |
| Age | | 22.03 ± 1.14 |
| Spherical Equivalent (RE) | | -3.04 ± 1.61 D |

Table 2: Mean of axial length measurements (SD) using both methods

| | Mean axial length (SD) (mm) | dF | *t* | *p*-value |
|---|---|---|---|---|
| Ultrasound biometry | 24.50 (0.86) | 0.33 | 7.09 | 0.00 |
| Optical biometry | 24.74 (0.90) | | | |

The Spearman's rho correlation coefficient was used to analyze the correlation between the degree of myopia and axial length measurement. This test indicated that there was a significant negative correlation between these two, $r_s = -0.609$, $p < 0.001$, N = 90. Figure 1 shows the correlation between the degree of myopia (D) and axial length (mm).

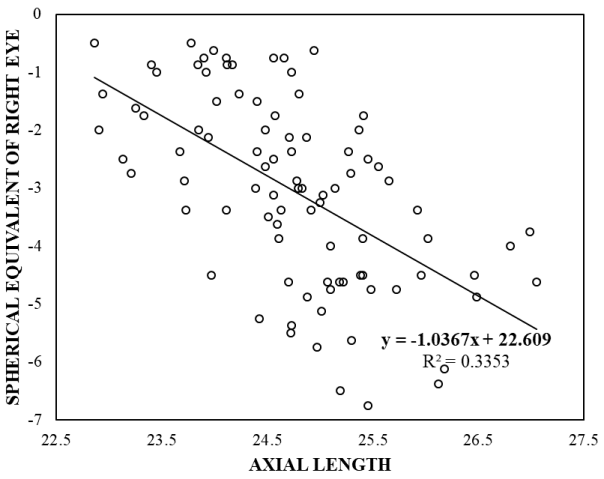


Figure 1: The correlation between the degree of myopia (D) and axial length (mm)

A simple linear regression was performed to predict the degree of myopia from AL measurement. Before interpreting the results of the simple linear regression, several assumptions were evaluated. First, the stem-and-leaf plots and boxplots indicated that each variable in the regression was normally distributed and free from univariate outliers. Second, inspection of the normal probability plot of standardized residuals as well as the scatterplot of standardized residuals against standardized predicted values indicated that the assumptions of normality, linearity and homoscedasticity of residuals were met.

In combination, the AL measurement accounted for a significant 33.5% of the degree of myopia, $R^2 = 0.335$, adjusted $R^2 = 0.328$, $F = (1, 88) = 44.38$, $p < 0.01$. Unstandardized (B) and standardized (β) regression coefficients and squared semi-partial correlations ($sr^2$) for the predictor in the regression model are reported in Table 3.

Table 3: Unstandardized (B) and standardized (β) regression coefficients and squared semi-partial correlations ($sr^2$) for the predictor in the regression model predicting the degree of myopia.

| Variable | B [95% CI] | B | $sr^2$ |
|---|---|---|---|
| Axial length | -1.04 [-1.35, -0.73] | -0.58 | 0.34 |

## Discussion:

This study investigated the comparison between axial length measurement between optical biometer (Lenstar 900™) and applanation ultrasound biometry in myopic subjects. From our findings, AL measured using the ultrasound biometry was significantly lower by 0.24 ± 0.33 mm than the measurement conducted using ultrasound ($p < 0.001$). Previous studies have demonstrated the differences in the AL measurements between non-contact A-scan and ultrasound A-scan. Wang et al. (2016) discovered that both Lenstar and IOL-Master non-contact biometry devices produced longer axial length values than the ultrasound device. A study from Atwa et al. (2019) demonstrated that, in eyes with a cataract or a clear lens, optical biometry produces longer mean measures than applanation ultrasound biometry, as represented by a difference of 0.05 mm in the AL measurement. Goyal et al. (2003) also reported that the average difference between the AL obtained using the non-contact interferometry method was higher by 0.20 mm than those measured using the ultrasound method.

The differences in the technique utilized to obtain the measurements and the variations in the system used by each instrument are the possible explanations for this difference in the AL measurement. Due to the need to position the probe directly on the cornea during ultrasound biometry, there is a chance that the cornea may be pressed inward. As a result, the measurements obtained are lower and more variable than with non-contact biometry (Wang et al. 2016). Additionally, the reflection of light provides another explanation. In ultrasound biometry, light is reflected on the ILM, while in optical biometry, Lenstar 900™, light is reflected on the retinal pigment epithelium (0.25 mm deeper than the ILM) (Atwa et al. 2019). Lenstar 900™ optical biometry instrument uses an 820 nm super luminescent diode (SLD) (Rohrer et al. 2009), which provides a higher resolution (O'Donnell et al. 2011), while ultrasound biometry produces a resolution of 200µm (Atwa et al. 2019). Furthermore, optical biometry uses light for measurement rather than using sound like ultrasound biometry, and this produces more accurate values (Pooja et al. 2018). Nakhli (2014) stated that resolution improves as wavelength decreases. Therefore, because light has a shorter wavelength than sound, laser light produces better resolution as used in contactless optical biometry. To monitor changes in axial length in patients, measurements of axial length should be conducted consistently using the same instrument in the clinic.

According to previous studies, non-contact biometry provides better repeatability and reliability compared to ultrasound biometry. Shen et al. (2013) reported that, in AL and ACD measurements in highly myopic eyes, the Lenstar LS 900 and IOLMaster biometry offered superior reproducibility and interchangeability than applanation ultrasound. Cruysberg et al. (2010) also mentioned that according to their study, Lenstar LS 900 provided excellent repeatability for CCT, ACD, LT, K values, and AL measurements. This is also supported by Rauscher et al. (2021) mentioning that in terms of CCT, AD, ACD, LT, and AL measurements, the Lenstar LS900 had outstanding repeatability. Thus, since non-contact biometry provides high resolution and low variability, it could result in more accurate measurements (Goyal et al. 2003).

The results of this study also found that there was a negative and strong linear correlation between axial length and degree of myopia in young adults. Similar findings were made by Chinawa et al. (2017) who reported a linear relationship between myopia and AL, indicating that AL increases with the degree of myopia. According to Chen et al. (2021), eyes with high myopia tend to have longer AL, shallower anterior spaces, thicker corneas, weaker lenses, and longer vitreous spaces. Xie et al. (2009) also reported that longitudinal studies showed that the depth of the anterior space increased in addition to the elongation of the vitreous with increased myopia. The AL measurements must be conducted during follow-up visits to monitor myopia progression in children.

The limitation of this study was that all AL measurements were carried out with undilated pupils, which made it easier for the subjects to fixate on the target during the examination. Nevertheless, without the use of cycloplegia, it is impossible to rule out the possibility that accommodation may have an impact on subsequent AL measurements. According to Gao et al. (2002), AL in myopic eyes is reduced following cycloplegia, contrary to studies by Cheng et al. (2014) and Bahar et al. (2021) which reported AL increases with cycloplegia. Future studies should be conducted on subjects with cycloplegia to determine the differences in measurements.

## Conclusion:

This study concludes that there is a significant difference in the measurements of AL using optical and ultrasound biometry in myopic subjects, in which the AL measured using ultrasound is shorter than using optical biometry. Axial length measurements must be conducted during follow-up visits to monitor myopia progression in children and should be done consistently with the same instrument to avoid any discrepancies.

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# The effectiveness of Bobath technique in treating children with cerebral palsy: A systematic review

***Shahid Mohd Dar, MPT.**
Department of Physical Rehabilitation Sciences,
Kulliyyah of Allied Health Sciences,
International Islamic University Malaysia,
Jalan Sultan Ahmad Shah,
Bandar Indera Mahkota,
25200 Kuantan, Pahang
shahiddar@iium.edu.my

**Nur Atiqah Johari, BSc.**
Department of Physical Rehabilitation Sciences,
Kulliyyah of Allied Health Sciences,
International Islamic University Malaysia,
Jalan Sultan Ahmad Shah,
Bandar Indera Mahkota,
25200 Kuantan, Pahang
nuratiqahjohari98@gmail.com

***Corresponding author:** Shahid Mohd Dar, shahiddar@iium.edu.my

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## Abstract:

**Aim:** To assess how Bobath therapy affects motor function and functional independence. **Method:** This systematic review was conducted following PRISMA guidelines. All randomized control trials (RCTs) that recruited cerebral palsy children and applied the Bobath approach as an intervention were collected through a comprehensive online database search. For quality assessment, the revised Cochrane risk-of-bias tool for randomized trial (RoB 2) was used. **Results:** Six eligible articles including five RCTs and one quasi-experimental study were retrieved from PEDro, MEDLINE, COCHRANE, EBSCO and PubMed since 2010, and all studies had low risk of bias. The Bobath therapy had shown positive effects on gross motor function, balance, upper extremity function and functional independence with no significant effects on gait parameters and disability involvement. **Conclusion:** The Bobath technique would not be effective on its own but may give more advantages if it is used as an adjunct to other conventional physiotherapy treatments.

**Keywords:** Neurodevelopmental therapy, Bobath, Cerebral palsy, Randomized control trials

## Introduction:

Cerebral palsy (CP) is a type of persistent, though not unchanging, disease of movement and/or posture and motor function that is attributed to the developmental or immature brain's non-progressive disturbance, injury, or abnormality (Sadowska et al., 2020). This definition is following Dr. Bobath, who defined cerebral palsy as the outcome of a laceration or underdeveloped part of the brain, non-progressive in nature and present since birth. The motor discrepancy results in atypical patterns of posture and movement, in relation to an abnormal postural tone. Due to the abnormalities faced by cerebral palsy (CP) children, there is an essential need for ongoing treatment to optimize their physical abilities, functional independence and their quality of life.

There are several interventions established in treating CP children, such as botulinum toxin-A injection (Multani et al., 2019), electromyographic feedback (Flux et al., 2023), heat-reinforcing needling (Zhang et al., 2014), Adeli suit therapy (AST) (Mahani, et al., 2011) and Bobath technique (Acar et al., 2016), to name a few. According to Vaughan-Graham et al., (2019), the Bobath concept is one of the most used techniques by physiotherapists in neurorehabilitation. The concept of treatment is that it is personalized according to the patient's condition and may involve manual contact and verbal commands, that provide facilitation and inhibit abnormal postural tone to achieve successful movements and task performance in terms of postural orientation, components of

movement, task recognition and motivation to complete any task. Even though the Bobath concept has been applied for more than 50 years, its effectiveness is still questionable, and a lot of studies have been conducted to determine whether there is evidence to accept it as an effective approach (Paci et al., 2003).

A lot of research is available regarding the effectiveness of the Bobath technique on neurological conditions and the results are inconsistent. For instance, Gray et al., (2018) reported significant improvement in the upper extremity function of patients compared to non-intervention group. On the other hand, studies also reported that physical functioning, trunk impairment scale and the 10-meter walk test did not improve significantly after the Bobath therapy compared to standard exercises. Due to these contradicting results, this review sought to assess the effectiveness of the Bobath approach towards cerebral palsied children by reviewing recent studies.

## Methodology:

### Identification

A systematic and broad search of the literature was performed to identify any randomized clinical trials that would meet the inclusion criteria. There were no imposed restrictions related to the publication status, language, or date of publication. Literature searches were performed in online databases such as MEDLINE, COCHRANE, PubMed, PEDro and EBSCO. The Boolean operators such as 'AND' or 'OR' and relevant keywords such as 'effectiveness' OR 'efficacy' OR 'effects OR 'evaluation' AND 'bobath concept' OR 'bobath technique' OR 'bobath approach' or 'neurodevelopment' AND 'cerebral palsy' OR 'cp' were used for searching processes. This systematic review followed strictly all recommendations from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement in preparing this article (Moher et al., 2009).

### Screening and Eligibility

The inclusion criteria were full text, English-published randomized controlled trials (RCT) and quasi-experimental studies limited to human studies, not older than 2010, and studies performed on cerebral palsy (CP) children, aged 0-15 years and Bobath (neurodevelopmental therapy -NDT) as a main treatment. Any RCT that compared Bobath to no treatment or conventional physiotherapy approaches was accepted. Studies that applied Bobath in conjunction with other treatments were also considered for inclusion. The exclusion criteria would be non-randomized trials or quasi-experimental, non-full text, non-published, non-English articles, articles related to animal study, articles older than 2010, and articles that were not related to CP children and Bobath therapy. The results from the studies would be narratively synthesized.

### Assessment of Risk of Included Studies

The selected articles were assessed for bias using the revised Cochrane risk-of-bias tool for randomized trials (Rob 2) (Sterne et al., 2019).

## Results:

### Study selection

A total of 90 articles were yielded from online databases. After removing 20 duplicate articles, the articles were further screened by the title and abstract. Then, the remaining 38 articles were assessed based on the inclusion and exclusion criteria. Thirty-two references were excluded for reasons mentioned in Figure 1. Finally, six full-text articles were included in the systematic review.

### Reporting results

The results obtained were illustrated in a table format (Table 1) adopted from the systematic review guidelines by the American Occupation Therapy Association, updated in March 2020.

### Study Characteristics

There were five randomized controlled trials (RCTs) and one quasi-experimental included in this research. The number of participants in the articles included in this systematic review ranged from 17 to 36, with ages ranging from 0 to 15 years old. All the studies recruited both male and female participants. All the participants recruited were diagnosed with cerebral palsy, not under the treatment of botulinum toxin, not candidates for surgery or other interventions, and researchers had obtained parents' consent for randomized assignment of their children into either group. The participant characteristics, intervention, outcome measures and results of the included articles were summarized in Table 1.

## Discussion:

### The Effects of Bobath in Terms of Motor Function

Labaf et al., (2015) presented positive results in the

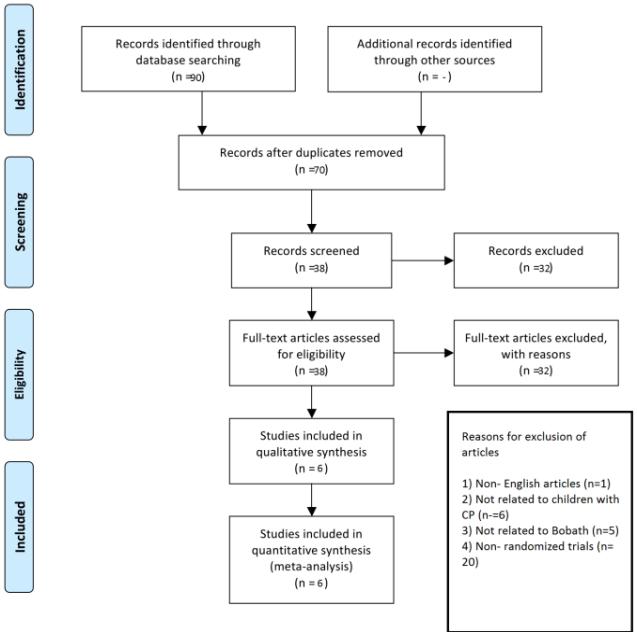


Figure 1: The Processes of Identification, Screening, Eligibility and Included by using PRISMA Guideline.

## Discussion:

**The Effects of Bobath in Terms of Motor Function**

Labaf et al., (2015) presented positive results in the Bobath group in terms of gross motor function (GMF) domains of lying and rolling, sitting, crawling, kneeling and standing abilities, but not in the domains of walking, running and jumping abilities. It was important to note that dynamic activities such as walking, running and jumping were far more difficult to be executed because they dealt with great core muscle strength to maintain their balance. Therefore, it was reasonable that no improvements were recorded in walking, running and jumping abilities.

In addition, there was not much difference in the GMF no matter how frequently the Bobath technique was applied to the children (Besios et al., 2018). This might be because of the inaccurate techniques applied by the therapists or probably the outcome gained during the treatment period was not assimilated into the children's daily lives.

Mahani et at., (2010) revealed superior improvements with modified Adeli suit therapy (AST), which was the combination of AST and Bobath. However, this idea contradicted another study by Kim et al., (2016) who claimed AST was as effective as Bobath in improving GMF. The varying results probably may be due to different ways of applying the Bobath treatment.

Additionally, a home program should be added to Bobath because it may encourage parents to supervise and motivate their children during rehabilitation. Behzadi et al., (2014) reported better results of GMF when children were treated with Bobath and were given a home program afterwards.

A study done by Kim et al., (2016) reported that the Bobath technique did not show any improvements in gait parameters. Walking is a complex activity that requires strength of muscles of the whole body, especially core muscles. If the children had abnormal movement patterns, which was a common problem in CP, their line of gravity and base of support would alter, so walking, even sitting or standing could be difficult. Kim et al., (2016) suggested that spatiotemporal parameters might improve with another treatment alongside Bobath as an adjunct. Their combination of treatment using Bobath or neurodevelopmental therapy (NDT) and AST presented significant improvement in the spatiotemporal parameters.

The upper extremity (UE) function was important for children to reach for things, for self-care and learning. A study by Acar et al, (2015) demonstrated significant improvements only if NDT acted as an adjunct to the main treatment. The treatment with NDT still showed progress in the Jebsen Taylor Hand Function Test (JTHFT), ABILHAND-Kids test and Quality of Upper Extremity Skills Test (QUEST) scores but only in the 'dissociated movements' domain. The significant increase in QUEST scores in NDT/NW (Neurodevelopmental Treatment/Nintendo Wii) group may be related to the children's effort to move their arms to better grasp and use the Nintendo Wii game console, which was proven through post-treatment clinical observation. The study also showed that children in the NDT/NW group improved their hand speed after the treatment period. Not only the Nintendo Wii was more attractive and entertaining to children, but some studies proved that outcome gained during the virtual environment treatments might be transmitted to real life.

**The Effect of Bobath in Terms of Functional Independence**

Besios et al., (2018) had used PEDI (Pediatric Evaluation of Disability Inventory) measure in their study and the results showed no significant effect on the PEDI scores regardless of the frequency of its application. The possible explanation for this outcome was because of most of the areas of assessment in PEDI such as behaviour, cognition, communication, language, problem-solving, and social relationships were not within the domains of Bobath therapy. The Bobath technique focuses on influencing the quality of motor response by applying therapeutic handling, facilitation and inhibitory techniques with specific key

points of control. So, Bobath was not effective in reducing the children's disability over time.

According to Acar et al., (2016), both Bobath (NDT) and NDT/Nintendo Wii groups revealed similar developments in terms of eating, care, bathing and upper and lower trunk dressing domains. The reason for the similar results was perhaps the outcome gained during the treatment was not immediately transmitted to their daily lives. Also, without the presence of the Nintendo Wii, the children would be less motivated and reluctant to perform regular exercises. This signified that Bobath alone was effective in improving functional independence through therapeutic handling together with the facilitation and inhibitory techniques which would progressively correct the abnormal postural tone in CP children.

Functional independence was essential because it was related to the quality of life (QOL). Compared to their normal developing peers, CP children's progressive limitations in the activities of daily living (ADLs) and participation restrictions might reduce their QOL, especially in their physical health and independence in basic functional activities (Chulliyil et al., 2014).

Future research should include more RCTs on Bobath effects on parameters such as spasticity, muscle activity, muscle strength and the QOL because it is crucial to know to what extent Bobath might impact the life of children with CP. Future research should also use consistent outcome measures to improve the validity of results. Researchers should experiment applying the Bobath technique as an adjunct therapy instead of a major treatment. Studies. The effects of Bobath (NDT) technique on different types of CP (spastic, ataxic & dyskinetic) and different topographical distributions (hemiplegia, diplegia & quadriplegia) could be addressed in future studies.

## Conclusion:

Overall, the Bobath technique was effective in improving cerebral palsy (CP) children's GMF, balance, UE function and functional independence. However, other aspects such as gait parameters and disability involvement did not show significant progression with it. Perhaps, the improvements might be observed if the Bobath technique becomes an adjunct to assist the main treatment, instead of becoming the main sole player. This research might benefit future therapists in terms of determining and choosing the right treatment combination for children with CP.

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Table 1: Description of included studies

| Author/Year | Level of Evidence Study Design Risk of Bias | Participants Inclusion Criteria | Intervention | Outcome Measures | Results |
|---|---|---|---|---|---|
| Behzadi, et.,al (2014) | Level 1B<br>RCT<br>Low risk | *N*= 30 (19 girls & 11 boys)<br>*Inclusion criteria*<br>Children age range 0-2 years old having motor dysfunction due to CP | n=15 (9 girls & 6 boys) , traditional Bobath group<br>n=15 (10 girls & 5 boys) , home-based group<br>Physiotherapist applied one-hour NDT-Bobath technique for 12 sessions. The traditional Bobath group received inhibitory and facilitation techniques. | *GMF*<br>GMFCS level | Bobath group showed significant improvements than home-base group ($p$= 0.007) |
| Besios et al.,(2018) | Level 1B<br>RCT<br>Low risk | *N*= 20 (age= 4.85±2.49 years<br>*Inclusion criteria*<br>Children diagnosed with CP | n=10, Low frequency intervention group (LFICP)<br>n=10, High frequency intervention group (HFICP)<br>The participants underwent two dissimilar intervention protocols with Bobath technique. LFICP group received only one session of (Bobath) a week that lasted for one hour. HFICP group received three intensive one-hour sessions each week. | *GMF*<br>GMFM-88<br>*Disability Involvement*<br>PEDI<br>*Fall Risk*<br>TUG | *GMF*<br>There were significant changes in GMFM-88 scores for both groups (p<0.001).<br>*Disability Involvement*<br>Participants from both groups showed no improvement in PEDI scores.<br>*Fall Risk*<br>Both groups revealed significant improvements in TUG scores (p<0.001). |
| Kim, et al.,(2016) | Level 1B<br>RCT<br>Low risk | *N*=17 (8 girls & 9 boys; mean age= 5.64 years)<br>*Inclusion criteria*<br>Children age range 4-7, diagnosed with CP, no history of orthopaedic surgery or spasticity- | n= 8(2 boys, 6 girls), AST/NDT<br>n= 9 (6 boys, 3 girls), NDT<br>Participants in the AST/NDT group received NDT for 30 minutes per session, 2 sessions per day, for 5 days per week. They also received Adeli suit treatment for 30 minutes per session for 5 times a week. The participants in the NDT group received only NDT with the duration same as received by AST/NDT group. | *GMF*<br>GMFM-88<br>*Functional Mobility*<br>TUG<br>*Balance*<br>PBS<br>*Gait Analysis*<br>GAITRite walkway system | *GMF*<br>Paired t tests revealed statistically significant improvements in GMFM in both AST and NDT groups (p<0.05).<br>*Functional Mobility and Balance*<br>TUG test and PBS disclosed significant improvements in all groups (p < 0.05).<br>*Gait*<br>The AST/NDT group displayed more significant effects on walking speed, cadence, and stride length (p<0.05) as compared to NDT group. |
| Mahani, et al.,(2010) | Level 1B<br>RCT<br>Low risk | *N*= 36 (11 girls & 25 boys; mean age=7.55 years)<br>*Inclusion criteria*<br>Children diagnosed with CP, no history of orthopaedic surgery or spasticity reduction intervention in the last 6 months, classified in level 1-4 of GMFCS. | n=12 (9 boys, 3 girls), MAST<br>n=12 (8 boys, 4 girls), AST<br>n=12 (8 boys, 4 girls), NDT<br>All children in the three groups received daily treatment for 2 hours, for 5 days per week for total of 20 sessions. The AST group underwent preparation session and wearing the Adeli suit. The NDT group underwent 2 hours of active and passive movements according to the NDT concept. The MAST group included passive stretching, followed by facilitation of normal movement patterns, then, the children wore Adeli suit and the loading system was applied. | *GMF and Functional Status*<br>GMFM-66 | All groups displayed positive effects in GMFM after treatment sessions (p<0.01). However, there were also significant differences between groups in the GMF scores after the treatment as well as at follow-up (p<0.01). |
| Acar, et al., (2015) | Level 1B<br>RCT<br>Low risk | *N*= 30 (16 girls & 14 boys)<br>*Inclusion criteria*<br>Children aged between 6 and 15 years, classified in level 1–3 of the MACS, level 1or 2 of the GMFCS, able to grasp and release an object, and no history of surgery or botulinum toxin injection to UE in the previous 6 months. | n=15 (7 girls, 8 boys), NDT/NW<br>n=15 (9 girls, 6 boys), NDT<br>The NDT group received standard NDT for 45 minutes per session, twice a week for 6 weeks. Participants in NDT/NW group played virtual reality games of tennis, baseball, and boxing (each game 5 minutes) for 15 minutes in addition to the standard NDT in each treatment session, which focused on the hemiplegic hand. | *Upper Extremity Function*<br>QUEST<br>*Hand Function and Speed*<br>JTHFT<br>*Hand Disability*<br>ABILHAND-Kids test<br>*Functional Independence*<br>WeeFIM | Both groups showed significant improvements in all aspects (except quality of function) after 6 weeks of treatment (all p<0.05). However, there is also significant difference in JTHFT scores between NDT/NW and NDT group. (p<0.001). The study revealed that NDT/NW showed more prominent results than NDT. |
| Labaf, et al., (2015) | Level 1B<br>Quasi-Experimental | *N*= 28 (14 girls & 14 boys; mean age= 4.65 years) | n=15(7 girls, 8 boys), NDT<br>n=13(7 girls, 6 boys), home exercise<br>The treatment group received standard | *GMF*<br>GMFM-88 | The groups were significantly different in lying, rolling, sitting, crawling, kneeling, and standing abilities (all p<0.05). However, |

| | | | | | |
|---|---|---|---|---|---|
| | Low risk | *Inclusion criteria* Children aged 2-6 years, diagnosed with CP, no other severe impairments such as seizure, no participation in other rehabilitation programs except for OT, and referred to the OT clinic of children with disabilities for a 3 month course of therapy. | NDT. In this study, the control group received home exercise, which included stretching, PROM, and AROM by the parents and controlled by an OT. Both groups received treatment for an hour, three sessions per week. | | there were no significant changes in walking, running, and jumping abilities between the two groups (p=0.09). |

*Note*: ABILHAND-Kids= Manual Ability Measure for CP Children; AROM= Active Range of Motion; AST= Adeli Suit Therapy; CP= Cerebral Palsy; GMF= Gross Motor Function; GMFM-88= Gross Motor Function Measure-88; GMFCS= Gross Motor Function Classification System; HFICP= High Frequency Intervention for Cerebral Palsy; JTHFT= Jebsen Taylor Hand Function Test; LFICP= Low Frequency Intervention for Cerebral Palsy; MACS= Manual Ability Classification System; MAST= Modified Adeli Suit Therapy; NDT= Neurodevelopmental Treatment; NW=Nintendo Wii; OT= Occupational Therapist; PBS= Pediatric Balance Scale; PEDI= Pediatric Evaluation of Disability Inventory; PROM= Passive Range of Motion; QUEST= Quality of Upper Extremity Skills Test; RCT= Randomized Controlled Trial; TUG= Time-up and Go; UE= Upper extremity; WeeFIM= Functional Independence Measure.

# Association between Eating Behaviour, Stress Level and Body Mass Index of University Students

**Janagar Manoharan, BSc.**
Dietetics Programme, School of Health Sciences, Universiti Sains Malaysia, Health Campus, 16150 Kubang Kerian, Kelatan.
janagarmano@gmail.com

*** Divya Vanoh, PhD**
Dietetics Programme, School of Health Sciences, Universiti Sains Malaysia, Health Campus, 16150 Kubang Kerian, Kelatan.
divyavanoh@usm.my

****Corresponding author:*** Divya Vanoh, divyavanoh@usm.my

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**Abstract:**

**Introduction**: Stress among university students is rising and affects eating behaviour and body mass index. This study aims to determine the relationship between stress and eating behaviour and its association with body mass index among undergraduate students in Universiti Sains Malaysia. **Method**: A total of 107 subjects were recruited using the convenience sampling method. Participants were given a questionnaire used composed of sociodemographic items, anthropometry measurements, items from the Cohen's Perceived stress scale questionnaire and eating behaviour (Three-factor eating questionnaire R21). **Results**: Analysis indicated that more than half of the subjects had moderate stress levels (69.2 %). However, there was no significant difference between stress and gender. The analysis between gender and all domains of eating behaviour (cognitive restrain, uncontrolled eating and emotional eating) showed no significant difference. The majority of participants presented a normal BMI. Male students had a significantly higher median BMI (22.68 ± 6.91 kg/m2) than female students (20.68 ± 4.07 kg/m2). The emotional eating was significant among students who were underweight. High perceived stress was significantly associated with a median BMI. There was a significant association between uncontrolled eating domain ($p$=0.041) and emotional eating domain with perceived stress level. **Conclusion**: Findings of this study can be considered as a preliminary study for intervention research investigating the effectiveness of multi-domain modules for managing eating behaviour and stress among students.

**Keywords:** Stress, Eating Habits, Emotional Eating, Body Weight

## Introduction:

In Asia, the prevalence of overweight and obesity among university students are 20.8% in Bangladesh, 2.9-14.3 % in China, 20-30.1 % in Malaysia, 31% in Thailand, 13-52.6% in Pakistan, and 11-37.5% in India (Peltzer, et al., 2014; Tapera, et al., 2017). University students often reported having higher stress levels, being sedentary and practicing unhealthy eating patterns comprising of processed foods, fried foods, and sweet beverages (Tapera, et al., 2017).

College or university students often feel stressed due to poor stress coping mechanisms (Fijar, et al., 2018). The prevalence of stress among Malaysian students was 40 % (Cheng and Muhammad Khair, 2020) while in Turkey, Hong Kong, and Australia reported 27%, 43% and 52.9%, respectively (Cheng and Muhammad Khair, 2020). The major stress contributing factor among university students is due to the poor ability to adapt to university life (Monteiro, et al., 2014). Various other challenges such as personal psychological issues, family problems, and low socioeconomic status may affect the students` eating behaviour (Kabir, et al., 2018). It is common for a student to experience stress during the exam period as they may have skipped breakfast, delayed mealtime or even taken meals in restaurant (Kabir et al., 2018).

There is a strong relationship between stress level and eating behaviour where high stress is always recognized as a reason for uncontrolled eating behaviour (Penaforte, et al., 2016; Ramadhani and Mahmudiono, 2021; Saat, et al., 2014). A study done among 914 university students in Malaysia stated that 87% of students consumed fried food at least 2-4 times per week, 57% of students consumed high fat food more than 4 times a week and reported lesser intake of fruit and vegetables in their daily diet (Nik Hairi, et al., 2015).

Since university students reported having troubled dietary habits, this study aims to determine the relationship between stress, eating behaviour and its association with BMI among Universiti Sains Malaysia undergraduate students.

## Materials and Methods:

### Study design

This was a cross-sectional study approved by the Human Research Ethics Committee in Universiti Sains Malaysia [code USM/JEPeM/21060449]. This research included 107 students from the School of Dental Sciences, School of Medical Sciences and School of Health Sciences. The participants were recruited via convenience sampling. Informed consent was obtained from all participants prior to their recruitment to the study. The inclusion criteria of the study participants were Malaysian undergraduate students aged 18 years and above. Students with clinical diagnosed mental health problems were excluded from this study.

### Research instrument

The data collection was conducted via a self-administered questionnaire in the English language distributed using the Google form. Items on sociodemographic characteristics included gender, age, ethnicity, school, year of study and current residence of the participants. BMI was self-reported as body weight(kg) divided by squared of height(m2). The WHO BMI cut-off points were used; BMI <18.5 kg/m² (underweight), between 18.5 and 24.9 kg/m² (normal), ≥25 kg/m² (overweight) and ≥ 30.0 kg/m² or above (obese) (World Health Organization, 2020).

The Cohen's Perceived Stress Scale (Cohen, et al., 1983) was used to determine the stress perception of an individual. There were 10 questions pertaining to their feelings and thoughts in the past month with answer option of 0 (Never), 1 (Almost never), 2 (Sometimes), 3 (Often) and 4 (Very often). The total score was calculated via adding the sum of the 10 items. Reverse scoring was applied for question 4, 5, 7 and 8. The Cronbach's alpha of this questionnaire was between 0.84 to 0.86. Scores ranging from 0-13 was considered as low stress, 14-26 was moderate stress and 27-40 was considered as high perceived stress (Cohen et al., 1983).

The three-factor eating questionnaire R21 (TFEQ-R21) was used to determine the eating behaviour of an individual (Stunkard and Messick, 1985). The TFEQ-R21 included three main domains of eating behaviour namely cognitive restrain (CR) (6 items), uncontrolled eating (UE) (6 items), and emotional eating (EE) (9 items). The cognitive restraint scale was used to assess the control over food consumption to influence body weight and shape, while the emotional eating assessed the tendency to over-eat when experiencing negative mood states such as loneliness, anxious or depressed. On the other hand, uncontrolled eating scale had been used to measure the tendency to lose control over eating when feeling hungry or when exposed to external stimuli (Tholin et al., 2005). Question 1 to 16 had similar response categories 1 (Definitely agree), 2 (Mostly agree), 3 (Mostly disagree), 4 (Definitely disagree). Reverse scoring was applied for the first 16

questions with scores of 1=4, 2=3, 3=2, 4=1 and for question 17-20, normal scoring was applied such as 1=1, 2=2, 3=3 and 4=4. Besides, for last question (question 21) it was recorded as 1–2 scores as 1; 3–4 as 2; 5–6 as 3; 7–8 as 4. Higher scores indicate worsening eating behaviour (Cappelleri et al., 2009).

**Data analysis**

Statistical analysis was done using the IBM SPSS version 26.0. Numerical data was presented as mean (SD) or median (IQR) based on the distribution normality. Categorical data were present as frequency (percentage). The association between eating behaviour domains and body mass index were tested using Pearson product-moment correlation or Spearman's rank correlation test. The relationship between the stress level with eating behaviour domains and body mass index were determined using the One-Way analysis of variance (ANOVA) if normally distributed and Kruskal-Wallis if not normally distributed. Significance level was set at *p* value less than 0.05.

## Results:

**Sociodemographic characteristics**

The sociodemographic characteristics of the participants who participated in this study are presented in Table 1. The majority of the study participants were Malay (59.81%) and female (65.40%).

Table 1 Frequency distribution table for demographic characteristic (N= 107)

| Characteristics | n | % |
|---|---|---|
| **Age** (y) (Median/IQR) | 22.00 ± 2.00 | |
| **Ethnicity** | | |
| Malay | 64 | 59.81 |
| Indian | 21 | 19.63 |
| Chinese | 15 | 14.02 |
| Others | 7 | 6.54 |
| **Gender** | | |
| Male | 37 | 34.60 |
| Female | 70 | 65.40 |

**Anthropometric characteristics, stress level and eating behaviour**

The majority of the participants had a normal body mass index (BMI) range with median of 21.60 ± 4.79 kg/m$^2$. Male students had a significantly higher median BMI (22.68 ± 6.91kg/m$^2$) compared to female students (20.68 ± 4.07kg/m$^2$) ($p$<0.05).

More than half of the study participants reported moderate stress levels (69.2%). Only 15% of the participants reported having high stress levels (15.0%). However, there were no significant gender differences between stress and eating behaviour domains (Table 2)

Table 2 Stress level, eating behaviour and BMI level according to gender.

| Parameters | Total (n = 107) | | Male (n= 37) | | Female (n=70) | | p value |
|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | |
| **Stress Level** | | | | | | | 0.550 |
| Low | 16 | 15.00 | 4 | 10.80 | 12 | 17.10 | |
| Moderate | 74 | 69.20 | 28 | 75.70 | 46 | 65.70 | |
| High | 17 | 15.90 | 5 | 13.50 | 12 | 17.10 | |
| **Eating Behaviour (Mean/SD) *** | | | | | | | |
| Cognitive Restrain | 2.57 ± 0.34 | | 2.55 ± 0.36 | | 2.59 ± 0.33 | | 0.581 |
| Uncontrolled Eating | 2.56 ± 0.43 | | 2.56 ± 0.46 | | 2.55 ± 0.42 | | 0.877 |

| | | | | |
|---|---|---|---|---|
| Emotional Eating | 2.80 ± 0.71 | 2.85 ± 0.76 | 2.77 ± 0.68 | 0.581 |
| **Body Mass Index (Median/IQR)** | 21.60 ± 4.79 | 22.68 ± 6.91 | 20.68 ± 4.07 | 0.001 |

*SD: Standard Deviation; IQR: Interquartile range

**Association Between Eating Behaviour and Body Mass Index (BMI)**

Higher emotional eating scores were associated with lower BMI ($p<0.02$). However, no significant association was found between uncontrolled eating behaviour and cognitive restraint with BMI. (Table 3).

Table 3 Association between eating behaviour with BMI

| Parameter | Eating Behaviour Domain | r-value | *p*-value |
|---|---|---|---|
| Body Mass Index (kg/m²) | Cognitive restraint | 0.008 | 0.933 |
| | Uncontrolled Eating | -0.178 | 0.067 |
| | Emotional Eating | -0.224 | 0.020* |

*$p<0.05$ significant using Spearman's rank correlation

**Association Between Eating Behaviour and BMI With Stress Level**

Subjects with low stress levels had significantly higher median values of emotional eating scores (3.50,0.96) as compared to those with moderate (2.67, 1.17) and high (2.83,1.08) perceived stress levels ($p<0.05$). Similarly, uncontrolled eating scores were highest in the low stress group.

Those with the highest perceived stress were reported to have higher BMI (22.60, 9.12 kg/m²) as compared to the those with moderate (21.62, 4.92 kg/m²) and low (19.78, 6.26 kg/m²) stress levels (Table 5).

Table 5 Association between stress level and eating behaviour

| Parameter | Low stress level (n=16) Median (IQR) | Moderate stress level (n=74) Median (IQR) | High perceived stress level (n=17) Median (IQR) | *p*-value |
|---|---|---|---|---|
| Cognitive Restrain | 2.42(0.29) | 2.67(0.50) | 2.50(0.42) | 0.358 |
| Uncontrolled Eating | 2.67(0.33) | 2.56(0.58) | 2.22(0.78) | 0.041* |
| Emotional Eating | 3.50(0.96) | 2.67(1.17) | 2.83(1.08) | 0.013* |
| Body Mass Index (kg/m²) | 19.78(6.26) | 21.62(4.92) | 22.60(9.12) | 0.001* |

IQR: Interquartile range
*Kruskal-Wallis test, significant at $p<0.05$

## Discussion:

In this study, males had a significantly higher median BMI than females. The overall median BMI of the subjects were in the normal weight category (World Health Organization, 2020). Cheng and Muhammad Khair (2020) reported that higher BMI in men is due to the tendency to consume higher calories compared to females. In general, young females are typically more health conscious and more likely to avoid high calorie foods for achieving weight loss or maintaining optimal body image (Cheng and Muhammad Khair, 2020).

More than half of the participants in the current study reported moderate stress. This finding is parallel with previous studies conducted in Saudi Arabia, India, and Malaysia (AlAteeq, et al., 2020; Bhavani Nivetha, et al., 2018; Sami, et al., 2014). This is most likely due to the fact that university students are emerging adults who are interested in exploring their identities, working for independence, and fulfilling various roles (AlAteeq, et al., 2020).

The findings of this study demonstrated a significant relationship between lower BMI with higher scores in the domain of emotional eating regardless of gender. The study by Kowalkowska and Poínhos (2021) stated that emotional eating was positively associated with BMI among female students. Students tend to eat more when they are emotionally disturbed which contributes to weight gain. Similarly, a study among Lebanese University students revealed that BMI was positively associated with emotional eating (Aoun, et al., 2019). (Poínhos, et al., 2015). The other two domains of eating behaviour such as cognitive restraint and uncontrolled eating were not associated with BMI. A previous study found a positive correlation between cognitive restrain and BMI (Kowalkowska and Poínhos, 2021) where cognitive restrain was associated with higher BMI. This may be because of self-initiated eating restrain for the purpose of weight control which will lead to weight gain (Tonja Thomas and Neela Badrie, 2010). Another study done among Sudanese medical students stated that eating behaviour is significantly associated with BMI (Yousif, et al., 2019). A study on the eating behaviour of Malaysian university students showed a significant positive association between abnormal eating and BMI (Mona Mohamed, et al., 2020).

This study found that high stress level was significantly associated with low BMI. The findings resonate with with previous study which found that higher perceived stress was associated with overweight or obesity (Pelletier, et al., 2016). Another study among medical students in China showed a significant increase in overweight and obesity with higher stress levels due to frequent examinations, tight curriculum schedules and long clinical hours (Chen, et al., 2020). Besides that, overweight and obesity among university students enrolled in health care courses were attributed to several factors such as having less time for family and friends, higher workload, talking to patients about personal problems, dealing with disease and death, and insufficient time for recreation (Gajjala, et al., 2016). However, some studies have reported no association between BMI and perceived stress (Nur Zakiah, et al., 2010; Saat, et al., 2014).

The findings of this study revealed that students with low stress levels was significantly associated with uncontrolled eating and emotional eating. This is in contrast with the findings of other studies which found stress to be related to a lower preference for healthy food (Choi, 2020). Students with higher stress levels tend to consume more fast food and sugar containing snacks as comfort food. On the other hand, a study by Serin (2018) stated that healthy people with normal body weight will have positive emotions that affect their food intake as positive emotion is based on the satisfaction of a person. Examples of positive emotions are happiness, gratitude, pleasure, enthusiasm, pride and healthy lifestyle (Serin, 2018). As for uncontrolled eating, students may eat more to satisfy themselves with caloric dense food or high fat food. Both positive and negative emotions can alter the eating behaviour of a person (Cheng and Wong, 2021). Positive emotions can increase the consumption of palatable food (Cheng and Wong, 2021). Individuals who engage in emotional eating as a coping strategy will have a greater tendency to consume palatable-snacks in response to stress (Amestoy and Fiocco, 2021). Most of the students who experienced negative emotions were more inclined to eat less but eat more when they had positive emotions (Alalwan, et al., 2019). Furthermore, boredom can drive emotional eating behaviour (Alalwan, et al., 2019). The findings of other studies showed that higher stress is associated with emotional eating and uncontrolled eating (Cheng and Muhammad Khair, 2020; Penaforte, et al., 2016).

This study had few limitations. The anthropometric data was self-reported and may be subjected to bias. Other confounding factors of stress level such as physical activity and dietary intake were not assessed in this study.

## Conclusion:

In this present study, it was found that most of the study participants were moderately stressed and had normal BMI. In addition, lower BMI was associated with higher emotional eating scores. Higher stress was associated with greater BMI, however subjects with lower stress levels had greater uncontrolled eating and emotional eating scores. It is essential for university management to screen for psychological problems among students as this may affect their eating habits and overall health status.

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# Effect of different solvent extracts on the yield and *in vitro* antibacterial activity, with GC-MS analysis of active extracts from *Vernonia amygdalina* leaves

**Nur Farid Amirul Mustafa, BSc.**
Department of Plant Science, Kulliyyah of Science, International Islamic University Malaysia, Jalan Sultan Ahmad Shah, 25200 Kuantan, Pahang Malaysia.
nurfaridamirul59@gmail.com

**Mohd Syahmi Salleh**
[1]Department of Plant Science, Kulliyyah of Science, International Islamic University Malaysia, Jalan Sultan Ahmad Shah, 25200 Kuantan, Pahang Malaysia.
[2]Sustainable Agriculture and Green Technology Research Unit (Ag-Tech), Kulliyyah of Science, International Islamic University Malaysia Kuantan Campus, Jalan Sultan Ahmad Shah, 25200 Kuantan, Pahang, Malaysia.
msyahmi@iium.edu.my

*** Noor Haslinda Noor Hashim, PhD**
[1]Department of Plant Science, Kulliyyah of Science, International Islamic University Malaysia, Jalan Sultan Ahmad Shah, 25200 Kuantan, Pahang Malaysia.
[2]Sustainable Agriculture and Green Technology Research Group (Ag-Tech), Kulliyyah of Science, International Islamic University Malaysia Kuantan Campus, Jalan Sultan Ahmad Shah, 25200 Kuantan, Pahang, Malaysia.
noorhaslinda@iium.edu.my

***Corresponding author:** Noor Haslinda Noor Hashim, noorhaslinda@iium.edu.my

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## Abstract:

**Introduction:** *Vernonia amygdalina* (*V.amygdalina*), commonly known as 'Bitter leaf', is a small perennial shrub with various medicinal properties including the treatment of stomach disorders, fever symptoms, diabetes, hypertension, and coughs. *V.amygdalina* is a potent source of antibacterial properties that may be beneficial in preventing bacterial infections and associated diseases such as fever and diarrhoea. *V. amygdalina* has been extensively studied for its antioxidant, anti-inflammatory, antifungal, anticancer and antidiabetic properties. Although existing literature emphasises the importance of selecting appropriate extraction solvents to preserve the quality and therapeutic properties of *V. amygdalina*, the ideal solvent for maximum extraction of bioactive components remains unclear. **Aim:** The present study aims to determine the most efficient solvent for producing antibacterial-rich *V. amygdalina* extracts. **Methodology:** Dried leaves of *V. amygdalina* were extracted using various solvents (methanol, ethanol, and dichloromethane) to assess the extraction yield. The antibacterial potential of all extracts against *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* was evaluated using the agar disc diffusion assay. The profiling of the active extract was accomplished using gas chromatography coupled with mass spectrometry (GC-MS). **Results:** Among the solvents tested, ethanol exhibited the highest extraction productivity, with a percentage yield of 49.20%. However, the findings of this study revealed that dichloromethane is the most efficient solvent for extracting antibacterial compounds from *V. amygdalina* leaves, with the inhibition zones against all bacteria strains ranging from 16.67 ± 1.20 mm to 21.33 ± 0.5 mm at 200 mg/mL. The GC-MS analysis of the dichloromethane extract identified compounds such as phytol, flavonoids, vitamin E, and squalene. **Conclusion:** The choice of the extraction solvent greatly affects the antibacterial efficacy of *V. amygdalina* leaves. The efficacy of *V. amygdalina* against pathogenic bacteria strains demonstrated in this study highlights its potential for further exploration in pharmaceutical applications.

**Keywords:** Bitter leaf, extraction solvent, extraction yield, zone of inhibition, agar disc diffusion

## Introduction:

Bacterial infections represent a significant burden on public health, affecting individuals of all ages and geographical regions (Baker, et al., 2021). Bacterial pathogens may cause a wide range of diseases, from common ailments such as urinary tract infections, respiratory tract infections, and skin infections to more severe conditions like sepsis and pneumonia. Bacterial infections can also complicate the management of chronic conditions, surgical operations, and immunosuppressive therapies, providing additional challenges in patient care. In order to overcome the problem, the global annual production of antibiotics is estimated to reach 100-200 thousand tonnes, with a total production of more than one billion tonnes since 1940 (Serwecińska, 2020). The extensive use of antibiotics has led to a significant rise in the excretion and environmental release of these drugs, thereby fueling the development of drug resistance in bacterial strains. Many antibacterial compounds, either synthetic or natural, have been developed to treat and combat infectious pathogens. However, the emergence of multidrug-resistant bacteria has further impacted the availability and affordability of many of the antibiotics currently prescribed worldwide. Consequently, the treatment will become less effective and increase morbidity, mortality, and medical costs. Therefore, finding a new antibiotic derived from nature is important to combat the harmful effects of multidrug-resistant pathogens.

*Vernonia amygdalina (V. amygdalina),* commonly known as "bitter leaf", is a perennial shrub of the Asteraceae family with dark green leaves and rough bark. It is native to tropical Africa although it has been cultivated in many parts across West Africa. The plant may reach a height of 1-6 meters. *V. amygdalina* is a multifunctional and fast-regenerating softwood shrub containing anti-nutritional compounds that contribute to its bitter taste. Nevertheless, its high mineral and vitamin content make it a valuable part of the human diet (Oyeyemi, et al., 2018). Traditionally, the leaves of *V. amygdalina* have been used to treat a variety of diseases, including hypertension, measles, constipation, uterine mobility induction, post-partum haemorrhage control, fever, viral disease and hypercholesterolemia. Moreover, it is also reported to be used to treat malaria, venereal illnesses, wounds, hepatitis, jaundice, and diabetes (Nursuhaili, et al., 2019). Previous pharmacological studies have reported *V. amygdalina* exhibiting antioxidant, antifungal, anti-inflammatory, anticancer, antidiabetic, hepatoprotective, neuroprotective, antimalarial, and antibacterial activities (Ugbogu, et al., 2021). The phytochemical compounds contained in *V. amygdalina* include alkaloids, saponins, terpenes, lignans, flavonoids, phenolic acids, steroids, anthraquinone, coumarins, sesquiterpenes, xanthones and edotides. However, the concentration and stability of these bioactive compounds can be influenced by pre- and post-harvest factors, such as drying processes and extraction solvents (Ejike and Ndukwu, 2017).

The extraction of natural bioactive compounds from plant materials is a crucial step in the isolation and separation processes. The most popular approach is solvent extraction and it is critical to select solvents that can effectively extract the relevant phytochemical constituents. Several factors, such as solvent properties, solvent-to-solid ratio, particle size of the plant material, extraction duration and extraction temperature should be considered as they may affect the extraction efficiency (Zhang, et al., 2018). Therefore, the purpose of this study is to extract bioactive compounds from *V. amygdalina* leaves using three different solvents, namely dichloromethane, methanol, and ethanol by using Soxhlet extraction. In addition, the study aims to determine the most potent antibacterial extracts followed by the determination of the bioactive compounds in the active extract of *V. amygdalina* using GC-MS.

## Materials and Methods:

### Sample preparation and extraction

Fresh *V. amygdalina* leaves were collected from the plants by the hand-picking method. Only healthy, disease-free leaves were selected and thoroughly washed under running tap water. The leaves were then dried in an oven for seven days before being pulverized into a fine powder using a blender and weighed. The powder samples were then stored in a Schott bottle and kept refrigerated until further use.
For the experiment, 35 g of the powder samples were placed in three thimbles. Each thimble was stuffed with cotton wool to prevent the sample from escaping before being placed in a Soxhlet extractor. Three solvents (dichloromethane, ethanol, and methanol) were used, with 300 mL of each being added to three round bottom flasks connected to the Soxhlet extractor and condenser. The Soxhlet extraction was carried out for nine hours. After the extraction was completed, the solution containing solvents and extracts was concentrated using a rotary evaporator to separate the solvent from the crude extracts. The extraction process was repeated three times. Finally, the extraction yield was determined using the following equation:

$$Y = \frac{\text{Weight of dried extract (g)}}{Dry\ weight\ of\ plant\ material\ (g)} \text{ x } 100\%$$

**Preparation of bacteria inoculum**

One gram-positive (*Staphylococcus aureus*) and two gram-negative (*Escherichia coli* and *Pseudomonas aeruginosa*) bacterial strains were used in this study. A single colony of each bacteria strain was cultivated on nutrient agar followed by incubation at 37°C for 24 hours. Then, one colony of each bacteria strain from the fresh bacterial subculture was transferred into 40 mL nutrient broth solution and incubated at 37 °C for 24 hours. After 24 hours, the broth containing the bacteria was stored in the chiller until further use.

**Agar disc diffusion assay**

The agar disc diffusion assay was carried out according to Balouiri, et al. (2016) to determine the antibacterial activity of *V. amygdalina* leaves extract. Various dilutions were achieved by reconstituting the *V. amygdalina* extracts in methanol using a two-fold dilution method to achieve concentrations of 25, 50, 100, and 200 mg/mL. 20 µL of each extract concentration was impregnated on the filter paper disc (6 mm in diameter) and left to dry. On nutrient agar plates, 200 µL of each bacterial strain were inoculated evenly using a sterile hockey stick spreader. The filter paper discs containing extracts were then placed on the bacteria-containing agar surface and incubated for 24 hours at 37 °C. The procedure was repeated three times for each bacterial strain. After 24 hours, the diameter of the inhibition zones on each plate was measured. Filter paper discs containing methanol were used as negative controls, whereas antibiotic discs containing gentamycin served as positive controls.

**Gas Chromatography-Mass Spectrometry analysis**

The dichloromethane extract was analysed using Agilent GC-MS equipment (Agilent 5975C inert, USA) together with a mass spectrometer MS 597C according to the method by Kalaiyarasan and Hariram (2021) with minor modification. The GC-MS is equipped with a DB-1MS capillary column length of 30 m, an inner diameter of 0.25 mm, and a film thickness of 0.25 µm. The initial temperature was 35°C and was raised to 95°C before reaching the final temperature of 300°C. Helium was used as the carrier gas with a flow rate of 1.0 mL/min and an ionisation voltage of 70 eV. The sample injection volume was 1 µL of extract solution, and the analysis was performed for 30 minutes. The chemical components in the extracts were identified by comparing the obtained spectra with those available in the NIST 05a library database (National Institute of Standards and Technology).

**Statistical analysis**

Data were analysed using Statistical Analysis System (SAS) software for Windows. Differences in means were determined using one-way ANOVA. Results were expressed as a mean of three determinations ± SD. The significance level was set as $p < 0.05$. Tukey's HSD method was used for pairwise mean comparisons.

## Results:

**Effects of different solvents on extraction yield**

Table 1 shows the effect of the extraction solvents on the extract yield of *V. amygdalina* leaves. The highest extraction yield was observed for ethanol extracts at 49.20%, followed by methanol extracts at 45.89%, and dichloromethane extracts at 7.69%.

Table 1. Extraction yield of *V. amygdalina* extracts.

| Solvents | Dry weight of plant material (g) | Weight of dry extract (g) | Extraction yield (%) |
|---|---|---|---|
| **Dichloromethane** | 35 | 2.69 ±0.16 | 7.69±0.45 |
| **Ethanol** | 35 | 17.22 ±0.33 | 49.20±0.93 |
| **Methanol** | 35 | 16.06±1.03 | 45.89±0.74 |

Values are expressed as mean ± SD (n=3).

**Disc diffusion assay**

Figure 1 presents the results of the disc diffusion assay of ethanol, methanol, and dichloromethane extract of *V. amygdalina* leaves against each bacterial strains used. Results showed that all extracts inhibited the bacterial strains at different concentrations ranging from 25 - 200 mg/mL.

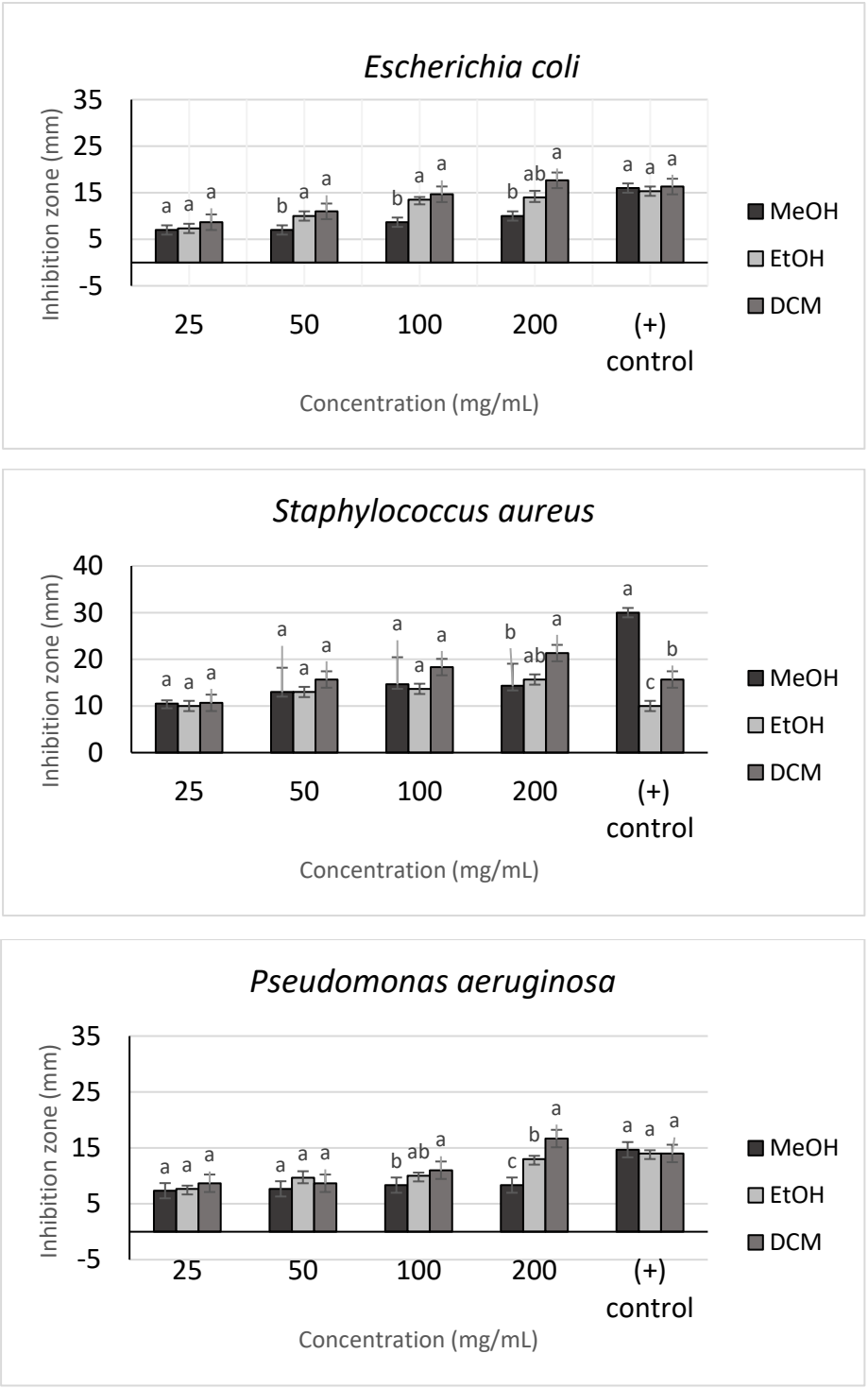


**Figure 1**. The zones of inhibition of three different solvents at different concentrations against selected bacteria. (+) control: positive control (gentamycin) at 10 ug/mL. Mean values with the same lowercase letter are not significantly different ($p > 0.05$) according to Tukey's HSD Test.

**GC-MS Analysis**

The GC/MS analysis was performed on the most active extracts of *V. amygdalina*, and the identified chemical constituents were listed with their corresponding retention time and peak area. Specifically, the GC/MS analysis of *V. amygdalina* indicated that the dichloromethane extract contained 26 compounds, as illustrated in Figure 2. Meanwhile, the ten most abundant compounds in the dichloromethane extract, as detected by GC-MS analysis are tabulated in Table 2.

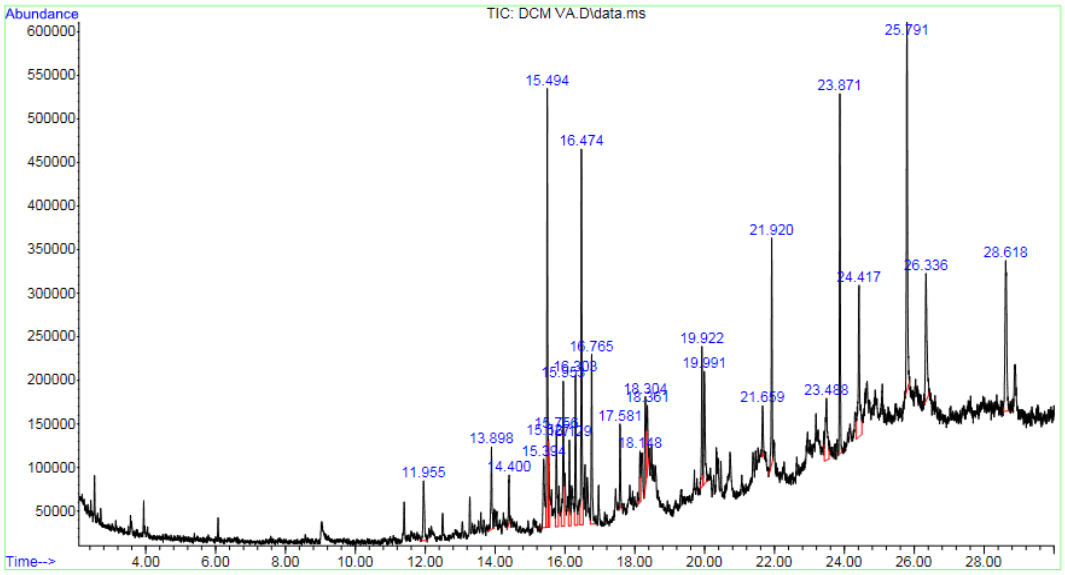


**Figure 2.** GC-MS chromatogram of the dichloromethane extract of *Vernonia amygdalina* leaves.

Table 2: Chemical constituents present in the dichloromethane extract of *Vernonia amygdalina* leaves.

| Retention time (min) | Compound Name | Peak area (%) |
|---|---|---|
| 25.791 | Octadecane, 1-iodo- | 9.8189 |
| 15.496 | Bicyclo[3.1.1]heptane, 2,6,6-trimethyl-, (1.alpha.,2.beta.,5.alpha.)- | 8.709 |
| 16.476 | 7,9-Di-tert-butyl-1-oxaspiro (4,5) deca-6,9-diene-2,8-dione | 8.434 |
| 23.872 | 2,6,10,15,19,23–hexamethyl-2,6,10,14,18,22-tetracosahexaene (Squalene) | 7.336 |
| 28.616 | Methylenebis(2,4,6-triisopropylphenylphosphine) | 6.326 |
| 24.417 | Eicosane | 5.615 |
| 26.336 | Vitamin E | 4.748 |
| 21.922 | Phthalic acid, 2-ethylhexyl tridecyl ester | 4.709 |
| 16.764 | .beta.-Methylfentanyl | 4.027 |
| 15.952 | 3,7,11,15-Tetramethyl-2-hexadecen-1-ol (Phytol) | 3.882 |

## Discussion:

The extraction yield revealed that ethanol exhibited the highest percentage yield at 49.20 % followed by methanol (45.89 %) and dichloromethane (7.69 %). This is because the content of bioactive compounds in the extract can vary greatly due to differences in the polarity of the extraction solvent. Higher extraction yields were observed for ethanol and methanol extracts compared to dichloromethane extract, suggesting that the extraction efficiency favours more

polar solvents (Truong, et al., 2019). The presence of hydroxyl groups in ethanol and methanol increases their ability to form hydrogen bonds and other polar interactions, thereby increasing their ability to dissolve a broader range of polar and semi-polar compounds (Srikacha and Ratananikom, 2020). In contrast, the inability of dichloromethane to form hydrogen bonds restricts its interactions with polar functional groups. This finding is consistent with a previous study by Ekam, et al. (2010), which reported a positive correlation between solvent polarity and extraction yield. Additionally, the lower extraction yield may result from the thermal decomposition of phytochemical compounds during the Soxhlet extraction process, as reported by Danlami, et al. (2014). Thermally sensitive phytochemicals compounds undergo degradation during the heating, resulting in low extraction yields (Danlami, et al., 2014).

Figure 1 indicates that *S. aureus* was the most susceptible to all solvent extracts at all concentrations, with an inhibition zone diameter ranging between 7 to 22 mm. A previous study by Bukar, et al. (2013) reported that the most susceptible bacteria strains to the ethanolic extract of *V. amygdalina* are *S. aureus* followed by *E. coli* and *P. aeruginosa*. The variation in inhibition zones can be attributed to the differences in the structure of the cell envelope between Gram-positive and Gram-negative bacteria (Fivenson, et al., 2023). The higher susceptibility observed in the *V. amygdalina* extracts may be associated with the presence of two cellular membranes, with an outer membrane coated with lipopolysaccharides in Gram-negative bacteria, acting as a powerful barrier that restricts the penetration of compounds. In contrast to the barrier of Gram-negative bacteria, the absence of an outer membrane in Gram-positive bacteria reduces the interference and facilitates the diffusion of compounds across the cell membrane (Fivenson, et al., 2023).

Among various solvents tested, dichloromethane extract displayed the highest antibacterial activity against all bacterial strains at various concentrations (25-200 mg/mL) when tested by the agar disc diffusion assay (Figure 1). However, the antibacterial activity of dichloromethane extract is not significantly different compared to all tested solvents at low concentrations. On the other hand, there are some significant differences at 200 mg/mL. Dichloromethane extracts exhibited inhibitory activity against *E. coli*, *P. aeruginosa* and *S. aureus,* with an inhibition zone ranging from 8 to 22 mm, exceeding the inhibitory activity of methanol and ethanol extracts. The non-polar nature of dichloromethane allows selective extraction of lipophilic or non-polar antibacterial compounds from *V. amygdalina* (Benramdane, et al., 2022). Furthermore, Gram-positive bacteria are more sensitive to lipophilic extracts than Gram-negative bacteria, which explains the larger inhibition zones observed for *S. aureus* in the dichloromethane extract (Benramdane, et al., 2022). Further GC-MS analysis of the dichloromethane extract revealed a predominance of lipophilic compounds as shown in Table 1. The identified compounds included those known for their antibacterial properties, such as squalene, phytol, β-methylfentanyl and octadecane (Hartmann, et al., 2020; Huang, et al., 2021; Olusola, et al., 2021; Oladunmoye, et al., 2019; Unlu, et al., 2021; Wijayanti and Dewi, 2022). These compounds may have a greater impact on the inhibition of bacterial growth in the dichloromethane extract.

## Conclusion:

Our findings highlight the influence of solvent selection on the extraction yield and antibacterial activity of *V. amygdalina* leaves extract. Ethanol and methanol, being more polar solvents, exhibited higher extraction yields, while dichloromethane selectively extracted lipophilic compounds due to its non-polar nature. Among the solvents tested, dichloromethane was found to be the most effective solvent for the production of antibacterial-rich extract, exhibiting potent antibacterial activity against *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*. In addition, GC-MS analysis identified 26 phytochemical compounds with potential antibacterial properties. Given the increasing demand for plant-derived antibacterial agents as a substitute for synthetic antibiotics, *V. amygdalina* may be a promising source for the development of new antibacterial drugs to prevent a variety of diseases. Future research may focus on the characterization of the active compounds as well as the elucidation of their mechanism of action for the development of antibiotics from *V. amygdalina*.

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# Herbs To Treat Female Sexual Dysfunction (*Mati Putik*) In Malay Medical Manuscripts

***Radiah Binti Abdul Ghani, PhD**
Department of Biomedical Science, Kulliyyah of Allied Health Sciences, International Islamic University Malaysia, Jln Sultan Ahmad Shah Bandar Indera Mahkota 25200 Kuantan, Pahang, Malaysia.
radiah@iium.edu.my

**Ain Ilmiah Binti Anhar, BSc.**
Department of Biomedical Science, Kulliyyah of Allied Health Sciences, International Islamic University Malaysia, Jln Sultan Ahmad Shah Bandar Indera Mahkota 25200 Kuantan, Pahang, Malaysia.
ain.anhar@gmail.com

**Mohd. Affendi Bin Mohd. Shafri, PhD**
Department of Biomedical Science, Kulliyyah of Allied Health Sciences, International Islamic University Malaysia, Jln Sultan Ahmad Shah Bandar Indera Mahkota 25200 Kuantan, Pahang, Malaysia.
affendishafri@iium.edu.my

***Corresponding author:*** Radiah Binti Abdul Ghani, radiah@iium.edu.my

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**Abstract:**

**Introduction:** Lack of libido is one of the most common symptoms of female sexual dysfunction among women in the global community. In Malaysia, low levels of libido have been demonstrated in women experiencing *mati putik* or female sexual dysfunction (FSD). Due to the lack of awareness about FSD, people commonly misunderstand that the signs and symptoms are due to the aging process. The most common signs of *mati putik* or FSD are fatigue and no desire or interest in engaging in sexual activity. To date, there has been no comprehensive review of the practice of Malay ancestors regarding FSD. Thus, the aim of this study was to document the formulations and practices recorded in Malay medical manuscripts for enhancing female sexual libido. **Methods:** The secondary texts of Malay medical manuscripts were reviewed to discover the ingredients used as aphrodisiac agents in the Malay Archipelago. The Malay term *shahwat* was the keyword used to describe sexual libido in the Malay community. A comparative analysis was then conducted to evaluate the materia medica found in the academic literature. **Results:** Four formulations were found that comprised four different aphrodisiac ingredients, including cabbage, fenugreek, kati, and honey. From all the ingredients, only fenugreek has found clinical evidence in the academic literature. **Conclusion:** Therefore, it is suggested that the materia medica found in the study be further explored to demonstrate its relationship with libido. This study is important as a part of preserving Malay medical knowledge and heritage, as well as providing insight into information on aphrodisiac plants for enhancing women's libido that can be applied in conventional medicine.

**Keywords:** Hypoactive sexual desire disorder, Malay medical manuscripts, Malay traditional medicine, *mati putik*

## Introduction:

*Mati putik* or female sexual dysfunction (FSD) is more frequent among women who are married and have children (Shahimi, 2017). The most common symptoms of *mati putik* among Malay women are low libido or a lack of interest in engaging in sexual activity, as well as extreme fatigue (Shahimi, 2017). It is believed that *mati putik* can be treated by Malay traditional practices such as *bertangas* (vaginal steam), *berurut* (massage), and consuming or using herbal-based products (Shahimi, 2017; Ahmad Zaidi, 2022). Although *mati putik* is common in the society, only a few are really concerned about the method of treating this problem. Some people prefer to keep it to themselves because they are ashamed and fear the treatment will hurt them (Shahimi, 2017; Ahmad Zaidi, 2022). According to a recent cross-sectional study by Malaysian researchers, the prevalence of FSD among women aged 50 years and older attending the outpatient clinic was 68.8 percent. The women appeared to have problems in all six FSD subdomains, including sexual desire, satisfaction, arousal, lubrication, pain, and orgasm and desire disorder, which is the most prevalent at 85.2 percent (Tey et al., 2022).

Low libido is defined as hypoactive sexual desire disorder In Diagnostic and Statistical Manual-5 this disorder is classified in the first class of Female Sexual Dysfunction (FSD), which is the Female Sexual Interest/Arousal Disorder. Flibanserin is the first FDA-approved drug for hypoactive sexual desire disorder. Bremelanotide is the most recent drug for enhancing female libido in evidence-based medicine. It is a successful drug that has passed all the clinical trial stages. It has proven the ability to increase libido, physical arousal, and sexual satisfaction (Koochaki et al., 2021). The current clinical trial studies provide some alternatives for enhancing female sexual libido. Vitamin E, ginseng, and Tribulus terrestris are found to be effective in improving sexual desires among women (Ghamari et al., 2020; Vale et al., 2018). The use of zinc supplementation is positive for increasing testosterone levels and improving sexual function in women. Free testosterone and estradiol (E2) are important hormones for regulating sexual desire and arousal in women (Mazaheri et al., 2021).

The Malay medical manuscript (MMM) is a wonderful treatise that portrays the high intelligence of our Malay ancestors in grasping myriads of medical knowledge. Like other races in Malaysia, the Malay community also have their own traditional beliefs and practices on medicine and health, which have been practiced and passed down from generation to generation either in the form of writings or verbally (Abd Aziz & Yunos, 2019). Studying MMM is crucial for research on its accessibility and usefulness in Malay society, known for its reliance on non-allopathic medicine (Sidik & Baharuddin, 2010). The study on MMM may provide information on the signs and symptoms of *mati putik* and potential treatment options for women suffering from FSD. Thus, the aim of this study is to document the formulations for enhancing female libido in the Malay medical scriptures.

## Materials and Methods:

### Reviewed Materials

The secondary texts of Malay medical manuscripts were reviewed to discover the ingredients used as aphrodisiac agents in the Malay Archipelago. The Malay term "shahwat" was the keyword used to describe sexual libido in the Malay community. To differentiate between "shahwat" for men and women, the study retrieved information that contained the benefits for women in the same formulation and discarded all formulations that had descriptions for men and women in general. From all the reviewed references, only three publications were selected that contained the intended information, including Kitab Kitab Perubatan Melayu: Khazinat al-Insan (Sarah Syazwani, 2017), Kitab Perubatan Melayu: Rumah Ubat Di Pulau Penyengat (Mohd Affendi Mohd Shafri, 2018), and Tib Ilmu Perubatan Melayu (Harun Mat Piah, 2019). In Kitab Tib Ilmu Perubatan Melayu, the book itself comprised of three fragments of manuscripts from MSS 2515, MSS 1292, and Hikayat Nurul Al-Lisan Menjawab Masalah (MSS 1792). Other publications were completed transliterated manuscripts.

### Comparative Analysis of the Content of the Manuscript to Contemporary Scientific Reports

Comparative analysis is a method in which the use of individual herbs, animals, or minerals in a traditional formulation in a text is compared to published papers in modern scientific databases. The presence of papers of related use or in support of the use in the manuscripts is an indication of verified use. However, the absence of the papers does not necessarily mean that the traditional use is unverified, as many of the traditional Malay formulations, or even the individual ingredients from the Malay world, have not been studied by modern scientists (Mohd Shafri, 2021). The study used two search engines, PubMed and Google

Scholar, to retrieve peer-reviewed journal articles and both peer-reviewed and non-peer-reviewed articles from a vast range of medical and science sub-disciplines. The scientific evidence search strategy used in this study includes: (a) In vitro study OR In/ex vivo study OR Animal study OR randomized controlled trial study OR human case study; and (b) Any parts of the materia medica that were used in the clinical study. The search strategy was established to ensure that the scientific evidence retrieved for any materia medica is reliable and relevant.

## Results and Discussion:

### Formulation of Herbs to Treat *Mati Putik* or Female Sexual Dysfunction

The results of the study discovered four formulations for enhancing female sexual libido in the Malay medical manuscripts from three different references. The formulations were depicted below with translations:

(1) *Yang kedelapan halba, maka kequwwatannya hangat darjah yang kedua, dan kering darjah yang pertama. Fa'idahnya membantutkan bengkak yang baharu, dan menyegerakan pecah bengkak yang lama. Maka, jika dimasak dengan manisan lebah, diminum, menghilangkan penyakit sejuk dan segala yang bertakung di dalam dada, dan menguatkan shahwat, dan membaikkan rahim perempuan, dan menyempurnakan 'aqal,* dan;

Eight is fenugreek. Its strength is hot on the second degree and dry on the first degree. Its benefits are to prevent new abscess; and treat chronic abscess. If cooked with honey and drink, this will get rid of cold diseases and all diseases that are located in the chest; and increase sexual desire; and improve womb; and increase the intellect.
(Kitab Perubatan Melayu Khazinat Al-Insan, Sarah Syazwani, 2017, p. 33)

(2) *Adalah fa'idah ini ma'jun menyembuhkan penyakit angin; dan mengeluarkan sekalian penyakit daripada sejuk; dan memberi quwwat akan shahwat; dan memberi sembuh sakit berdebar; atau sakit duka cita; dan sangat memberi manfaat perempuan, dan mantapkan 'aqal iaitu dimakan pagi, petang; sekali makan satu butir, kira-kira besar ibu tangan tiap-tiap sebutirnya, in sha' Allah Ta'ala, mujarrab dengan sebabnya adanya. Tamm.*

The benefits of this electuary [fenugreek] are to heal diseases related to imbalance in the wind element; and to get rid of all cold diseases; and increase desire for sex; and to resolve nervousness and grief; and this is especially beneficial to women; and to enhance the intellect. Eat one thumb-size piece in the morning and evening.

(Kitab Perubatan Melayu Rumah Ubat di Pulau Penyengat, Mohd Affendi Mohd Shafri, 2018, p.

(3) *(Kata tabib), "Daripada kurnub (kubis)". Jawabnya, "Panas kering lagi lembut isinya dan daunnya panas lembut. Dan pergunaannya jika dimakan akan dia nescaya menambahi syahwat jimak dan jadi daripadanya angin. Dan menghilangkan berat lidah jika selalu memakan dia dan molekkan suaranya dan jika diasap di bawah faraj perempuan nescaya keluar uri-uri; dan demikian bijinya memudahkan keluar uri dan jika diminum air perahan daunnya nescaya keluar uri dengan mudah dan jika dimakan oleh perempuan kemudian daripada beranak nescaya menyucikan peranakan akan sebagai cuci yang elok. Dan jika dihantarkan daunnya pada tempat disengat oleh kala nescaya mengisap ia akan bisanya kepada luar dan jika dimakan akan dia nescaya menghilangkan penyakit safara dan dapat tidur; dan jika selalu meminum air rebus daunnya nescaya melicin akan suara serta moleknya".*

Said physician, "From kurnub (cabbage)". Her replies, "Its flesh is hot, dry and soft whereas the leaves are hot and soft. Its usage is if eaten, it will increase desire for sex and cause angin. If consumed regularly, it will reduce heaviness in the tongue; and smoothen the voice; and if smoked over her vagina, it will remove the lochia; and the seed eases the process of removing lochia; and if consumed the juice from the leaves, the lochia will be removed easily; and if consumed by woman after giving birth, it will cleanse her womb, which is good as cleansing. And if the leaves are applied on the site stung by scorpions, it will take out the venom; and if consumed, this will treat safara diseases; and aid sleeping. If the boiled water is taken regularly, this will smoothen the voice.

([Hikayat Nurul Lisan Menjawab Masalah (MSS 1792)] Kitab Tib Ilmu Perubatan Melayu, Harun Mat Piah 2019, p. 289)

(4) *(Kata tabib), "Daripada karfas (kati). Jawabnya, "Panas kering; pergunaannya menghilangkan bengkak dan membukakan lubang urat yang tersumbat dengan balgham dan membaikkan bahu mulut dan menghilangkan sebak nafas dan membanyakkan air kencing serta memudahkan keluarnya dan membangkitkan syahwat jimak daripada laki-laki dan perempuan. Dan jika dimakan akan dia nescaya menghilangkan air titik air kencing".*

Said physician, "From karfas (kati)". Her replies, "Its nature is hot and dry. Its usage is to reduce swelling; and to remove the blockage in the vein caused by phlegm; and improve bad breath (halitosis); and treat

sebak nafas; and increase the amount of urine; also ease in urination; and initiate the desire for sex in both men and women. If consumed, this will treat dribbling".

([Hikayat Nurul Lisan Menjawab Masalah (MSS 1792)] Kitab Tib Ilmu Perubatan Melayu, Harun Mat Piah 2019, p. 289)

**Comparative Analysis with Scientific Literatures**

In this study, four different ingredients were discovered from the formulations. The use of a single ingredient is more preferred than preparing in combination with other material. The prescription of the formulation is either by drinking the boiled remedy, eating as an electuary, or eating the leafy parts of the plants. All the ingredients discovered in the study do not only boost up the women's arousal, but they have more than one medicinal benefit.

Table 1: Summary of the findings (the ingredients, part or form used, and prescription)

| No. | Ingredient | Part/ Form used | Direction of usage |
|---|---|---|---|
| 1. | *Halba* (Fenugreek)<br>Manisan lebah (Honey) | Seed<br>Liquid | Drink the cooked mixture of fenugreek and honey |
| 2. | *Halba* (Fenugreek) | Seed | Eat one thumb-size piece of fenugreek electuary in the morning and evening |
| 3. | *Kubis* (Cabbage) | Flesh and Leaf | Eat the flesh and leaves of the cabbage |
| 4. | *Kati* | Not stated | Not stated |

Fenugreek is a bitter, strong-scented spice (Omar, 2018) used to enhance the flavour in some Malay dishes. This herb has been utilized in the treatment of uterine infections, vaginitis, induce childbirth and lactation in the Middle East (Shahrajabian et al., 2021). In Malay traditional medicine, drinking the pounded seed of fenugreek is good for breastfeeding mothers to improve lactation (Mohamed Rehan et al., 2021). Clinical evidence supported fenugreek could increase women's sexual libido by increasing the level of circulating hormones and sexual function in healthy menstruating women (Rao et al., 2015). The study administered 600 mg of Trigonella foenum-graecum seed extract (Libifem) to 80 women in the age of 20 and 40 years old, and the results revealed a significant increase in free testosterone and estradiol (E2) and improvement in sexual desire and arousal among women compared to the placebo (Rao et al., 2015). In the study, the Malay medical manuscripts described the use of *halba* or fenugreek, in combination with honey for drinking and *halba* electuary for women's libido.

Table 2: Clinical Evidence of The Materia Medica in the Scientific Literatures

| No | Vernacular Name | Scientific Name | Scientific literature evidence |
|---|---|---|---|
| **Plant-based** | | | |
| 1. | *Kubis* (Cabbage) | *Brassica oleracea* | Not found |
| 2. | *Kati* | *Aganosma marginata*[1]<br>*Ligusticum acutilobum*[2] | Not found |
| 3. | *Halba* (Fenugreek) | *Trigonella foenum-graecum* | Influence of a Specialized Trigonella foenum-graecum Seed Extract (Libifem), on Testosterone, Estradiol and Sexual Function in Healthy Menstruating Women, a Randomised Placebo Controlled Study (Rao et al., 2015) |
| 4. | *Manisan lebah (Honey)* | - | Not found |

[1] *Kati* may refer to *sekati lima* plant (https://prpm.dbp.gov.my/)
[2] *Kati* may refer to *ganti* plant (MSS 1292)

*Kubis* or cabbage is a traditional salad food (ulam), not only among Malay community but all races in Malaysia. It can be found in many cultivated forms such as cabbage (*kubis*), broccoli (*kubis bunga hijau*), cauliflower (*kubis bunga*) and brussel sprouts (*kubis brussel*). They are also being called cruciferous vegetables. By applying the leaves of cabbage on the mother's breast, this will help relieve breast engorgement during the postpartum period (Muhammad Rehan et al., 2021). Cabbage is among the food that is prohibited to be consumed among women after childbirth due to its cold nature. In the Malay traditional view, these mothers should always remain in the hot condition to ensure the recovery process runs smoothly (KKM, 2017). Cabbage is high in sulfur and enriched with vitamins and has medicinal benefit in the treatment of scurvy in Mediterranean (Stefan & Andreaa, 2021). The seed from spring cabbage (Brassica oleracea L. var. capitata L.) has been traditionally used as an aphrodisiac in Turkey (Tufan et al., 2018). Fenugreek and cabbage are found to be effective in the alleviation of breast engorgement among breastfeeding mothers (Hassan et al., 2020). However, there was no scientific evidence that relates between cabbage as aphrodisiac herbs.

The next herb that was recorded to be used as ingredients to treat *mati putik* is called *kati* in the manuscripts. There are two types of plants referred to as *kati*. The first plant is *Aganosma marginata*, or called by its local name as *sekati lima*. In MSS 2515, the leaves and roots of *sekati lima* are used as remedy for coughing. By drinking the boiled water of the stem, flowers and pulur of teberau, leaves of *sekati lima*, fenugreek, garlic and onion, this will relieve asthmatic coughs (Raja Perdaus et al., 2021). The second plant is *Ligusticum acutilobum* or called by the local as *ganti*. It is one of the ingredients used in a remedy for typhoid fever as chronicled in MSS 4106. By mixing the grounded leaves of climbing ferns and *susuk baju*, *costus, kanti* and massoy bark with water and sprinkle over the whole body, this formulation is believed to heal typhoid fever (Ruzaidi et al., 2021). This plant is well known in Chinese medicine and called as *dang quai*, it is an essential ingredient for anaemia and gynaecological conditions (Dennis et al., 2007).

Based on the findings, it has been observed that only one ingredient, which is fenugreek, has been scientifically proven for their ability in enhancing libido. The remaining ingredients may not yet be explored as female aphrodisiac agents. Consumption of these herbs often may increase the libido in women. Therefore, it is suggested for women experiencing low libido to add this herb into their daily intake, although their effectiveness is still not proven in the academic literatures.

## Conclusion:

Low libido is one of the reasons why married couples experience less satisfaction in their sexual experience which may lead to marital dissatisfaction. Besides the awareness regarding the signs and symptoms and modern medicinal treatment, a complementary study on the practices of Malay ancestors could be one of the initiatives which need to be highlighted. It has been shown in this study that medical manuscripts have shown the practice of our ancestors in preserving their libido by consumption of certain ingredients accessible to their home. However, most of the herbs found in the study has no scientific evidence on the treatment for female sexual dysfunction except fenugreek. Therefore, further investigation of those herbs such as cabbage, *kati* and honey is warranted in order to establish a proper formulation of the ingredients which will be effective for the FSD treatment.

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# Dietary adherence component of modified end-stage renal disease adherence questionnaire (ESRD-AQ): translation and validation

**Sarah Muneera Karami, BSc**
Department of Nutrition Sciences,
Kulliyyah of Allied Health Sciences,
International Islamic University Malaysia,
Jalan Sultan Ahmad Shah,
Bandar Indera Mahkota,
25200 Kuantan, Pahang
sarahmuneera@gmail.com

**Wan Azdie Mohd Abu Bakar, PhD**
[1]Food Security and Public Health Nutrition Research Group (FOSTER),
[2]Department of Nutrition Sciences,
Kulliyyah of Allied Health Sciences,
International Islamic University Malaysia,
Jalan Sultan Ahmad Shah,
Bandar Indera Mahkota,
25200 Kuantan, Pahang
wazdie@iium.edu.my

**Roselawati Mat Ya, PhD**
Department of Community Medicine,
Kulliyyah of Medicine,
International Islamic University Malaysia,
Jalan Sultan Ahmad Shah,
Bandar Indera Mahkota,
25200 Kuantan, Pahang
rosematya@iium.edu.my

**Norhasmah Sulaiman, PhD**
Department of Nutrition,
Faculty of Medicine & Health Sciences,
Universiti Putra Malaysia,
Jln Universiti,
43400 Serdang, Selangor
norhasmah@upm.edu.my

***Nor Azwani Mohd Shukri, PhD**
[1]Food Security and Public Health Nutrition Research Group (FOSTER),
[2]Department of Nutrition Sciences,
Kulliyyah of Allied Health Sciences,
International Islamic University Malaysia,
Jalan Sultan Ahmad Shah,
Bandar Indera Mahkota,
25200 Kuantan, Pahang
norazwani@iium.edu.my

***Corresponding author:** Nor Azwani Mohd Shukri, norazwani@iium.edu.my

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## Abstract:

**Introduction:** A nutritionally balanced diet is crucial among end-stage renal disease (ESRD) patients to maintain their health status. An appropriate instrument is needed to assess ESRD patients' adherence towards dietary recommendations. Several questionnaires to measure adherence behaviours of ESRD patients are available but none has ever been translated into the Malay language. Therefore, this study aimed to translate the modified version of the End-stage Renal Disease Adherence Questionnaire (ESRD-AQ), focusing on the dietary adherence component, from English to Malay. **Methodology:** Forward and backward translations of the questionnaire were conducted involving experts in dietetics and linguistics to produce a pre-harmonized Malay translation and two backward English translations according to established guidelines. An expert committee reviewed these translated questionnaires to produce a harmonized version. This then underwent a pre-test conducted using cognitive interview, as well as face validity assessment,

involving 15 haemodialysis patients. **Results:** Minor amendments were made to several phrases during the expert committee review to ensure the translated questionnaire was contextually appropriate and culturally adapted to the Malay language. All questions in the Malay version of the modified ESRD-AQ achieved a Face Validity Index (FVI) value of 1.00, indicating high validity. **Conclusion:** The Malay version of the modified ESRD-AQ (Dietary Adherence Component) underwent translation and validation protocols, the findings of which indicate that it is clear and comprehensible for use in assessing dietary adherence among ESRD patients in Malaysia.

**Keywords:** Dietary adherence, End-stage renal disease, ESRD-AQ, Malay, Translation

## Introduction:

End-stage renal disease (ESRD), also known as chronic kidney disease (CKD) stage 5, refers to a condition characterized by the permanent impairment of kidney function, resulting in a significant decrease in its ability to remove harmful waste substances from the body (Kidney Disease Improving Global Outcomes, 2013). The incidence of CKD rises with age, peaking in those sixty years of age or beyond. Diabetes mellitus is the leading cause of the disease, alongside hypertension and vascular disease, in both developed and developing countries (Hashmi, Benjamin & Lappin, 2023). According to the Global Burden of Disease Study (2017), accessibility of renal replacement therapy has greatly increased from 1990 to 2017. This is much needed as the worldwide occurrence of dialysis and kidney transplantation has risen by 43.1% and 34.4%, respectively, across all age groups (Bikbov et al., 2020).

Hemodialysis, a method of cleansing the blood extracorporeally using a catheter to eliminate metabolic waste in patients with kidney failure, is a procedure that has significant physical, psychological, economic, and social impacts on patients, leading to a decrease in their quality of life (Hackett & Jardine, 2017; Ronco & Clark, 2018). A nutritionally balanced diet is essential for individuals undergoing hemodialysis. End-stage renal disease patients frequently experience a range of dietary issues, including protein-energy depletion, mineral-bone abnormalities, electrolyte imbalance, and anemia, due to their kidneys not functioning at their maximum potential (Lee et al. 2020; Lim et al., 2020). Furthermore, patients' appetite and dietary consumption might potentially be affected due to side effects of hemodialysis such as headache, nausea, vomiting, and fatigue (Himmelfarb, 2005). Thus, individuals must adhere to the dietary guidelines by consuming an appropriate quantity of protein, calories, fluids, vitamins, and minerals to maintain good health.

Adherence, as defined by the World Health Organization, WHO (2003), refers to the extent to which a person's behaviour such as taking medication, following a diet, and executing lifestyle changes corresponds with agreed recommendations from a healthcare provider (Al-Salmi, Cook & D'Souza, 2022). Adherence behaviours assessment among ESRD patients usually includes four dimensions which are dietary intake, fluid restriction, adherence to medications, and dialysis attendance. There are several available questionnaires to assess adherence among ESRD patients such as the Renal Adherence Behaviour Questionnaire (RABQ), Renal Adherence Attitudes Questionnaire (RAAQ), Dialysis Diet and Fluid Non-adherence Questionnaire (DDFQ), as well as End-stage Renal Disease Adherence Questionnaire (ESRD-AQ). The RAAQ, a scale consisting of 26 items, RABQ (25 items), and DDFQ (eight subscales) measure adherence to dietary and fluid intake recommendations (Rushe & McGee, 1998; Vlaminck et al., 2001). On the other hand, the ESRD-AQ measures adherence to all four dimensions (Kim et al., 2010). According to Lim (2021), the ESRD-AQ is simple to administer and has been used locally by the author. However, none of these adherence questionnaires for dialysis patients has ever been translated into the Malay language.

In this study, we aimed to translate the dietary adherence subscale of the modified ESRD-AQ by Lim (2021) into the Malay language and validate it. The availability of the validated Malay version of ESRD-AQ (Dietary Adherence Component) would benefit

researchers as well as healthcare professionals in Malaysia to assess ESRD patients' dietary compliance and may contribute to better diet management among them.

## Methodology:

### End-stage Renal Disease Adherence Questionnaire (ESRD-AQ)

The original ESRD-AQ was developed in the English language by Kim et al. (2010). It comprises four subscales that assess treatment adherence behaviours across four dimensions: attendance to hemodialysis sessions (14 items), utilization of prescribed medications (9 items), adherence to fluid restrictions (10 items), and compliance with dietary recommendations (8 items). All subscales have demonstrated content validity scores exceeding 0.86 and exhibit strong reliability with an intraclass correlation coefficient (ICC) of more than 0.83. To focus on dietary compliance among hemodialysis patients, a local researcher adopted three questions from the dietary adherence component of ESRD-AQ, added a new question to measure self-reported dietary adherence on a continuous scale, and validated it (Lim, 2021). This modified ESRD-AQ (Dietary Adherence Component) which consists of four items was then used in the current study to be translated into Malay and validated. The first two pertain to the frequency and timing of the patient's most recent dietary education obtained from a healthcare professional. The rest of the questions are related to the patient's self-reported dietary adherence in the previous week. The responses for items no. 1, 2, and 3 are provided as multiple choice, while the final item (the dietary adherence level rating) is evaluated using a continuous scale of 0 to 100%, with a higher score indicating better compliance.

### Study Design

The current study conducted the translation and validation of a questionnaire, which was originally in English, into the Malay language. This was accomplished following the instrument translation guideline by the WHO (2019).

### Phase 1: Questionnaire Translation

The translation of the modified ESRD-AQ (Dietary Adherence Component) (E0) was conducted in five stages (Figure 1). The process began with forward translation from English to Malay by two independent bilingual translators, who are proficient in both languages. The first translator, who possessed expertise in terminologies used in healthcare and was familiar with the content of the questionnaire in both languages produced the first version of Malay translation (M1). Meanwhile, the other translator, a Malay language expert who was not aware of the purpose of the questionnaire, generated the second Malay translation (M2) to identify any slight variations from the original questionnaire (E0) (Tsang, Royse & Terkawi, 2017).

The second stage is the synthesis of the M1 and M2 to create a unified pre-harmonized Malay version (MH1) of the modified ESRD-AQ (Dietary Adherence Component). The MH1 then underwent a backward translation process by two proficient English translators who were blinded from the original version (E0) into two distinct English versions (E1 and E2, respectively) (Lau et al., 2017).

The next stage involved the harmonization process of E1 and E2 among expert committee members, which consisted of three senior lecturers with expertise in dietetics, public health nutrition, and community medicine, respectively. The E1 and E2 were deliberated upon, compared with the original version (E0), and harmonized to address and resolve any disparity, ambiguity, and inconsistency in the words and sentences of the items derived from the adopted questionnaire. Simultaneously, the MH1 was also deliberated by the expert committee and underwent necessary revision and modification, in line with the E1 and E2. After all versions of translations were thoroughly reviewed and concluded that both the translated and original versions exhibited semantic, idiomatic, experiential, and conceptual similarity, a consensus on all items was achieved to develop the harmonized version of the translated questionnaire (MH2) (Lau et al., 2017; Tsang et al., 2017).

Finally, the MH2 was pre-tested among 15 respondents from the target population using cognitive interviews. It was done on the hemodialysis patients that undergo routine hemodialysis three times per week (with each session lasting about four

hours) at the Pusat Dialisis Majlis Ugama Islam dan Adat Resam Melayu Pahang (MUIP), located in Kuantan, Pahang. The inclusion criteria also included patients who were not suffering from any major acute diseases or psychological disorders and had undergone dialysis for at least three months before enrolment into the study. The respondents were interviewed by the researcher on what they understood by each question and what they thought of when they heard a certain term or phrase. This was to ensure the translated items maintained the same meaning as the original items and to prevent any confusion regarding the translated questionnaire (Tsang et al., 2017; Geshina, 2019).

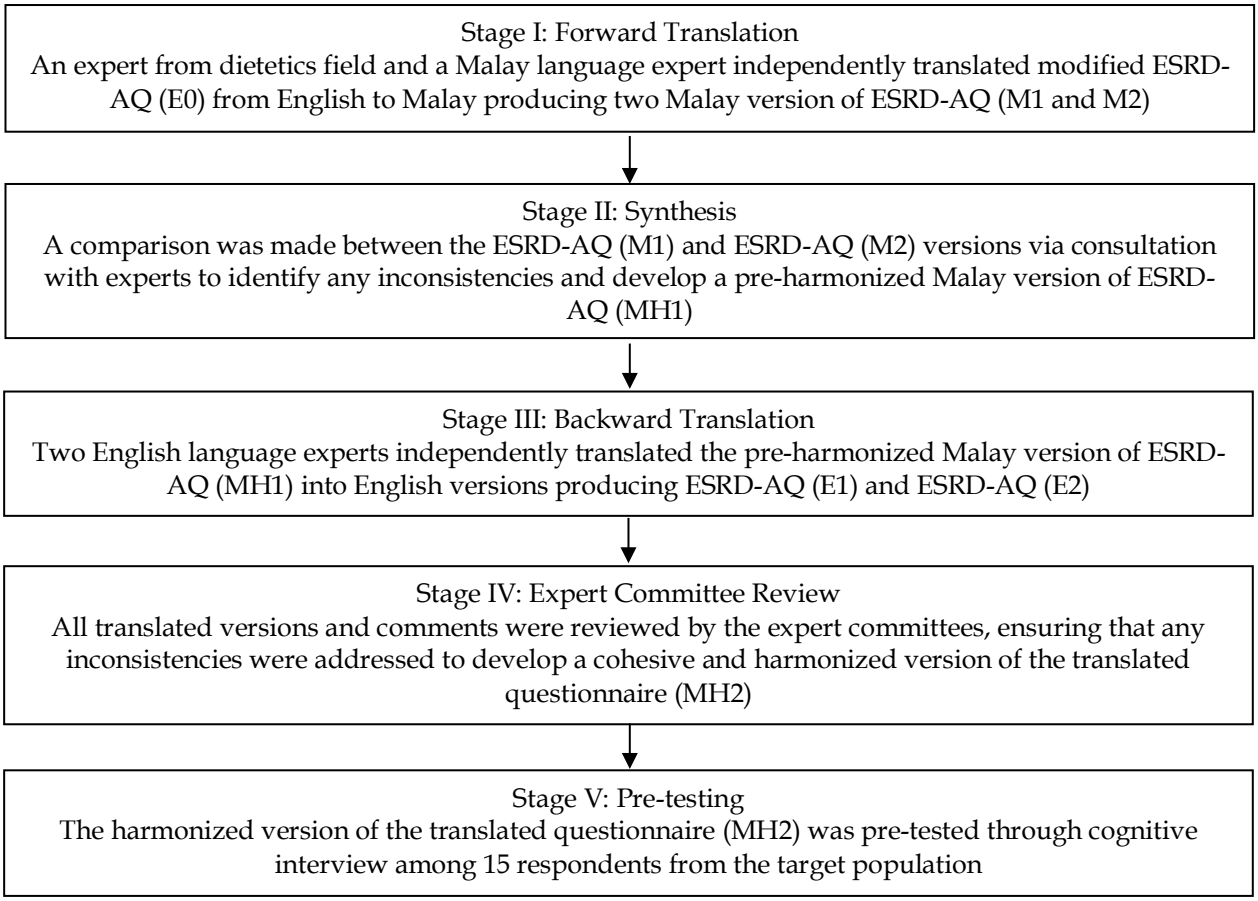


Figure 1: Flow chart of questionnaire translation procedure

**Phase 2: Questionnaire Validation**

Concurrently with the cognitive interview, a face validity assessment was undertaken by a similar group of hemodialysis patients (N=15). A minimum of 10 raters is acceptable for face validation (Yusoff, 2019) and to assess the suitability of the language in pre-testing (Geshina, 2019). The face validity was assessed using the MH2 where the respondents were required to rate their understandability and clarity of each question using a four-point Likert scale ranging from 'Item is not clear and understandable' to 'Item is very clear and understandable'. According to Yusoff (2019), the raters' understanding, and interpretation of the items will affect how well an assessment tool measures the intended construct. The questionnaire item with a face validation index (FVI) value of at least 0.80 was retained.

The FVI was calculated in two forms, i.e. FVI for item (I-FVI) and FVI for scale (S-FVI). Before calculating the FVI, the clarity and comprehension rating should be converted into a binary variable. A rating of 3 or 4 was recoded as 1, indicating clear and comprehensible, while a rating of 1 or 2 was recoded as 0, indicating not clear and not comprehended. Based on Yusoff (2019), the I-FVI value is the

percentage of raters that assign a clarity and comprehension rating of 3 or 4 to an item or question. The S-FVI/Ave is the mean value of the I-FVI scores for all questions on the scale, or the average of the proportion of clarity and comprehension as assessed by all raters. The proportion of clarity and comprehension was determined by calculating the average rating given by each rater. Meanwhile, the S-FVI/UA is an index that measures the percentage of questions that were rated as having a clarity and comprehension score of 3 or 4 by all raters. The Universal Agreement (UA) score was assigned a value of 1 when the item achieves 100% agreement among raters. Otherwise, the UA score was assigned a value of 0 (Yusoff, 2019).

No content validation was conducted in the current study. The purpose of the content validity assessment is to evaluate the degree to which an instrument measures the targeted construct and this depends on how well the items represent the content domains that the questionnaire is supposed to address (Fitzpatrick, 1983). The modified ESRD-AQ (Dietary Adherence Component) does not have any specific domains, but rather all its items assess a single construct (dietary adherence). In addition, the response to the items is in multiple choices; for instance, one of the items requires respondents to report when they last received diet education, and the answer options provided are 'last week', 'last month', 'irregularly', etc. Due to these reasons, a content validity assessment of the modified questionnaire was therefore not deemed necessary.

**Ethical Approval and Participant Consent**

The current study obtained its ethical approval from the International Islamic University Malaysia Research Ethics Committee (Reference No.: IIUM/504/14/11/2/IREC2024-001) and permission to conduct research activities from the Pusat Dialisis MUIP management. All the participants provided informed consent prior to their participation in the study.

**Statistical Analysis**

Descriptive statistics were performed with the presentation of continuous data through mean and standard deviation, and categorical data through absolute number and percentage.

## Results:

**Phase 1: Translation**

The evaluation process demonstrated that pre-harmonized Malay version (MH1) did not require additional adjustment during the backward translation (from Malay to English) since the meaning of the sentences in both back-translated versions (E1 and E2) remained the same as in the original English version (E0).

During the expert committee review, however, a few phrases in the MH1 were revised to ensure they are contextually appropriate and accurately convey the same meaning as the original terminologies. For instance, the phrase "*Jarang sekali*" in the answer options for Item No. 2 was replaced with the phrase "*Jarang-jarang*" because it gives a more accurate meaning to the word 'Rarely'. Other than that, the phrase "*Cadangan pemakanan*" for Items No. 3 and 4 was replaced with "*Saranan pemakanan*". This is because it is a more apt translation for the term 'Dietary recommendation' and is more commonly used by nutritionists and dietitians in Malaysia. No comment about the misunderstanding of phrases or sentence contexts of the translated questionnaire was reported by the respondents during the cognitive interview.

**Phase 2: Validation**

Five males (33.3%) and 10 females (66.7%) aged between 24 and 72 years were involved in this assessment (Table 1). All the respondents were Malay and their dialysis vintage varied from six months to 22 years (mean ± SD, 51 ± 61 months).

The study participants (N=15) assessed the clarity and comprehension of the items as either 3 or 4, producing an index of 1.00 for all the items (Table 2). Therefore, the Malay version of the modified ESRD-AQ (Dietary Adherence Component) can be considered valid to be used among hemodialysis patients in Malaysia.

## Discussion:

Assessing the dietary adherence of patients undergoing maintenance hemodialysis treatment is crucial for their overall well-being and quality of life

Table 1: Demographic characteristics of study participants (N=15)

| Demographics | n | % | Mean ± SD |
|---|---|---|---|
| **Age (years)** | | | 52.7 ± 12.6 |
| **Gender** | | | |
| Male | 5 | 33.3 | |
| Female | 10 | 66.7 | |
| **Ethnicity** | | | |
| Malay | 15 | 100 | |
| **Dialysis vintage (months)** | | | 50.5 ± 60.9 |

Table 2: Face Validity Index for the Malay Version of the modified ESRD-AQ (N=15)

| Items | Question | | | |
|---|---|---|---|---|
| | 1 | 2 | 3 | 4 |
| S-FVI/Ave | 1.00 | 1.00 | 1.00 | 1.00 |
| S-FVI/UA | 1.00 | 1.00 | 1.00 | 1.00 |
| Proportion Clarity/Comprehensible | 1.00 | 1.00 | 1.00 | 1.00 |

The original version of ESRD-AQ developed by Kim et al. (2010) has been translated and validated in several languages such as Arabic (Naalweh et al., 2017), Sinhalese (Lasanthika et al., 2023), and Portuguese language (Poveda et al., 2016). This study involved five stages of translation of the modified ESRD-AQ (Dietary Adherence Component) into the Malay language and face validation that was done concurrently with the cognitive interview of the translated questionnaire. During the translation process, only minor amendments were needed to ensure that certain phrases would convey the precise meaning of the original terms used in the English version.

It is crucial to accurately translate and adapt instruments in a manner that adheres to established criteria and ensures cultural and conceptual appropriateness, rather than merely focusing on linguistic or literal equivalency (Streiner, Norman & Cairney, 2015). The cultural equivalency of a translated instrument refers to the degree to which a word, concept, scale, or normative structure can be regarded as relevant and applicable to cultural groups other than the one in which these elements originated (Marsella & Kameoka, 1989). A stepwise validation for cross-cultural equivalence based on Flaherty et al. (1988) consists of five dimensions which are content, semantic, technical, criterion and conceptual equivalence but they are mutually exclusive of each other. On one or more of these dimensions, an instrument may be considered cross-culturally equivalent, but it may not be on the other dimensions (as cited in Beck, Bernal & Froman, 2003). This study examined the content, semantic, and conceptual equivalence of the translated questionnaire that was done through forward and backward translations, as well as an expert committee review. The goal was to ensure that the questionnaire could accurately assess the same theoretical constructs and maintain their meaning in the culture of interest. Furthermore, most of the words used in the original English version of the questionnaire were easily translatable and did not have multiple meanings in the Malay language. Consequently, when translated into Malay, there was no significant concern in terms of cultural equivalence.

Positive feedback and the absence of comments received from the target population regarding their inability to comprehend any phrase or sentence during the cognitive interview provides evidence that the translated questionnaire incorporates precise phrases and structured sentences that remain faithful to the original intent and concept of the questionnaire. Additionally, the face validation revealed good FVI values which indicates that the Malay version of the modified ESRD-AQ (Dietary Adherence Component) is clear and easily comprehensible.

To the best of our knowledge, the Malay version of the modified ESRD-AQ (Dietary Adherence

Component) is the only one that has been translated into the Malay language for use among our local populations. Since our investigation was focused on measuring dietary adherence among the respondents, we did not adopt all the available items in the original ESRD-AQ that was developed by Kim and colleagues (2010). However, the translation and validation of the whole ESRD-AQ, comprising four subscales, i.e., adherence to dialysis sessions, drug prescription, fluid restriction, and dietary guidelines, may be conducted by other researchers if they are interested in using the complete questionnaire. Other than that, the current study only involved Malay respondents. Although the selection of participants was based on purposive sampling for the stated inclusion criteria, the lack of non-Malay patients at the dialysis centre (where the study was conducted) which is in an east-coast state in the Peninsular Malaysia made this demographically typical. Nonetheless, the availability of this validated Malay version of modified ESRD-AQ (Dietary Adherence Component) could fill the gap for a tool to aid researchers and healthcare professionals in Malaysia in assessing ESRD patients' dietary compliance and improving their dietary management for better nutritional outcomes.

## Conclusion:

The Malay version of the modified ESRD-AQ (Dietary Adherence Component) has been translated according to established guidelines and validated with good FVI values indicating its clarity and comprehensibility. Therefore, this questionnaire can be used to assess dietary compliance among ESRD patients in Malaysia.

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## Conflict of interest:

The authors declare no conflict of interest.

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