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Labisia pumila: A Review on its Traditional, Phytochemical and Biological Uses

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Abstract: *Labisia pumila* is traditionally used by Malay woman to maintain healthy female reproductive function and as postpartum medicine. *In vitro* and *in vivo* studies indicated that *Labisia pumila* exerts a wide range of biological activities such as phytoestrogenic, anti-inflammatory, antioxidant and anti-aging, anti-microbial and anti-carcinogenic activities. These biological activities are related to the presence of the bioactive phytochemical constituents comprising of phenolic, flavonoid and other antioxidant compounds. In addition, saponin, alkenyl compounds and benzoquinone derivatives are also present and these compounds are known to be linked with useful biological activities. In this article, we carried out a critical review on the current knowledge on the traditional usage, phytochemical constituents and biological activities of *Labisia pumila*.

Key words: Labisia pumila · Kacip Fatimah · Myrsinaceae · Traditional uses · Biological activities · Phytochemistry

INTRODUCTION

*Labisia pumila (*Myrsinaceae*)* is also known as Kacip Fatimah in Malaysia. The other local names for the plant include Selusoh Fatimah, Kacit Fatimah, Tadah Matahari, Mata Pelanduk Rimba and Sangkoh (Iban). It can be widely found throughout the rain forest of Indochina, particularly Malaysia. It grows wildly at 80-100 meter above the sea level. According to Stone [1], there are three varieties of *L. pumila* in Malaysia which are var. *pumila*, var. *alata* and var. *lanceolata*. However, the most common variety is *L. pumila* var. *alata*. These varieties can be differentiated from each other by their petiole and leaf characteristics [2]. *L. pumila* var. *alata* has a winged petiole with red veins, while var. *pumila* has a marginate petiole with ovate leaf blade shape. However, the var. *lanceolata* has a long and non-winged petiole. Jamia *et al*. [3-4] reported that the var. *alata* is more frequently used in traditional medicine preparations.

Traditionally, the decoction of this plant is consumed by the indigenous women of the Malay Archipelago to facilitate child birth delivery and to improve their post-partum health [11]. Interestingly, the root of *Ardisia mamillata* which is also from the family of Myrsinaceae is also used to treat respiratory tract infection and menstrual disorders [5]. Although *L. pumila* is traditionally used by women to promote the health of female reproductive system, men of several ethnic groups in Sarawak, Malaysia are also consumed this herb to maintain and increase stamina [6]. Nowadays, it is taken on regular basis because of its health enhancing effect. Therefore, the demand for *L. pumila* based products is in the increasing trend, mainly due to the renewed interest by public on herbal medicine application [4]. This review article is intended to provide an up-to-date and comprehensive review on *L. pumila*, especially its phytochemical constituents such as flavonoids and phenolic compounds, beta carotene and ascorbic acid, saponins, alkenyl compounds and benzoquinone derivative. This article also covers about the biological activities and common extraction method of *L. pumila*.

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Fig. 1: Photo of *Labisia pumila* Benth. var. *alata*

Green House Cultivation of *Labisia Pumila:* Mostly, *L. pumila* plant is harvested from its natural habitat in tropical forest. Owing to the increasingly demand, the supply of the plant from natural habitat is getting limited. Furthermore, the propagation and growth rate of this herb is relatively slow [7]. The plant propagates from its seed in natural habitat. The dependence on seeds for propagation is inappropriate since the seeds are extremely scarce. In order to accommodate the future demand of this herb by herbal industry, several research teams such as Forest Research Institute Malaysia [5] and Universiti Putra Malaysia [4] have intensively carried out the experiments to domesticate and cultivate this herb since 2002 and 2008, respectively. Rozihawati *et al*. [8] reported their propagation techniques by using the leaf, petiole and stem of the plant. These cuttings were treated with rooting hormone and placed in the media of sand, sawdust and the mixture of sand and sawdust. Their findings showed that *L. pumila* var. *pumila* could be easily propagated by the leaf and petiole cuttings with or without hormone treatment. However, the stem cuttings required the application of hormone for good rooting percentage. Both sand and the mixture of sand and sawdust were the best rooting media for leaf cuttings. On the other hand, the petiole and stem cuttings were rooting better in 100% sand media. Despite with the encouraging findings, the cultivation effort still cannot produce this herb in commercial scale for local demand till to date.

According to Jaafar *et al*. [9], this herb is very sensitive to changes in microclimate, especially light intensity, temperature and relative humidity. Therefore, the authors suggested growing the herb under greenhouse condition. This might be the most appropriate solution for commercial scale of cultivation. This is because the microclimate in greenhouse can be controlled to provide suitable growing condition for the plant. In open field, the plants might receive higher sunlight intensity for photo-synthesis, hence producing more NADPH and ATP than those plants grow in the greenhouse [8]. Consequently, the accumulation of redox and energy could decrease the plastoquinone pool and inhibit the water splitting complex, thus leading to the inactivation of photosystem, PSII. This phenomenon is called photo-inhibition [10].

In the subsequent year, the same group of researchers conducted the study on photosynthetic response of the three varieties of *L. pumila* under different microclimate parameters such as temperature, CO_2 concentration and photosynthetic photon flux density in both open field and greenhouse conditions [10]. Ibrahim and Jaafar [11] reported that all varieties grown in greenhouse exhibited higher light-saturated photosynthetic capacity than those grown in open field. Their study also indicated that plants grown under greenhouse encountered less photo-inhibition. It is also noteworthy that *L. pumila* var. *alata* and var. *pumila* were found to be acclimatized better under both growing conditions compared to var. *lanceolata*.

Phytochemicals from *Labisia pumila:* Several studies have been conducted to identify the phytochemicals from *L. pumila*. Table 1 lists the identified phytochemicals from the herb and their corresponding chemical structures along with the disease that can be cured using the identified phytochemicals. Some of the studies reported that the phytochemicals such as phenolic, flavonoid, carotenoids, ascorbic acids, saponin, alkenyl compounds and benzoquinone derivatives might contribute to numerous pharmacological activities. These pharmacological properties have created deep interest from researchers for further investigation. Nowadays, the plant derived drugs are increasingly accepted by public due to unfavorable side effect of chemically synthesized drugs.

Phenolics and Flavonoids: Phenolic compounds are the secondary metabolites that can be found abundantly in most of the land plants. Phenolic compounds were reported to have the most antioxidant potential. It is believed that phenolic acids can be easily absorbed by

Table 1: Identified antioxidant compounds in *Labisia pumila* and its chemical structures.

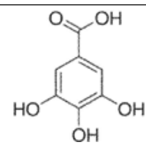
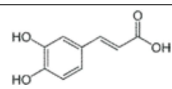
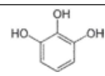
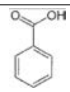
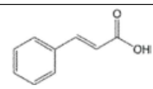
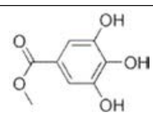
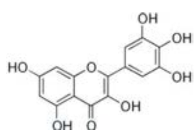
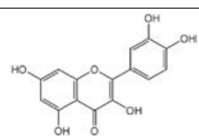
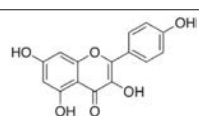
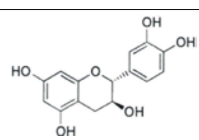
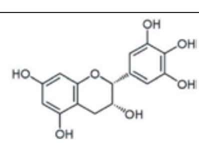
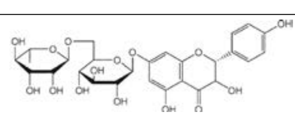
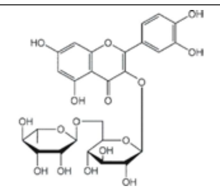
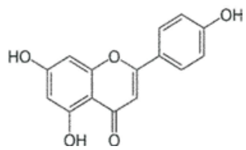
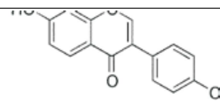
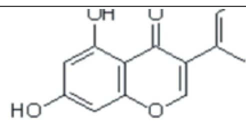
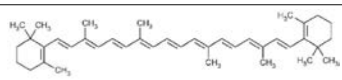
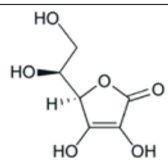
Phytochemical	Chemical structure	Author	Biological activities
Phenolics			
Gallic acid		[13]	antioxidant, antityrosinase, antimicrobial, anti-inflammatory and anticancer activities
Caffeic acid		[13]	
Pyrogallol		[13]	
Benzoic acid		[14]	
Cinnamic acid		[14]	
Methyl gallate		[17]	
Flavonoids			
Quercetin		[13-14]	Anti-inflammatory, Anti tumor, Anti thrombogenic, antiosteoporotic, Antiviral, Antibacterial, antifungi, antiatherosclerotic
Myricetin		[13-14]	
Kaempferol		[13-14]	
Catechin		[14]	
Epigallocatechin		[14]	
Naringin		[13]	

Table 1: Continued

Phytochemical	Chemical structure	Author	Biological activities
Rutin		[13]	
Apigenin		Ehsan and Hawa (2011)	
Daidzein		Ehsan and Hawa (2011)	
Genistein.		Ehsan and Hawa (2011)	
Beta carotene		[12]	Anti oxidant, anti cancer,
Ascorbic acid		[12]	

the digestive system and they offer numerous anti-aging benefits. Therefore, many studies are extensively carrying out to identify phenolic compounds that exhibiting strong antioxidant activity. The antioxidant activity might indirectly contribute to the reported anti-carcinogenic, anti-bacterial, anti-viral and anti-inflammatory properties.

Total phenolic content in *L. pumila* were studied by many researchers till to date. Norhaiza *et al*. [12] reported that the plant contained significant level of phenolic compounds with the amount value ranging from 2.53 to 2.55 mg/g. Interestingly, there was no significant difference between the amount of phenolic content in different varieties of *L. pumila* such as var. *alata* and var. *pumila*. However, they reported the difference in the total flavonoid content, which was higher in *L. pumila* var. *pumila* than to var. *alata*. In good agreement with Ehsan *et al*. [13], who reported that *L. pumila* var. *pumila* contained higher total flavonoids content than var. *alata* and var. *lanceolata*, particularly the methanolic extract of the leaves compared to the other parts of the plant. Their reversed phase chromatographic results showed that kaempferol, myricetin, naringin, quercetin and rutin as the main flavonoids in all three varieties of *L. pumila*. The same group of researchers also detected isoflavonoids such as daidzein and genistein in all three varieties of *L. pumila* [23]. Based on the mass spectrometric data of Chua *et al*. [14], the identified flavonoids in methanolic extract of *L. pumila* included nine types of ?avonols from the basic chemical structure of quercetin, myricetin and kaempferol and two types of ?avanols, namely catechin and epigallocatechin. On the other hand, the total anthocyanin content in *L. pumila* var. *alata* was higher than var. *pumila*. It was an interesting finding because anthocyanin was reported to be effective in reducing the risk of chronic metabolic disorders [15].

In the following year, Ehsan *et al*. [13] reported the presence of gallic acid and caffeic acid in all the three varieties of *L. pumila*. However, it was found that higher content of gallic acid and pyrogallol were detected in var. *alata* compared to the two other varieties. Chua *et al*. [14] identified nine phenolic acids from the family of benzoic acid and cinnamic acid spectrometrically. Quantitative determination of alkenated-phenolics from the leaves, leaves/stems and roots of *L. pumila* using a HPLC-UV-ELSD system had been conducted by Avula *et al*. [16]. The authors discovered that all parts of the plant contained specific phenolic compounds such as irisresorcinol, belamcandol B and demethyl belamcandaquinone B. Recent study conducted by Hisham *et al*. [17] had successfully identified and purified methyl gallate from the leaves of *L. pumila* through an open column chromatography. They demonstrated that methyl gallate could exhibit various types of biological activities such as anti-oxidant and pro-oxidant, anti-microbial, anti-asthmatic, collagenase inhibitor and protein tyrosine kinases inhibitor [18].

Flavonoid which is also called polyphenol, is another class of secondary plant metabolites. Recently, flavonoids have gained tremendous interest among the researchers, mainly because of their potential benefits for health promotion. Similarly, they have been reported to have anti-viral, anti-allergic, anti-platelet, anti-inflammatory and anti-diarrheal and anti-tumor properties [19]. These pharmacological activities might be contributed to the existence of anti-oxidative flavonoids in the plant. Interestingly, flavonoids contained in grape seed proanthocyanidin extract were believed to appeared to be more powerful than the most common antioxidants, namely vitamin C and vitamin E in preventing cellular damage by free radicals [20].

β-Carotene and ascorbic acid: The protective effect of *L. pumila* was further confirmed after detection of β-carotene in the plant extract [14]. The β-carotene content was found to be higher in var. *alata* than var. *pumila*. It provides nutritional protection against skin damage from sunlight. Meta-analysis conducted by Kopcke and Krutmann [21] also indicated that β-carotene supplementation was effective to provide protection against sunburn reaction. Besides β-carotene, another powerful antioxidative compound such as ascorbic acid (vitamin C) was detected in the extract of *L. pumila* var. *pumila* and var. *alata* [14]. It is believed that ascorbic acid could reduce the risk of chronic disease and strokes through small reduction in systolic blood pressure [22]. Many people are taking this vitamin to increase their immune system because of its capacity to inhibit oxidation by free radicals accumulated in human body.

Saponin: Saponins are another group of secondary metabolites in plant and they are biologically active with a wide range of medicinal properties including hypo-cholesterolemic, anticarcinogenic, anti-inflammatory, antimicrobial and antioxidant activities [23]. Saponins can be found in various parts of *L. pumila* including leaves, stems, roots, bulbs, fruits and blossom. Ehsan *et al*. [13] reported that the total saponin content in the leaves was higher than in the stems and roots of the plant. In particular, the leaves of var. *pumila* contained higher amount of the total saponin content than var. *alata* and var. *lanceolata*. Recently, Avula *et al*. [16] demonstrated that four triterpenoids saponin compounds, namely ardisicrenoside B, ardisiacrispin A, 3-O-α-L-rhamnopyranosyl-(1>2)-β-D-glucopyranosyl-(1?4)-α-L-arabinopynanosyl cyclamiretin A and ardisimamilloside H from the roots, leaves and stem of *L. pumila* using an HPLC-UV-ELSD system. Through their finding, they detected that both ardisiacrispin A and irisresorcinol compounds at a concentration as low as 10.0 and 0.2?µg/mL, respectively. In line with the findings of Huang *et al*. [24], they also detected triterpernoid and steroid saponin in *Ardisia mamillata* in the same family of Myrsinaceae. Panax ginseng is another type of herbal plant that well known for its saponin content [28]. Triterpenoid saponins have been proven for their biological activities such as anti-bacterial, anti-neoplastic and anti-cancer properties. The chemoprevention activity of triterpenoids against several types of cancer has been reviewed by Laszczyk [25] and Petronelli *et al*. [26].

Alkenyl Compounds and Benzoquinone Derivative: Many years ago, another group of researchers found alkenyl compounds and benzoquinone derivatives in the leaves and the roots of *L. pumila* [32, 33]. Indeed, the family of Myrsinaceae are known to produce and accumulate many benzoquinone compounds [27]. Benzoquinone is derived from quinone that exists abundantly in plant kingdom. Its anti-bacterial activity has been reviewed by numerous researchers [28-30]. The identified alkenyl resorcinols derivatives by the group included (Z)-5-(pentadec-4'-enyl)-resorcinol, (Z)-5-(pentadec-8'-enyl)-resorcinol and (Z)-5-(pentadec-10'-enyl)-resorcinol [37]. While, alkenyl resorcinols are unsaturated resorcinol lipids that exhibiting medical property based on epidemiological studies on the treatment of gastrointestinal cancer and cardiovascular diseases [31]. They concluded that the positive effect was mainly due to the presence of alkenyl resorcinols and phenolic acids in cereal grain based diets. Alkenyl resorcinols are compounds commonly found in cereal grain [32] and their composition vary between 15% for rye, 1% for wheat and 0.5% for barley.

Biological Activities

Phytoestrogenic Effects: *L. pumila* is believed to have phytoestrogen acting as primary female sex hormone, particularly estrogen. This is because the plant is widely used as woman post-partum medicine traditionally. The phytoestrogens could be coumestans, isoflavones and/or flavonoids because these compounds showed significant phytoestrogenic activity. *In vitro* study conducted by Jamia *et al*. [3] showed that the ethanolic extract of the roots of *L. pumila* var. *alata* exhibited significant estrogenic effect on the human endometrial adenocarcinoma cells in estrogen-free basal medium, thus enhancing secretion of alkaline phosphatase. Researchers also demonstrated that the plant extract exhibited the estrogenic property acting as estrogen receptor modulators [33]. The water extract displaced the binding to antibodies and raised against estradiol, making it similar to other estrogens such as esterone and estradiol [33].

On the other hand, the estrogenic property could be due to the capability of the plant extract in modulating post-menopausal adiposity. The finding was made based on the observation of Al-Wahabi *et al*. [34] who conducted *in vivo* experiments on ovariectomized rats treated with 17.5 mg/kg/day of water extract of *L. pumila* var. *alata* orally and used 120μg/kg/day of estrogen replacement therapy (ERT) as a positive control. They found that the water extract of the plant could modulate post-menopause adiposity similar to the result from ERT treatment by initiating lipolysis in adipose tissues, thus reducing obesity symptom. The plant extract (10-50 mg/kg/day) was found regulating the body weight gain of Sprague-Dawley rats through uterotrophic action on the uterus of tested rats [35]. Plasma leptin of treated rats with water extract of *L. pumila* significantly increased to a higher level or comparable to ovariectomized rats treated with ERT. The promising effect of *L. pumila* had also been proven from the body composition and metabolic features of female rats treated continuously with dihydrotesterone to induce polycyctic ovary syndrome (PCOS). It was found that 50 mg/kg/day of the water extract increased uterine weight up to 27% and improved insulin sensitivity up to 36% as well as improved the lipid profile in PCOS rats without affecting body composition [36].

Not only obesity, the health problem of post-menopause always accompanies by osteoporosis. Shuid *et al*. [37] reported that the administration of 17.5 mg/kg/day of the plant extract could prevent the changes in bone biochemical markers. The reduction of change suggested that the plant extract could be another alternative for ERT treatment. This is because ERT treatment is known for its chronic side effects such as breast and uterine cancer.

It is also noteworthy that menopause will always cause the aorta wall to stiffen. The aortic stiffness consequently leads to the risk of cardiovascular disease in menopause women. In recent years, phytoestrogens were found to have a potential role in treating post-menopausal women's diseases. Anthony *et al*. [38] reported that phytoestrogen from soy protein inhibited atherosclerosis. Furthermore, isoflavones from soy could be used to improve endothelial-dependent vascular reactivity that commonly affected by post-menopausal women. Therefore, studies had been carried out to investigate the effects of the plant extract on the integrity of the aortic wall in ovariectomized rats. Al- Wahaibi *et al*. [39] reported the phytoestrogenic property of *L. pumila* could maintain the elastic lamellae architecture of the aorta in ovariectomized rats. They claimed the protective effect of *L. pumila* in modulating post-menopausal cardiovascular risk was comparable to ERT.

Anti-oxidant and Anti-aging Activities: Plant antioxidants are believed to play a crucial role in protection against several of diseases and delaying aging process. The advantages of antioxidant from plant are probably because of their protective effects against reactive oxygen species (ROS). ROS is a term referring to all highly reactive molecules that contain oxygen. One of them is called free radical molecules. Free radical molecules are molecules that have electric charges and tend to affect healthy cells of the body causing the cells to lose their structure and functions. Antioxidants are believed to have the ability to reduce free radical that can cause cell damage in human bodies. Cell damage caused by free radicals may lead to aging and other degenerative diseases like cancer, cataracts, immune system decline and brain dysfunctionality [40].

Till to date, several studies have been conducted to investigate the anti-oxidant activities of *L. pumila*, in terms of free radical scavenging activity, ferric reducing power and β-carotene bleaching method [14, 16, 23, 49]. Based on the results, *L. pumila* var. *alata* was found to be the highest anti-oxidative variety compared to the other two varieties such as var. *pumila* and var. *lanceolata.* Norhaiza *et al*. [12] reported that the anti-oxidant activities of the plant extract were due to the presence of β-carotene, ascorbic acid, anthocyanins, flavonoid and phenolic compounds.

Anti-bacterial and Anti-fungal: The anti-microbial activity of *L. pumila* was studied by Ehsan *et al*. [13] and Ali and Khan [41], both groups of researchers agreed the exhibition of anti-bacterial and anti-fungal activities of the plant extract. A wide range of microbial strains including bacteria, fungi, or protozoans were tested in their studies. Ehsan *et al*. [13] reported higher activity of *L. pumila* var. *pumila* against Gram positive bacteria (*Micrococcus luteus, Bacillus subtilis* B145, *Bacillus cereus* B43, *Staphylococcus aureus* S1431) compared to *L. pumila* var. *alata* and var. *lanceolata.* However, *L. pumila* var. *alata* showed higher activity against Gram negative bacteria (*Enterobacter aerogenes*, *Klebsiella pneumonia* K36, *Escherichia coli* E256, *Pseudomonas aeruginosa* PI96) compared to var. *pumila* and var. *lanceolata*. Nevertheless, the antibacterial activity of this extract was lower than the activity of standard antibiotic, kanamycin. The 50% inhibition of MRSA (*Methicillin-resistant Staphylococcus aureu*) by *L. pumila* extract was decreased from 19. 41 µg/ml to 3.76 and 0.83 µg/ml after tested with the purified belamcandol B and 1,3-dihydroxy-5-[10(Z)-pentadecenyl]benzene, respectively from the herb [54]. The results indicated that the plant extract contained strong anti-bacterial phytochemicals. Similarly, the anti-fungal property of the plant extract against *Fusarium* sp., *Candida* sp. and *Mucor* sp. exhibited appreciable activities compared to streptomycin.

Anti-carcinogenic: The anti-carcinogenic activity of this herb was first reported by Pihie *et al*. [42]. They conducted *in vivo* studies on croton oil-induced mouse skin carcinogenesis models for 20 weeks by using ethanolic extract of the plant. Their finding suggested that *L. pumila* not only decreased the tumor incidence, tumor burden and tumor volume in DMBA-croton oil-induced mice, but also delayed skin tumor. It was conclusively declared that *L. pumila* exhibited significant anti-carcinogenic activity in a dose dependent manner.

Extraction Method for *Labisia pumila*: In the recent years, there has been growing interest in the use of medicinal plant-based product all over the world. Due to this increasing demand, many plant extracts have been studied for their potential activity and compounds. This valuable compound that possess certain bioactivity can be derived from any parts of the plant like bark, leaves, stems, fruits, roots and flowers. In order to acquire maximum potential of this said compound, the utilization of appropriate extraction technologies and parameters must be applied. The parts of plant that possess the most active compound and have been studied by researchers on *Labisia pumila* for various bioactivity and compound are presented in this section. This section also covered about the variation types of extraction techniques used by researchers in their study.

While in some cases in which the active ingredients are distributed all over the plants, most researchers extracted the whole plant of *Labisia pumila* without left behind any parts. However, the number of researchers using leaves of this plant is quiet significant also. The reason these researchers extracted leaves only is because of the fact that plant leaves generally are more favourable for storing active compounds compared to the other parts [13].

Successful extraction and isolation of bioactive compound from plants is also greatly dependent on the type of solvent and method used in the extraction process. Most of the extraction techniques used in *Labisia pumila* extract is conventional techniques. Whether soaking or maceration technique, generally most researchers prefer to extract the desired bioactive compound traditionally because historically in Malay Archipelago culture practices, decoction of *Labisia pumila* in water is commonly employed before consuming it. That is why, it can be said that almost all the researchers use water as a solvent to extract the bioactive compound in *Labisia pumila*. The reason behind the preparation of *Labisia pumila* water extract is also so that this extract can be consumed by subject in *in vivo* studies. Ayida [34] successfully proved that *Labisia pumila* can potentially modulating postmenopausal cardiovascular risks by administering Sprague Dawley rats with water extract of *Labisia pumila.* Water extract of this plant also were used to evaluate toxicity level in this plant in term of genotoxicity or teratogenic and reproductive toxicity [43-45].

Solvent extraction method using methanol, ethanol and hexane were also applied. The Soxhlet extraction technique for anticarcinogenic activity of *Labisia pumila* was done by utilizing ethanol [42]. Other than that, modern extraction method such as microwave assisted extraction (MAE) was used to study the accumulation of flavonoids, isoflavonoids and phenolics in the leaves of *Labisia pumila*. This non conventional method offer huge advantages of short extraction time, increasing the yield in shorter periods and use less solvent [13]. In conclusion, if the extraction technique used in plant studies are lacking in term of engineering aspect, the process of extraction are not optimized and the potential of the plant will not be fully discovered.

CONCLUSION

Based on the review, *Labisia pumila* indicated a significant potential of this plant to address a number of human health conditions. *Labisia pumila* indicated phytoestrogenic effect that can be used in the treatment of conditions related to estrogen hormone imbalance in women. Besides that, *Labisia pumila* also exhibit other beneficial biological activities such antioxidant, anti-aging and collagen synthesis abilities, antimicrobial and currently discovered anticarcinogenic activities. Nevertheless, all these biological activities have only been studied *in vitro* using cell lines and *in vivo* using laboratory animal. These results require further study to be applicable to humans. Truthfully, gaps in conducted studies do exist and these gap need to be bridged in order to fully exploit the potential of *Labisia pumila*. Even so, it is very clear that *Labisia pumila* is in fact have many uses and hold tremendous potential for the future that need to be discovered.

Abbreviations: AP-1, activator protein 1; ATP, adenosine triphosphate; DMBA, 7,12-dimethylbenz(a)anthracene; DPPH, 2,2-diphenyl-1-picrylhydrazyl; EFBM, estrogen-free basal medium; ERT, estrogen replacement therapy; FRAP, ferric reducing antioxidant power; FSC_{50}, 50% free radical scavenging activity; HPLC, high-performance liquid chromatography; HPLC-UV-ELSD, high-performance liquid chromatography-ultraviolet-evaporative light scattering detector; ICR, imprinting control region; NADPH, nicotinamide adenine dinucleotide phosphate; NOAEL, non-observable adverse effect level; MMPs, matrix metalloproteinases; MRSA, *Methicillin-resistant Staphylococcus aureus*; PCOS, polycyctic ovary syndrome; ROS, reactive oxygen species; RP-HPLC, reverse phase-high-performance liquid chromatography; SERM, selective estrogen receptor modulator; SPE, solid phase extraction; TEAC, trolox equivalent capacity; TGF, transforming growth factor; UPLC-ESI-MS/MS, ultra-performance liquid chromatography-electrospray ionization tandem mass spectrometry;

REFERENCES

1. Stone, B.C., 1988. Notes on the genus Labisia Lindl. (Myrsinaceae), Malay. Nat. J., 42: 43-51.
2. Sunarno, B., 2005. Revision of the genus Labisia (Myrsinaceae), BLUMEA, 50: 579-97.
3. Jamia, A.J., P.J. Houghton, S.R. Milligan, J. Ibrahim, 2003. The oestrogenic and cytotoxic effects of the extracts of *Labisia pumila* var. *alata* and *Labisia pumila* var. pumila in vitro, Sains Kesihatan, 1: 53-60.
4. Jaafar, H.Z.E., N.B. Mohamed Haris and A. Rahmat, 2008. Accumulation and partitioning of total phenols in two varieties of *Labisia pumila* Benth under manipulation of greenhouse irradiance, Acta Hortic, 797: 387-92.
5. Huang, J., Y. Ogihara, H. Zhang, N. Shimizu and T. Takeda, 2000. Triterpenoid saponins from Ardisia mamillata, Phytochem, 54: 817-22.
6. Runi, S.P., 2001. Studies on medicinal plant in Sarawak, in: Chang, YS (Ed.), Seminar on Medicinal and Aromatic Plants, Forest Research Institute Malaysia, Kepong, pp: 112-9.
7. Mohd Noh, H.J., B. Mohd Jelani and A.H. Mohd Akhir, 2002. Prestasi Pertumbuhan Empat varieti Kacip Fatimah di ladang semaian Sungkai, Perak, Seminar on Medicinal Plants, FRIM Kepong.
8. Rohizawati, Z., H. Aminah and N. Lokman, 2003. Preliminary trial on rooting ability of *Labisia pumila* cuttings, Malaysian Science and Technology Congress 2003, Agriculture Science, Cititel, Mid Valley, Kuala Lumpur.
9. Jaafar, H.Z.E., I. Mohd Hafiz and E. Philip, 2009. Leaf gas exchange properties of three varieties of *Labisia pumila* Benth. under greenhouse conditions, J. Trop. Ple. Physiol, 3: 16-24.
10. Karpinski, S., H. Reynolds and B. Karpinska, 1997. Photosynthesis electron transport regulates the expression of cytosolic ascorbate peroxidase genes in Arabidopsis during excess light stress, Plant Cell, 9: 627-40.
11. Ibrahim, M.H. and H.Z.E. Jaafar, 2011. Photosynthetic capacity, photochemical efficiency and chlorophyll content of three varieties of *Labisia pumila* Benth exposed to open field and greenhouse growing conditions, Acta Physiol. Plant, 33: 2179-85.
12. Norhaiza, M., M. Maziah and M. Hakiman, 2009. Antioxidative properties of leaf extracts of a popular Malaysian herb, *Labisia pumila*, J. Med. Plants Res., 3: 217-23.
13. Ehsan, K., Z.E.J. Hawa and A. Sahida, 2011. Phytochemical analysis and antimicrobial activities of methanolic extracts of leaf, stem and root from different varieties of *Labisia pumila* Benth, Molecules, 16: 4438-50.

14. Chua, L.S., A.L. Norliza, S.Y. Lee, C.T. Lee, M.R. Sarmidi and R.A. Aziz, 2011. Flavonoids and phenolic acids from *Labisia pumila* (Kacip Fatimah). Food Chem., 127: 1186-92.
15. Wang, S.Y. and H. Jiao, 2000. Scavenging capacity of berry crops on superoxide radicals, hydrogen peroxide, hydroxyl radicals and singlet oxygen, J. Agric Food Chem., 48: 5677-84.
16. Avula, B., Y.H. Wang, Z. Ali, T.J. Smillie and I.A. Khan, 2011. Quantitative determination of triperpene saponins and alkenated-phenolics from *Labisia pumila* using an LC-UV/ELSD method and confirmation by LC-ESI-TOF, Planta Medica, 77: 1742-8.
17. Mohd Nazrul Hisham, D., J. Mohd Lip, J. Mohd Noh, A. Normah and M.F. Nurul Nabilah, 2011. Indentification and isolation of methyl gallate as a polar chemical marker for *Labisia pumila* Benth, J. Trop. Agr. Food Sci., 39: 279-84.
18. Chaubal, R., V.H. Deshpande and N.R. Deshpande, 2005. Methyl gallate, the medicinally important compound: A review, Elec. J. Env. Agricult. Food Chem., 4: 956-62.
19. Proestos, C. and M. Komaitis, 2006. Ultrasonically assisted extraction of phenolic compounds from aromatic plants: Comparison with conventional extraction techniques, J. Food Quality, 29: 567-82.
20. Bagchi, M., M. Mark, W. Casey, B. Jaya, Y. Xumei, S. Sidney, *et al*., 1999. Acute and chronic stress-induced oxidative gastrointestinal injury in rats and the protective ability of a novel grape seed proanthocyanidin extract, Nutr. Res., 19: 1189-99.
21. Köpcke, W. and J. Krutmann, 2008. Protection from sunburn with beta-carotene: A meta-analysis, Photochem. Photobiol, 84: 284-8.
22. Fotherby, M.D., J.C. Williams, L.A. Forster, P. Craner and G.A. Ferns, 2000. Effect of vitamin C on ambulatory blood pressure and plasma lipids in older persons, J. Hypertens, 18: 411-5.
23. Corea, G., E. Fattorusso, V. Lanzotti, R. Capasso, A.A. Izzo, 2005. Antispasmodic Saponins from Bulbs of Red Onion, Allium cepa L. Var. Tropea, J. Agric. Food Chem., 53: 935-40.
24. Huang, J., H. Zhang, N. Shimizu and T. Takeda, 2003. Ardisimamillosides G and H, two new triterpenoid saponins from Ardisia mamillata, Chem. Pharm. Bull, 51: 875-7.
25. Laszczyk, M.N., 2009. Pentacyclic triterpenes of the lupane, oleanane and ursane group as tools in cancer therapy, Planta Medica, 75: 1549-60.
26. Petronelli, A., G. Pannitteri and U. Testa, 2009. Triterpenoids as new promising anticancer drugs, Anticancer Drugs, 20: 880-92.
27. Seigler, D.S., 1998. Plant Secondary Metabolism, Kluwer Academic Publisher, Massachusetts.
28. Kim, M.H., S.H. Jo, K.S. Ha, J.H. Song, H.D. Jang and Y.I. Kwon, 2010. Antimicrobial activities of 1, 4-benzoquinones and wheat germ extract, J. Microbiol. Biotechnol, 20: 1204-9.
29. Ignacimuthu, S., M. Pavunraj, V. Duraipandiyan, N. Raja and C. Muthu, 2009. Antibacterial activity of a novel quinone from the leaves of Pergularia daemia (Forsk.), a traditional medicinal plant, AJTM, 4: 36-40.
30. Koyama, J., 2006. Anti-infective quinone derivatives of recent patents, Recent Pat. Antiinfect. Drug Discov, 1: 113-25.
31. Slavin, J.L., M.C. Martini, D.R. Jr. Jacobs and L. Marquart, 1999. Plausible mechanisms for the protectiveness of whole grains, Am. J. Clin. Nutr, 70: 459S-63S.
32. Ross, A.B., M.J. Shepherd, M. Schüpphaus, V. Sinclair, B. Alfaro, A. Kamal-Eldin and P. Aman, 2003. Alkylresorcinols in cereals and cereal products, J. Agric. Food Chem., 51: 4111-8.
33. Institute for Medical Research, I., 2002. Estrogenic and androgenic activities of Kacip Fatimah (*Labisia pumila*). Abstracts of Research Projects, Ministry of Health Malaysia, Kuala Lumpur, pp: 8.
34. Ayida Al-Wahabi, W.M. Wan Nazaimoon, H.S. Farihah and A.L. Azian, 2007. Effect of ovariectomy, *Labisia pumila* var. alata treatment and estrogen replacement therapy on the morphology of adipose tissue in ovariectomized Sprague Dawley rats, J. Medicine, 1: 1-7.
35. Fazliana, M., W.M. Wan Nazaimoon, H.F. Gu, C.G. Ostenson, 2009. *Labisia pumila* extract regulates body weight and adipokines in ovariectomized rats, Maturitas, 20: 91-7.
36. Mannerås, L., M. Fazliana and W.M. Wan Nazaimoon, 2010. Beneficial metabolic effects of the Malaysian herb *Labisia pumila* var. alata in a rat model of polycystic ovary syndrome, J. Ethnopharmacol, 127: 346-51.
37. Shuid, A.N., L.L. Ping, N. Muhammad, N. Mohamed and I.N. Soelaiman, 2011. The effects of *Labisia pumila* var. alata on bone markers and bone calcium in a rat model of post-menopausal osteoporosis, J. Ethnopharmacol, 133: 538-42.

38. Anthony, M.S., T.B. Clarkson, B.C. Bullock and J.D. Wagner, 1997. Soy protein versus soy phytoestrogens in the prevention of diet-induced coronary artery atherosclerosis of male cynomolgus monkeys, Arterioscl. Throm. Vas., 17: 2524-31.
39. Al-Wahaibi, A., W.M. Wan Nazaimoon, W.N. Norsyam, H.S. Farihah and A.L. Azian, 2008. Effect of water extracts of *Labisia pumila* var. alata on aorta of ovariectomized Sprague-Dawley rats, Pak. J. Nutr., 7: 208-13.
40. Sies, H., W. Stahl and A.R. Sundquist, 1992. Antioxidant Function of Vitamins, Ann. NY Acad. Sci., 669: 7-20.
41. Ali, Z. And I.A. Khan, 2011. Alkyl phenols and saponins from the roots of *Labisia pumila* (Kacip Fatimah), Phytochem., 72: 2075-80.
42. Pihie, A.H.L., F. Othman and Z.A. Zakaria, 2011. Anticarcinogenic activity of *Labisia pumila* against 7, 12- dimethylbenz (a) anthracene (DMBA)/croton oil-induced mouse skin carcinogenesis, Afr. J. Pharm. Pharmacol, 5: 823-32.
43. Zaizuhana, S., J.N.M.B. Puteri, Y. Noral'ashikin, H. Muhammad, A.B. Rohana and I. Zakiah, 2006. The *in vivo* rodent micronucleus assay of Kacip Fatimah (*Labisia pumila*) extract, Trop. Biomed, 23: 214-9.
44. Ezumi, M.F.W., S.S. Amrah, M.I. Nazrul, A.W.M. Suhaimi and S.S.J. Mohsin, 2005. Evaluation of the teratogenicity of aqueous extract of *Labisia pumila* var. *alata* in rats, Malays. J. Med. Sci., 12: 13-21.
45. Singh, G.D., M. Ganjoo, M.S. Youssouf, A. Koul, R. Sharma, S. Singh, P.L. Sangwan, S. Koul, D.B. Ahamad and R.K. Johri, 2009. Sub-acute toxicity evaluation of an aqueous extract of *Labisia pumila*, a Malaysian herb, Food Chem. Toxicol, 47: 2661-5.