



#### RA JOURNAL OF APPLIED RESEARCH

ISSN: 2394-6709

DOI:10.47191/rajar/v10i06.01 Volume: 10 Issue: 06 June-2024



Impact Factor- 8.174

Page no.- 114-123

## **Unlocking the Medicinal Benefits of Local Herbal Remedies**

#### Mohamad Noor Hadi Nordin<sup>1</sup>, Han Yih Lau<sup>2</sup>, Mohammad Malek Faizal Azizi<sup>3</sup>, Sohana Romeli<sup>2</sup>

- <sup>1</sup>Koperasi Kolej Kemahiran Tinggi MARA Lenggong, Mukim Durian Pipit, 33400 Lenggong, Perak, Malaysia.
- <sup>2</sup>Agrotechnology and Bioscience Division, Malaysian Nuclear Agency, 43000 Kajang, Selangor, Malaysia.
- <sup>3</sup>Biotechnology and Nanotechnology Research Centre, Malaysian Agricultural Research and Development Institute (MARDI), Persiaran MARDI-UPM, Serdang 43400, Selangor, Malaysia.

ARTICLE INFO	ABSTRACT
Published Online:	This study explores the medicinal potential of indigenous herbs in Southeast Asia. They are
04 June 2024	categorized herbs based on their flavor, taxonomy, and plant part, with an emphasis on their
	wide-ranging applications. The discussion focuses on five key herbs: Tongkat Ali, Misai
	Kucing, Hempedu Bumi, Kacip Fatimah, and Limau Purut, all of which are renowned for their
	specific therapeutic benefits. While these herbs offer promising medicinal properties,
	precautions must be exercised due to the potential for adverse effects and interactions. The
	findings of previous research shed light on the rich medicinal heritage of local herbs,
	providing valuable insights for future studies and pharmaceutical development. This review
Corresponding Author:	comprehensively discusses both the benefits and precautions associated with the use of local
Han Yih Lau	herbs.

I. INTRODUCTION

In recent years, there has been a resurgence of interest in traditional herbal remedies for their potential medicinal properties. Among the myriad of botanical treasures found in various regions worldwide, Southeast Asia boasts a rich diversity of indigenous plants known for their therapeutic benefits. Malaysia stands out as a treasure trove of local herbs with purported medicinal properties, cherished for generations by traditional healers and modern practitioners alike.

In herbal medicine the term herbs are used loosely to refer not only to herbaceous plants but also to bark; roots; leaves; seeds; flowers and fruit of trees, shrubs, and woody vines; and extracts of the same that are valued for their savoury, aromatic, or medicinal qualities. The botanical term herb refers to seed-producing plants with nonwoody stems that die down at the end of the growing season (Craig, 1999). Plants have played a significant role in maintaining human health and improving the quality of human life for thousands of years and have served humans well as valuable components of seasonings, beverages, cosmetics, dyes, and medicines (Craig, 1999).

Plants were once considered as a daily food. Now, plants are popular used as a common source in medicinal agents, food additives, cosmeceuticals, and nutraceuticals (Hendra et al., 2011). Although, the medicinal properties of plants have

gained attention, many research studies are still conducted to discover their values because the utilisation of synthetic drugs to heal or control most chronic diseases have caused several long-term effects. There is rising approach regarding the application of herbal medicinal plants in treating diseases with minimal or no aftereffects (Abd Aziz et al., 2021).

An easy way to comply with the conference paper formatting requirements is to use this document as a template and simply type your text into it. Wherever Times is specified, Times Roman or Times New Roman may be used.

#### II. CLASSIFICATION OF SPICES AND HERBS

Herbs come from leaves of a plant while spices come from various parts of a plant other than the leaves. Spices and herbs can be classified into various groups based on flavour/taste, taxonomy, or part of the plant where they came from. Based on flavour or taste, spices and herbs can be classified into four groups: hot spices (black and white peppers, cayenne pepper, mustard, chilies), mild-flavour spices (paprika, coriander), aromatic spices (clove, cumin, dill, fennel, nutmeg, mace, cinnamon), and aromatic herbs and vegetables (thyme, basil, bay leaf, marjoram, shallot, onion, garlic). Table 1 shows the part of the plant from which different spices originate.

Table 1. Sources of spices and herbs

Table 1. Sources of spices and herbs			
Part of the plant	Spice/Herb		
Leaves	Basil, oregano, bay leaf,		
	thyme, tarragon		
Bark	Cinnamon, cassia		
Seed	Fennel, fenugreek, dill mustard		
Flower/bud, pistil	Clove, saffron		
Fruits/berries	Clove, chili, black pepper,		
	allspice		
Bulbs	Onion, garlic, leek		
Root	Ginger, turmeric		
Aril	Mace		

#### III. BENEFITIAL OF LOCAL HERBS

#### A. Tongkat ali (Eurycoma longifolia)

Eurycoma longifolia Jack (known as tongkat ali), a popular traditional herbal medicine, is a flowering plant of the family Simaroubaceae, native to Indonesia, Malaysia, Vietnam and Cambodia, Myanmar, Laos, and Thailand. E. longifolia, is one of the well-known folk medicines for aphrodisiac effects as well as intermittent fever (malaria) in Asia. Decoctions of E. longifolia leaves are used for washing itches, while its fruits are used in curing dysentery. Its bark is mostly used as a vermifuge, while the taproots are used to treat high blood pressure, and the root bark is used for the treatment of diarrhea and fever. Mostly, the roots extract of E. longifolia are used as folk medicine for sexual dysfunction, aging, malaria, cancer, diabetes, anxiety, aches, constipation, exercise recovery, fever, increased energy, increased strength, leukaemia, osteoporosis, stress, syphilis, and glandular swelling. The roots are also used as an aphrodisiac, antibiotic, appetite stimulant and health supplement (Rehman et al., 2016).

Tongkat Ali is popular for its aphrodisiac property and has been commonly used as an energy enhancer. Tongkat Ali on ED remains unknown, it was postulated that a wide range of bioactive compounds including phenolic compounds, polypeptides, diterpenoids, alkaloids, and quassinoids may contribute to such effect (Abd Aziz et al., 2021).

To the best of our knowledge, a study by Farouk and Benafri in (2007) explored the antibacterial activity of *E. longifolia* plant (Abd-Elaziem Farouk & Asma Benafri, 2007). In this experiment, leaves, stem, and roots were extracted separately with different extraction solvent which are methanol, ethanol, acetone, and aqueous water, by using maceration techniques. The results revealed that all parts of the plant that used alcoholic and acetone extract, except the roots, had potential as antibacterial agents against Grampositive bacteria and Gram-negative bacteria. Water was chosen as the best solvent for extract *E. longifolia* roots as mentioned in the Malaysian standard (MS 2409:2011) due to the high content of the major compound, which is

eurycomanone. In this experiment, leaves and stem of *E. longifolia* prefer alcoholic and acetone solvents to extract several bioactive compounds to act as an agent for antimicrobial due to their efficacy against bacteria.

Furthermore, different parts of plants from Kuala Keniam, Taman Negara, Pahang, Malaysia were collected to determine their phytochemical and biological activity (Khanijo & Jiraungkoorskul, 2016). Stem and leaves of E. longifolia were soaked with dichloromethane and methanol successively like other plants. Then, the plants were screened for the presence of alkaloids and flavonoids. In the case of E. longifolia plant, the stem consisted of flavonoids but not alkaloids and vice versa for leaves of E. longifolia. Since this plant consisted of less amount of flavonoids and alkaloids, the results did not give high data in free radical scavenging activity and antimicrobial activity as compared to the other plants. This was because both compounds worked together to give an effect in a therapeutic activity, such as antioxidant, antimicrobial, anticancer and others, which can be proven by the previous study (Farouk & Benafri, 2007).

Next, a study conducted by Tajul Ariff and co-worker in (2012) investigated the effects of E. longifolia roots on growth and production of testosterone levels in a male chicken (Tajul Ariff et al., 2012). The powdered roots were extracted by using 70% acetone and 70% ethanol as extraction solvent via maceration techniques. The results indicated 70% acetone spot on a TLC plate was larger as compared to 70% ethanol. Although, the total yield crude extract of 70% ethanol was higher with data at 0.1358 g and 70% acetone had only 0.0934 g. Besides, phytochemistry test was done to detect the presence of secondary metabolites in E. longifolia 70% acetone extract. The crude extract only showed the presence of alkaloid, saponin and steroid metabolites. However, the result on the male chicken did not show any increase in the concentration of testosterone levels after treatment with acetone extract of E. longifolia as compared to the control. In conclusion, the acetone extract does not have aphrodisiac activity even though there is the presence of steroids in the extract.

Then, the effects of solvents on *E. longifolia* stem and leaves were carried out (Zakaria et al., 2021). The study was conducted by using two different solvents (water and ethanol) and two different extractions technique (reflux and maceration) for both stems and leaves. The findings of this study showed that ethanol was the best solvent for extract leaves due to the high content of phospholipid, flavonoids and saponin. Meanwhile, total protein content and total phenolic content both high in leaves when water was used as extraction solvent even though the stem contained more phenolic compounds in general. Maceration was the best method when water was used as a solvent for extraction overnight at 60 °C as compared to reflux. This showed that

#### "Unlocking the Medicinal Benefits of Local Herbal Remedies"

temperature cause degradation of bioactive compounds. To concludes, there was a variety of factors that may affect the content and yield of the bioactive component of extracts.

The summary of studies on *E. longifolia* plants regarding extraction techniques and solvent used to extract a high yield of crude extract including major compounds, eurycomanone

#### B. Misai Kucing (Orthosiphon aristatus)

Orthosiphon stamineus is commonly known as misai kucing and kumis kucing. O. stamineus is widely grown in Southeast Asia and the tropical countries. Leaves of this plant are known as "Java tea" and are mainly used for the purpose of making herbal tea commonly in Southeast Asia and European countries. Other names for O. stamineus include Orthosiphon aristatus, Orthosiphon spicatus, Orthosiphon blaetter, kumis kucing, Indischer Nierentee, Feuilles de Barbiflore, and de Java. Orthosiphon species is categorized into two varieties: one with the white flowers (white variety) and the other with the light purple flowers (purple variety). Purple variety contains more bioactive compounds than the white one. Normally, the leaves and stem tips have medicinal values. Due to this property, this plant has extensively been subjugated traditionally to treat several human ailments and conditions such as diuretic, rheumatism, abdominal pain, kidney and bladder inflammation, edema, gout, and hypertension. The leaves of O. stamineus exhibit excellent pharmacological activities such as antioxidant, antibacterial, hepatoprotective, anticytotoxic, antihypertensive, inflammatory, vasodilatation. Many pharmacopoeias such as French, Indonesian, Dutch, and Swiss have listed this plant for the treatment related to renal cleansing and function, and related disorders that include nephritis, cystitis, and urethritis. In Europe, people use the leaves of O. stamineus extract as a tonic for kidney and bladder stones, liver and gallbladder problems, and urinary tract infections. This can be used to reduce cholesterol and blood pressure. Earlier report showed that this plant contains high number of flavones, polyphenols, bioactive proteins, glycosides, a volatile oil, and vast quantities of potassium (Ashraf et al., 2018).

Orthosiphon aristatus (OA), Eurycoma longifolia (EL) and Andrographis paniculata (AP) are among popular medicinal herbs in Southeast Asia. The major compounds for these medicinal plants are polar bioactive compounds (rosmarinic acid, eurycomanone and andrographolide) which have multiple benefits to human health. The bioactive compounds are used as a drug to function against a variety of diseases with the support of scientific evidence. This paper was intended to prepare a complete review about the extraction techniques (e.g., OA, EL and AP) of these medicinal plants based on existing studies and scientific works. Suitable solvents and techniques to obtain their

major bioactive compounds and their therapeutic potentials were discussed (Abd Aziz et al., 2021).

O. aristatus was extracted by using either classical or modern technique. Start with Akowuah et al. (2005) investigated the effects of different extraction solvents on varying polarities for the extraction of major polyphenols in O. aristatus leaves (Akowuah et al., 2005). O. aristatus leaf powder was extracted by using solvents, such as water, 50% methanol, absolute methanol, 70% acetone and chloroform for 2 h, 4 h, and 8 h in a water bath at 40°C. The results indicated that chloroform extraction from 4 h to 8 h at 40°C gave the highest amount of sinensetin and eupatorine. The extraction method with 70% methanol at 4 h and 8 h produced a higher TMF yield. Meanwhile, it was observed that the use of 50% methanol for 8 h of extraction yielded higher rosmarinic acid (RA).

Then, Hossain and Ismail (2010) carried out maceration techniques to investigate the best solvent system for qualitative and quantitative determination of caffeic acid and RA with various extraction solvents (100% methanol, 50% methanol, 100% acetone, 70% acetone, 100% ethanol, 50% ethanol, chloroform, and water) and extraction time (2 h, 4 h, 6 h and 8 h) from leaves of *O. aristatus* (Hossain & Ismail, 2010). The data were analysed qualitatively and quantitatively by using thin-layer chromatography (TLC), high-performance thin-layer chromatography (HPTLC) and HPLC. The confirmed chosen solvent to extract a high yield of RA were 70% acetone and 100% ethanol as the best solvent to extract caffeic acid after a two-hour extraction. Therefore, the semi-polar solvent was also suitable to extract a high yield of RA by using maceration techniques.

In another study, the leaves of O. aristatus were extracted via maceration by using absolute ethanol, 50% ethanol and water as solvents. The experiment was conducted for 6 h at room temperature. The biomarker (RA, sinensetin and eupatorin) contents of the extracts were evaluated by using TLC and were found to have all three biomarkers (Mansor et al., 2016). Besides, the extraction of bioactive compounds also used Soxhlet extraction and reflux extraction techniques for 6 h. Based on these findings, the study revealed that reflux method generated a high vield of total extraction (72.73%) as compared to Soxhlet and maceration techniques by using 50% ethanol as the best solvent as compared to absolute ethanol and water. These findings suggested that the binary solvent system was able to extract both non-polar and polar bioactive compounds and together enriched the RA quantity in the extract.

#### C. Hempedu Bumi (Andrographis paniculate)

Andrographis paniculata Wall (family Acanthaceae) is one of the most popular medicinal plants used traditionally for the treatment of array of diseases such as cancer, diabetes, high blood pressure, ulcer, leprosy, bronchitis, skin diseases, flatulence, colic, influenza, dysentery, dyspepsia,

and malaria for centuries in Asia, America, and Africa continents. It possesses several photochemical constituents with unique and interesting biological properties. This review describes the past and present state of research on A. paniculata with respect to the medicinal usage, phytochemistry, pharmacological activities, toxicity profile and therapeutic usage, to bridge the gap requiring future research opportunities. This review is based on literature study on scientific journals and books from library and electronic sources. Diterpenes, flavonoids, xanthones, noriridoides and other miscellaneous compounds have been isolated from the plant. Extract and pure compounds of the plant have been reported for their anti-microbial, cytotoxicity, anti-protozoan, anti-inflammatory, antioxidant, immunostimulant, anti-diabetic. anti-infective, angiogenic, hepato-renal protective, sex hormone/sexual function modulation, liver enzymes modulation insecticidal and toxicity activities. The results of numerous toxicity evaluations of extracts and metabolites isolated from this plant did not show any significant acute toxicity in experimental animals. Detailed and more comprehensive toxicity profile on mammalian tissues and organs is needed in future studies (Menzel, 1998).

A study by Phansawan and Poungbangpho (2007) investigated five medicinal plants including A. paniculata by varying the polarity of extraction solvents and study the antioxidant activity (Phansawan and Poungbangpho, 2007). The solvent used in this experiment were ethanol, methanol, acetone, acetic acid, and distilled water. Maceration techniques were applied for 24 h and maintained at room temperature. Ethanol was chosen as the best solvent for extraction of all medicinal plants due to the highest recorded antioxidant activity. The result was followed by acetone, methanol, distilled water, and acetic acid as extraction solvent for these medicinal plants (Pueraria mirifica, Stevia rebaudiana Bertoni, Curcuma longa Linn, A. paniculata and Cassia alata Linn). Focusing on A. paniculata, the results obtained high antioxidant activity at 0.77±0.13 µmol of Trolox / mg of ethanol crude extraction, followed by distilled water, acetic acid, and methanol.

Soxhlet techniques have also been used to extract leaves and roots of A. paniculata by using ethanol and methanol as extraction solvents (C Kuppusamy & K Murugan, 2010). This study determined the effects of both extracts on growth, development, and reproduction of malarial vector *Anopheles stephensi Liston*. The result showed that ethanol extract was able to inhibit the emergence of larvae at 88.60% when treated with 35 ppm after 8 days. Meanwhile, methanol extract obtained lower emergence inhibition than ethanol extract at 85.25%. This result was like a study by Pushpalatha & Muthukrishnan (1995) (Pushpalatha & Muthukrishnan, 1995).

(Saranya et al., 2010) aimed a suitable solvent that contained a high yield of andrographolide compounds and then an extract possessed high antioxidant and antiulcer activities (Saranya et al., 2010). The leaves of *A. paniculata* were subjected to a serial extraction and set temperature within 60 °C – 80 °C with the following order of solvent polarity: petroleum ether, ethyl acetate, ethanol, and hydro alcohol. The result revealed hydro alcohol fractions indicated significant free radical scavenging activity and was able to influence antiulcer activity due to the ability in preventing the formation, and the negative effects of toxic oxygen free radical on gastric mucosa. Thus, this study suggested further investigations on gastro protective trait of *A. paniculata*.

A study conducted by Jadhao and Thorat (2014) focused on the effect of different solvents, such as ethanol, methanol, acetone, ethyl acetate, petroleum ether, and dichloromethane on total yield extraction (Jadhao & Thorat, 2014). The experiments were done by using reflux techniques and the results revealed that methanol extraction gave the highest extraction yield as compared to other solvents. High yield of major constituents, andrographolide was obtained when extracted with polar solvents as compared to non-polar solvents, especially methanol although solubility parameters ethanol and acetone were closer to andrographolide compounds. Meanwhile, water extract contained less andrographolide content due to the hydrolysis and thermal degradation that might affects the results. To conclude, the polar solvent (methanol) was the best solvent to extract andrographolide compounds as compared to other solvents (Mishra et al., 2011).

#### D. Kacip Fatimah (Labisia pumila)

Kacip Fatimah (Labisia pumila) Fern. -Vill., locally termed as Kacip Fatimah (KF), is a popular herb in Southeast Asian countries. It belongs to the Myrsinaceae family. Recently it has been identified as one of the top five herbs used in Malaysia for treating variety of ailments (Karimi et al., 2013). Traditionally, KF is mainly used in a wide spectrum of women's health related issues; the effects are presumed as attributable to the presence of estrogen-like compounds. KF is often taken during and after pregnancy for its beneficial effects on uterine function and delivery. The primary route of administration of KF is oral, whereby the leaves, roots, or whole plant are boiled in water and consumed. Additionally, it is sold commercially in the form of herbal tea, powder, capsules, and tablets in many countries (Abdul Kadir et al., 2012). Clinical studies have also suggested the usefulness of KF extract in treating postmenopausal symptoms with no acute toxicity (Singh et al., 2009). Furthermore, the extract and constituents of KF have been shown to possess anticancer, antioxidant, antiosteoporosis, and anti-inflammatory properties (Fathilah et al., 2013; Nadia et al., 2012).

Numerous studies had reported the health benefits of LP on the prevention and treatment of diseases related to estrogen deficiencies. The antioxidant property of LP is one of the factors that contribute to the health benefits. Currently, various types of phytochemicals had been identified by the extraction of LP, and most possess beneficial properties and are consistent in their traditional uses. The LP extract mainly contains flavonoids, polyphenols, phenolic acids, and saponins (Chua et al., 2011). Much research had suggested that total flavonoid is important secondary metabolite that promotes strong bioactivity such as free radical scavenging, antioxidant, anti-flammatory, and anticancer (Norhaiza M. et al., 2009). The total flavonoid mainly composes of flavonoids, isoflavones, flavanols, isoflavanones, and dihydroisoflavones. The compound of flavonoids is quercetin, myricetin, kaempferol, rutin, protocatechunic acid, catechin, naringin, daidzein, genistein, and anthocyanin (Wu et al., 2019). It was proven that total flavonoids had been effectively scavenging the free radicals of most types of oxidizing molecules, including the singlet oxygen and various free radicals (Bravo, 2009).

Studies from (Nurdiana et al., 2018) reported on oxidative stress on rat model of postmenopausal osteoporosis. The study group of ovariectomized was treated with LP (10 mg/kg, 20 mg/kg, and 40 mg/kg). The treatment was administered for 8 weeks. The results showed that the levels of serum malondialdehyde were significantly reduced by the treatment of LP reaching the levels comparable to the control group. The serum levels of superoxide dismutase were significantly higher in the group of ovariectomized rats compared to the control group. This showed that the administration of 20 mg/kg treatment of LP significantly lowered the superoxide stress relative to group of ovariectomized control. The administration of 20 mg/kg of LP had given the best result on oxidative stress. It was found that the administration of 40 mg/kg did not give any good result. This could be that the administration of 40 mg/kg treatment of LP was toxic to the ovariectomized rat model. However, further study is needed to confirm the toxicity effect of LP dosage.

#### E. Limau Purut (Citrus hystrix)

The fruits, leaves, and rind of *C. hystrix* are the most common parts traditionally used to reduce the severity of certain illnesses. The fruits are used for the treatment of stomach ache by hilly Tripura tribes in northeastern India (Das et al., 2013) while the leaves and fruits are both used in steam-bathing for postpartum mothers, to relieve headache, rheumatism, fever, and to treat diabetes mellitus in North Sumatra, Indonesia (Silalahi & Nisyawati, 2019). In Malaysia, the fruits are used in hair shampoo to decrease dandruff and to promote hair growth (Lim, 2015). The leaves and fruits are also used to boost sexual performance and to treat hypertension, heart disease, and diarrhea (Abirami et al., 2014).

Abirami's team demonstrated in an in vitro study that the powdered rind and pulp of C. hystrix exhibited higher concentration-dependent glucose adsorption capacity than that of xanthan and guar gum, and that the capacity was augmented with increasing concentration of glucose (Abirami et al., 2014). This finding suggests that the extract could decrease postprandial glucose levels. The extract also decreased glucose dialysis retardation index and starch digestibility, suggesting a delay in glucose absorption possibly due to lower starch assimilation in the gastrointestinal tract. The extract could be beneficial in decreasing postprandial glycaemic and insulinemic response in type 2 diabetics, thus controlling the uptake of glucose. However, the active phytochemical compounds responsible for the activity were not identified. The functional groups responsible for the glucose absorbency were most likely hydroxyl group and possibly methyl ester group of galacturonic acid detected in the C. hystrix extract.

In a study by (Rekasih et al., 2021), a functional food drink was created containing various medicinal plants: Orthosiphon aristatus (Blume) Miq., Zingiber officinale Roscoe, Caesalpinia sappan L., Curcuma xanthorriza Roxb., Citrus limon (L.) Osbeck, Citrus aurantifolia (Christm.) Swingle, and C. hystrix. The drink contained 1% C. hystrix fruit juice and was administered at a dose of 18.2 mL/kg body weight to streptozotocin-induced diabetic rats for two weeks ready-to-drink, microencapsulated, nanoencapsulated formulations. The exact concentration of the C. hystrix juice in the drink could not be determined as the yield percentage was not reported. All formulations significantly reduced fasting blood glucose and elevated pancreatic β-cell and Langerhans islet viability in the rats, but the improvements were more significant in the microencapsulated and nanoencapsulated formulations. Encapsulation was believed to have increased the contact surface and improved the bioavailability of the bioactive phytocompounds in the drink (Jang et al., 2014). The study demonstrated possible synergistic interactions among the components of the drink. Possible mechanisms of the hypoglycaemic effects were not elucidated.

A study reported positive findings regarding the blood lipid profile of rats fed a high-fat diet following treatment with orally administered *C. hystrix* peel extract at 500 mg/kg (Zajmi et al., 2020). The extract reduced serum TC, LDL, triglyceride (TG), and HDL in rats after 14 days of treatment. However, the baseline level for each blood parameter was not similar among the groups, which could have resulted in a false significant difference between groups. (Sukalingam et al., 2016) demonstrated that ovariectomized rats fed a high-fat diet containing 2% cholesterol and 15% heated oil supplemented with 1% *C. hystrix* extract during heating had reduced cardiac TG and free fatty acid levels after 6 months.

# IV. PRECAUTIONS AND CONSIDERATIONS OF USING HERBS

#### A. Kava (Piper methysticum)

Kava is known for its CNS depressant activity, and it is commonly used as an anxiolytic agent. Commonly reported side effects of this medicinal plant include headache, gastrointestinal discomfort, and localized dizziness, numbness after oral ingestion. Large dosages have been shown to be capable of giving rise to dry, scaly skin, and discoloration of skin vellowish the and nails, photosensitivity and redness of the eye. Excessive consumption of kava may also lead to photophobia and diplopia (Boullata & Nace, 2000). The muscle relaxant and anticonvulsant effects of this plant have been attributed to its active pyrone's constituent. Significant interaction of kava with other CNS depressants which may lead to a comatose state has been reported and as such concurrent use with these agents is usually not advised (Almeida, 1996; Wong et al., 1998). In 2002, the US Food and Drug Administration received several reports of liver-related injuries alongside that of a previously healthy young female who eventually required liver transplantation following consumption of kava-containing products. This prompted the FDA to alert consumers on the potential risk of severe liver injury associated with the use of kava-containing dietary supplements. This liver-related risks also prompted regulatory agencies in other countries including Germany, Switzerland, France, Canada, and the UK to warn consumers about the potential risks of kava use and went on to consider the withdrawal of kava-containing products from the market (Hickmann M.A., 2003). In over 25 reports of adverse events outside the US, kava-containing products were associated with liver-related injuries like hepatitis, cirrhosis, and liver failure with some of the affected patients eventually requiring liver transplants (Hickmann M.A., 2003).

#### B. Ephedra sinica

Ephedra is a very popular herb with long history of traditional use in respiratory conditions (Dan Bensky et al., 2004; Zhongjing Zhang et al., 1999). This herb, whose efficacy has been demonstrated in several randomized double-blind clinical trials (Boozer et al., 2002; Haller et al., 2005; H.-J. Kim et al., 2008), is currently included in the Chinese Pharmacopoeia for therapeutic use and classified as non-toxic. It is an ingredient in commonly used formulary preparations such as Xiaoqinglong Heji for common cold and Zhisou Dingchuan Koufuye for asthma (Chinese Pharmacopoeia Commission, 2010). Ephedra has been marketed in the US as a weight-loss dietary supplement and its use associated with several serious cardiovascular and central nervous systems (CNSs) adverse effects (Chen et al., 2010; Hackman et al., 2006; Hallas et al., 2008; Verduin M.L. & Labbate L.A., 2002). Several case reports have also linked the use of Ephedra sinica and Ephedra-containing

dietary supplements to adverse events such as hepatotoxicity (Schoepfer et al., 2007; Skoulidis et al., 2005), neurotoxicity (Varlibas et al., 2009), and transient blindness (Moawad et al., 2006).

### C. Tussilago farfara

Traditionally, *Tussilago farfara* has been used effectively for thousands of years for the treatment of acute and chronic cough and it is generally regarded as non-toxic (Chinese Pharmacopoeia Commission, 2010). Total alkaloids as well as senkirkine isolated from this plant and have been demonstrated to be hepatotoxic (Zhang et al., 2008). Recently, the potential health effects of the pyrrolizidine alkaloids found in *T. farfara* was reviewed and hepatic veno-occlusive disease and cirrhosis were suggested as the major potential disease outcome in human (Edgar et al., 2011). However, restrictions in intake of pyrrolizidine-containing herbs and further investigations were recommended because of paucity of data on toxicity assessment in human (E. J. Y. Kim et al., 2013).

#### D. Ginkgo biloba and Ginseng

Ginkgo biloba has found widespread use in a variety of conditions and several products such as elixirs, extracts, tea, as well as capsules and tablets that may differ in terms of content, have been made from the dried root (Sparreboom et al., 2004). The whole root which contains ginsenosides is usually used because these compounds possess specific pharmacologic effects that may oppose each other (Chong & Oberholzer, 1988). Over 30 ginsenosides have been identified and these compounds are being investigated for their ability to inhibit cell proliferation, tumor cell invasion, and/or metastasis (He, 2011; J.-W. Kim et al., 2012). Recently, the ability of ginsenosides to modulate signaling pathways involving cell cycle, inflammatory, or growth factor pathways, was demonstrated (Dunnick & Nyska, 2013; Nag, 2012). The leaf extracts of ginkgo had also been demonstrated to contain active compounds that had found usefulness in improving circulation and cognition (Boullata & Nace, 2000).

The plant extracts appear to be relatively safe, although headache, dizziness, restlessness, nausea, vomiting, diarrhea, and dermal sensitivity are the most common side effects that have been observed. Ginkgo has been demonstrated to be capable of inhibiting platelet-activating factor and altering bleeding times. Therefore, cautious use had been advised in individuals or patients on anticoagulants therapy (Boullata & Nace, 2000). The ability of ginkgo to induce liver cancer in experimental model was reported recently and genotoxic mechanisms were suggested to play some role in the carcinogenic process (Dunnick & Nyska, 2013). Similar observation was made in the thyroid gland and further studies are required to determine whether the mechanisms for the ginkgo-induced thyroid tumors are also found in humans (Dunnick & Nyska, 2013). In addition to the

#### "Unlocking the Medicinal Benefits of Local Herbal Remedies"

carcinogenic effects in the liver and thyroid, ginkgo has also been shown to be capable of inducing tumorigenesis in the nasal cavity. The pathogenesis of the nasal lesions was suggested to be related to toxic metabolites of ginkgo reaching the nasal cavity from the systemic circulation (Reed, 1993; Sells et al., 2007). Some other authors, however, have attributed the nasal lesions to gastric reflux/post gavage reflux through the nasopharyngeal duct (Damsch, Eichenbaum, Looszova, et al., 2011; Damsch, Eichenbaum, Tonelli, et al., 2011).

#### V. CONCLUSION

The exploration of the medicinal potential of local herbs, particularly those found in Southeast Asia, is an intriguing field that combines traditional knowledge with modern scientific research. The introduction beautifully sets the stage for delving into the therapeutic properties of various indigenous plants found in Malaysia. The classification of spices and herbs provides a helpful framework for understanding their diverse uses and origins. Categorizing them based on flavor, taxonomy, or the part of the plant from which they are derived gives readers a comprehensive overview. The detailed examination of specific herbs like Tongkat Ali, Misai Kucing, Hempedu Bumi, Kacip Fatimah, and Limau Purut provides valuable insights into their traditional uses and the scientific evidence supporting their medicinal properties. Each herb is discussed in terms of its botanical characteristics, traditional uses, phytochemical composition, extraction techniques, and pharmacological activities. This thorough approach helps readers understand the holistic potential of these herbs in various health contexts. Furthermore, the inclusion of precautions and considerations regarding herbs like Kava, Garlic, Ephedra sinica, Tussilago farfara, Ginkgo biloba, and Ginseng adds a critical dimension to the discussion. Highlighting potential side effects, drug interactions, and safety concerns ensures that readers have a balanced understanding of the risks and benefits associated with herbal remedies. Overall, the exploration of the medicinal potential of local herbs is comprehensive, informative, and well-researched, providing valuable insights for both traditional healers and modern practitioners alike.

#### VI. ACKNOWLEDGEMENT

We would like to thank to the Malaysian Agricultural Research and Development Institute (MARDI) for publication funding.

#### REFERENCES

1. Abd Aziz, N. A., Hasham, R., Sarmidi, M. R., Suhaimi, S. H., & Idris, M. K. H. (2021). A review on extraction techniques and therapeutic value of polar bioactives from Asian medicinal herbs: Case study on *Orthosiphon aristatus*, *Eurycoma longifolia* 

- and *Andrographis paniculata*. *Saudi Pharmaceutical Journal*, 29(2), 143–165. https://doi.org/10.1016/j.jsps.2020.12.016
- Abd-Elaziem Farouk, & Asma Benafri. (2007). Antibacterial activity of *Eurycoma longifolia* Jack. A Malaysian medicinal plant. *Saudi Med J*., 28(9), 1422–1424.
- 3. Abdul Kadir, A., Nik Hussain, N. H., Wan Bebakar, W. M., Mohd, D. M., Wan Mohammad, W. M. Z., Hassan, I. I., Shukor, N., Kamaruddin, N. A., & Wan Mohamud, W. N. (2012). The Effect of *Labisia pumila* var. *alata* on Postmenopausal Women: A Pilot Study. *Evidence-Based Complementary and Alternative Medicine*, 2012, 1–6. https://doi.org/10.1155/2012/216525
- Abirami, A., Nagarani, G., & Siddhuraju, P. (2014). In vitro antioxidant, anti-diabetic, cholinesterase and tyrosinase inhibitory potential of fresh juice from *Citrus hystrix* and *C. maxima* fruits. *Food Science and Human Wellness*, 3(1), 16–25. https://doi.org/10.1016/j.fshw.2014.02.001
- Akowuah, G. A., Ismail, Z., Norhayati, I., & Sadikun, A. (2005). The effects of different extraction solvents of varying polarities on polyphenols of *Orthosiphon stamineus* and evaluation of the free radical-scavenging activity. *Food Chemistry*, 93(2), 311–317. https://doi.org/10.1016/j.foodchem.2004.09.028
- Almeida, J. C. (1996). Coma from the Health Food Store: Interaction between Kava and Alprazolam. *Annals of Internal Medicine*, 125(11), 940. https://doi.org/10.7326/0003-4819-125-11-199612010-00023
- Ashraf, K., Sultan, S., & Adam, A. (2018).
   Orthosiphon stamineus Benth. is an outstanding food medicine: Review of phytochemical and pharmacological activities. Journal of Pharmacy And Bioallied Sciences, 10(3), 109.
   https://doi.org/10.4103/JPBS.JPBS 253 17
- Boozer, C., Daly, P., Homel, P., Solomon, J., Blanchard, D., Nasser, J., Strauss, R., & Meredith, T. (2002). Herbal ephedra/caffeine for weight loss: a 6month randomized safety and efficacy trial. *International Journal of Obesity*, 26(5), 593–604. https://doi.org/10.1038/sj.ijo.0802023
- 9. Boullata, J. I., & Nace, A. M. (2000). Safety Issues with Herbal Medicine. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, 20(3), 257–269.
  - https://doi.org/10.1592/phco.20.4.257.34886
- Bravo, L. (2009). Polyphenols: Chemistry, Dietary Sources, Metabolism, and Nutritional Significance. *Nutrition Reviews*, 56(11), 317–333. https://doi.org/10.1111/j.1753-4887.1998.tb01670.x

- 11. Buran Phansawan, & Supak Poungbangpho. (2007). Antioxidant Capacities of *Pueraria mirifica*, *Stevia rebaudiana* Bertoni, *Curcuma longa* Linn., *Andrographis paniculata* (Burm.f.) Nees. and *Cassia alata* Linn. for the Development of Dietary Supplement. *Agriculture and Natural Resources*, 41(3), 548–554.
- 12. C Kuppusamy, & K Murugan. (2010). Effects of Andrographis paniculata Nees on growth, development and reproduction of malarial vector *Anopheles stephensi* Liston (Diptera: Culicidae). *Tropical Biomedicine*, 27(3), 509–516.
- Chen, W.-L., Tsai, T.-H., Yang, C. C. H., & Kuo, T. B. J. (2010). Acute Effects of Ephedra on Autonomic Nervous Modulation in Healthy Young Adults. *Clinical Pharmacology & Therapeutics*, 88(1), 39–44. https://doi.org/10.1038/clpt.2010.66
- 14. Chinese Pharmacopoeia Commission. (2010). Pharmacopoeia of the People's Republic of China (English edition). Ministry of Health of the People's Republic of China.
- 15. Chong, S. K. F., & Oberholzer, V. G. (1988). Ginseng--is there a use in clinical medicine? *Postgraduate Medical Journal*, 64(757), 841–846. https://doi.org/10.1136/pgmj.64.757.841
- Chua, L. S., Latiff, N. A., Lee, S. Y., Lee, C. T., Sarmidi, M. R., & Aziz, R. A. (2011). Flavonoids and phenolic acids from *Labisia pumila* (Kacip Fatimah). *Food Chemistry*, 127(3), 1186–1192. https://doi.org/10.1016/j.foodchem.2011.01.122
- Craig, W. J. (1999). Health-promoting properties of common herbs. *The American Journal of Clinical Nutrition*, 70(3), 491S-499S. https://doi.org/10.1093/ajcn/70.3.491s
- Damsch, S., Eichenbaum, G., Looszova, A., Lammens, L., Feyen, B., Bulck, K. Van den, Knight, E., Kelley, M., & Tonelli, A. (2011). Unexpected Nasal Changes in Rats Related to Reflux after Gavage Dosing. *Toxicologic Pathology*, 39(2), 337– 347. https://doi.org/10.1177/0192623310388430
- 19. Damsch, S., Eichenbaum, G., Tonelli, A., Lammens, L., Bulck, K. Van den, Feyen, B., Vandenberghe, J., Megens, A., Knight, E., & Kelley, M. (2011). Gavage-Related Reflux in Rats. *Toxicologic Pathology*, *39*(2), 348–360. https://doi.org/10.1177/0192623310388431
- Dan Bensky, Steven Clavey, & Erich Stöger. (2004).
   Chinese Herbal Medicine: Materia Medica (3rd ed.).
   WA: Eastland Press.
- 21. Das, S. C., Prakash, J., Deb, A. K., & Biswas, T. (2013). Medicinal value of underutilized fruits in hilly tripura. *Acta Horticulturae*, 972, 135–141. https://doi.org/10.17660/ActaHortic.2013.972.17
- 22. Dunnick, J. K., & Nyska, A. (2013). The Toxicity and Pathology of Selected Dietary Herbal Medicines.

- *Toxicologic Pathology*, *41*(2), 374–386. https://doi.org/10.1177/0192623312466451
- Edgar, J. A., Colegate, S. M., Boppré, M., & Molyneux, R. J. (2011). Pyrrolizidine alkaloids in food: a spectrum of potential health consequences. Food Additives & Contaminants: Part A, 28(3), 308–324. https://doi.org/10.1080/19440049.2010.547520
- Fathilah, S. N., Mohamed, N., Muhammad, N., Mohamed, I. N., Soelaiman, I. N., & Shuid, A. N. (2013). Labisia pumila regulates bone-related genes expressions in postmenopausal osteoporosis model. BMC Complementary and Alternative Medicine, 13(1), 217. https://doi.org/10.1186/1472-6882-13-217
- 25. Hackman, R. M., Havel, P. J., Schwartz, H. J., Rutledge, J. C., Watnik, M. R., Noceti, E. M., Stohs, S. J., Stern, J. S., & Keen, C. L. (2006). Multinutrient supplement containing ephedra and caffeine causes weight loss and improves metabolic risk factors in obese women: a randomized controlled trial. *International Journal of Obesity*, 30(10), 1545–1556. https://doi.org/10.1038/sj.ijo.0803283
- 26. Hallas, J., Bjerrum, L., Stovring, H., & Andersen, M. (2008). Use of a Prescribed Ephedrine/Caffeine Combination and the Risk of Serious Cardiovascular Events: A Registry-based Case-Crossover Study. American Journal of Epidemiology, 168(8), 966–973. https://doi.org/10.1093/aje/kwn191
- 27. Haller, C., JACOBIII, P., & BENOWITZ, N. (2005). Short-term metabolic and hemodynamic effects of ephedra and guarana combinations. *Clinical Pharmacology & Therapeutics*, 77(6), 560–571. https://doi.org/10.1016/j.clpt.2005.01.023
- 28. He, B., Gao, J., Luo, X., Luo, J. et. al. (2011). Ginsenoside Rg3 inhibits colorectal tumor growth through the down-regulation of Wnt/β-catenin signaling. *International Journal of Oncology*, 38(2). https://doi.org/10.3892/ijo.2010.858
- 29. Hendra, R., Ahmad, S., Oskoueian, E., Sukari, A., & Shukor, M. Y. (2011).Antioxidant, Antiinflammatory and Cytotoxicity of Phaleria macrocarpa (Boerl.) Scheff Fruit. BMCComplementary and Alternative Medicine, 11(1), 110. https://doi.org/10.1186/1472-6882-11-110
- 30. Hickmann M.A. (2003). *The Food and Drug Administration (FDA)* (Hickmann M. A., Ed.). Nova Science Publishers.
- 31. Hossain, M. A., & Ismail, Z. (2010). High performance thin layer chromatographic determination of caffeic acid and rosmarinic acid from the leaves of *Orthosiphon stamineus*. *Indonesian Journal of Chemistry*, 9(1), 137–141. https://doi.org/10.22146/ijc.21575
- 32. Jadhao D., & Thorat B. (2014). Purification (crystallization) of biotactive ingredient

- andrographolide from *Andrographis paniculata*. *World Journal of Pharmacy and Pharmaceutical Sciences*, *3*, 747–763.
- 33. Jang, D.-J., Kim, S. T., Oh, E., & Lee, K. (2014). Enhanced oral bioavailability and antiasthmatic efficacy of curcumin using redispersible dry emulsion. *Bio-Medical Materials and Engineering*, 24(1), 917–930. https://doi.org/10.3233/BME-130886
- 34. Karimi, E., Jaafar, H. Z., & Ahmad, S. (2013). Antifungal, anti-inflammatory and cytotoxicity activities of three varieties of *Labisia pumila* benth: from microwave obtained extracts. *BMC Complementary and Alternative Medicine*, *13*(1), 20. https://doi.org/10.1186/1472-6882-13-20
- 35. Khanijo, T., & Jiraungkoorskul, W. (2016). Review ergogenic effect of long jack, *Eurycoma longifolia*. *Pharmacognosy Reviews*, *10*(20), 139. https://doi.org/10.4103/0973-7847.194041
- 36. Kim, E. J. Y., Chen Y., Huang J. Q., Li K. M., Valentina R. N., Poon J., Chan K., Roufogalis B. D., McLachlan A. J., Mo, S.-L., Yang D., Yao M., Liu Z., Liu J., & Li G. Q. (2013). Evidence-based toxicity evaluation and scheduling of Chinese herbal medicines. *Journal of Ethnopharmacology*, *146*(1), 40–61. https://doi.org/10.1016/j.jep.2012.12.027
- 37. Kim, H.-J., Park, J.-M., Kim, J.-A., & Ko, B.-P. (2008). Effect of Herbal *Ephedra sinica* and *Evodia rutaecarpa* on Body Composition and Resting Metabolic Rate: A Randomized, Double-blind Clinical Trial in Korean Premenopausal Women. *Journal of Acupuncture and Meridian Studies*, *1*(2), 128–138. https://doi.org/10.1016/S2005-2901(09)60033-9
- 38. Kim, J.-W., Jung, S.-Y., Kwon, Y.-H., Lee, J.-H., Lee, Y. M., Lee, B.-Y., & Kwon, S.-M. (2012). Ginsenoside Rg3 attenuates tumor angiogenesis via inhibiting bioactivities of endothelial progenitor cells. *Cancer Biology & Therapy*, *13*(7), 504–515. https://doi.org/10.4161/cbt.19599
- 39. Lim, T. K. (2015). *Edible Medicinal and Non Medicinal Plants*. Springer Netherlands. https://doi.org/10.1007/978-94-017-9511-1
- Mansor, C. N. A. N. C., Latip, J., & Markom, M. (2016). Preparation of Orthosiphon stamineus enriched-extracts and evaluation of their free radical scavenging activity. 030013. https://doi.org/10.1063/1.4966751
- 41. Menzel, D. C. (1998). www. ethics. gov: Issues and Challenges Facing Public Managers. *Public Administration Review*, *58*(5), 445. https://doi.org/10.2307/977553
- 42. Mishra, K., Dash, A. P., & Dey, N. (2011). Andrographolide: A Novel Antimalarial Diterpene Lactone Compound from *Andrographis paniculata*

- and Its Interaction with Curcumin and Artesunate. *Journal of Tropical Medicine*, 2011, 1–6. https://doi.org/10.1155/2011/579518
- 43. Moawad, F. J., Hartzell, J. D., Biega, T. J., & Lettieri, C. J. (2006). Transient Blindness Due to Posterior Reversible Encephalopathy Syndrome Following Ephedra Overdose. *Southern Medical Journal*, 99(5), 511–514. https://doi.org/10.1097/01.smj.0000215739.90211.3b
- 44. Nadia, M. E., Nazrun, A. S., Norazlina, M., Isa, N. M., Norliza, M., & Ima Nirwana, S. (2012). The Anti-Inflammatory, Phytoestrogenic, and Antioxidative Role of *Labisia pumila* in Prevention of Postmenopausal Osteoporosis. *Advances in Pharmacological Sciences*, 2012, 1–7. https://doi.org/10.1155/2012/706905
- 45. Nag, S. A. (2012). Ginsenosides as anticancer agents: In vitro and in vivo activities, structure—activity relationships, and molecular mechanisms of action. *Frontiers in Pharmacology*, 3. https://doi.org/10.3389/fphar.2012.00025
- Norhaiza M., Maziah M., & Hakiman M. (2009).
   Antioxidative properties of leaf extracts of a popular Malaysian herb, *Labisia pumila*. *Journal of Medicinal Plants Research*, 3(4), 217–223.
- 47. Nurdiana, N., Mariati, N., Noorhamdani, N., Setiawan, B., Budhiparama, N., & Noor, Z. (2018). Effects of Labisia pumila on bone turnover markers and OPG/RANKL system in a rat model of postmenopausal osteoporosis. *Clinical Nutrition Experimental*, 20, 41–47. https://doi.org/10.1016/j.yclnex.2018.01.002
- 48. Pushpalatha, E., & Muthukrishnan, J. (1995). Larvicidal activity of a few plant extracts against *Culex quinquefasciatus* and *Anopheles stephensi*. *Indian Journal of Malariology*, 32(1), 14–23.
- Reed, C. J. (1993). Drug Metabolism in the Nasal Cavity: Relevance to Toxicology. *Drug Metabolism Reviews*, 25(1–2), 173–205. https://doi.org/10.3109/03602539308993975
- Rehman, S., Choe, K., & Yoo, H. (2016). Review on a Traditional Herbal Medicine, *Eurycoma longifolia* Jack (Tongkat Ali): Its Traditional Uses, Chemistry, Evidence-Based Pharmacology and Toxicology. *Molecules*, 21(3), 331. https://doi.org/10.3390/molecules21030331
- Rekasih, M., Muhandri, T., Safithri, M., & Wijaya,
   C. H. (2021). Antihyperglycemic Activity of Java Tea-Based Functional Drink-Loaded Chitosan Nanoparticle in Streptozotocin-Induced Diabetic Rats. *HAYATI Journal of Biosciences*, 28(3), 212. https://doi.org/10.4308/hjb.28.3.212
- 52. S. Saranya, R. Ushakumari, Sosamma Jacob, & Babu M. Philip. (2010). Efficacy of different entomopathogenic fungi against cowpea aphid, *Aphis*

- *craccivora* (Koch). *Journal of Biopesticides*, *3*(1), 138–142.
- 53. Schoepfer, A. M., Engel, A., Fattinger, K., Marbet, U. A., Criblez, D., Reichen, J., Zimmermann, A., & Oneta, C. M. (2007). Herbal does not mean innocuous: Ten cases of severe hepatotoxicity associated with dietary supplements from Herbalife® products. *Journal of Hepatology*, 47(4), 521–526. https://doi.org/10.1016/j.jhep.2007.06.014
- 54. Sells, D. M., Brix, A. E., Nyska, A., Jokinen, M. P., Orzech, D. P., & Walker, N. J. (2007). Respiratory Tract Lesions in Noninhalation Studies. *Toxicologic Pathology*, 35(1), 170–177. https://doi.org/10.1080/01926230601059969
- 55. Silalahi, M., & Nisyawati. (2019). An ethnobotanical study of traditional steam-bathing by the Batak people of North Sumatra, Indonesia. *Pacific Conservation Biology*, 25(3), 266. https://doi.org/10.1071/PC18038
- Singh, G. D., Ganjoo, M., Youssouf, M. S., Koul, A., Sharma, R., Singh, S., Sangwan, P. L., Koul, S., Ahamad, D. B., & Johri, R. K. (2009). Sub-acute toxicity evaluation of an aqueous extract of *Labisia* pumila, a Malaysian herb. Food and Chemical Toxicology, 47(10), 2661–2665. https://doi.org/10.1016/j.fct.2009.07.031
- 57. Skoulidis, F., Alexander, G. J. M., & Davies, S. E. (2005). Ma huang associated acute liver failure requiring liver transplantation. *European Journal of Gastroenterology & Hepatology*, 17(5), 581–584. https://doi.org/10.1097/00042737-200505000-00017
- Sparreboom, A., Cox, M. C., Acharya, M. R., & Figg, W. D. (2004). Herbal Remedies in the United States: Potential Adverse Interactions With Anticancer Agents. *Journal of Clinical Oncology*, 22(12), 2489–2503. https://doi.org/10.1200/JCO.2004.08.182
- 59. Sukalingam, K., Jaarin, K., Saad, Q. H. M., Mohamed, S., & Othman, F. (2016). Consumption of ADD-X and Repeatedly Heated Palm Oil on the Blood Pressure and Oxidative Stress Markers in Ovarectmized Rats. *International Journal of Pharmacology*, 12(5), 514–522. https://doi.org/10.3923/ijp.2016.514.522
- Tajul Ariff, A. S., Soelaiman, I. N., Pramanik, J., & Shuid, A. N. (2012). Effects of *Eurycoma longifolia* on Testosterone Level and Bone Structure in an Aged Orchidectomised Rat Model. *Evidence-Based Complementary and Alternative Medicine*, 2012, 1–7. https://doi.org/10.1155/2012/818072
- Varlibas, F., Delipoyraz, I., Yuksel, G., Filiz, G., Tireli, H., & Gecim, N. O. (2009). Neurotoxicity following chronic intravenous use of "Russian Cocktail." *Clinical Toxicology*, 47(2), 157–160. https://doi.org/10.1080/15563650802010388

- 62. Verduin M.L., & Labbate L.A. (2002). Psychosis and delirium following metabolife use. *Psychopharmacol Bull.*, *36*(3), 42–45.
- 63. Wong, A. H. C., Smith, M., & Boon, H. S. (1998). Herbal Remedies in Psychiatric Practice. *Archives of General Psychiatry*, *55*(11), 1033. https://doi.org/10.1001/archpsyc.55.11.1033
- 64. Wu, H., Xi, H., Lai, F., Ma, J., Chen, W., & Liu, H. (2019). Cellular antioxidant activity and Caco-2 cell uptake characteristics of flavone extracts from *Labisia pumila*. *International Journal of Food Science & Technology*, *54*(2), 536–549. https://doi.org/10.1111/ijfs.13968
- 65. Zajmi, A., Ramli, L. H., Al-Abd, N., & Othman, Z. (2020). Anti-hyperlipidemia activity of key lime (*Citrus aurantifolia*) and kaffir lime (*Citrus hystrix*) peel extracts on high fat diet induced hyperlipidemic rats. *Solid State Tech.*, 63, 2925–2932.
- 66. Zakaria, A. A., Noor, M. H. M., Ahmad, H., Hassim, H. A., Mazlan, M., & Latip, M. Q. A. (2021). A Review on Therapeutic Effects of *Labisia pumila* on Female Reproductive Diseases. *BioMed Research International*, 2021, 1–9. https://doi.org/10.1155/2021/9928199
- 67. Zhang, B., Xu, D., Guo, Y., Ping, J., Chen, L., & Wang, H. (2008). Protection by and anti-oxidant mechanism of berberine against rat liver fibrosis induced by multiple hepatotoxic factors. *Clinical and Experimental Pharmacology and Physiology*, *35*(3), 303–309. https://doi.org/10.1111/j.1440-1681.2007.04819.x
- 68. Zhongjing Zhang, Craig Mitchell, Ye Feng, & Nigel Wiseman. (1999). *On Cold Damage*. Paradigm Publications.