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Bioactive Compound and Therapeutic Value of the Some Malaysia Medicinal Plants: A Review

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ABSTRACT

There are many medicinal plants that have been used since folk ages. These plants have been recognized to have pharmaceutical properties and beneficial impact on health. This study discusses the use of ten medicinal plants in the traditional medicinal system of Malaysia and related scientific on their antioxidant activity, which demonstrate their pharmaceutical properties. The plants viewed are *Andrographis paniculata*, *Cosmos caudatus*, *Eurycoma longifolia*, *Ficus deltoidea*, *Gynura procumbens*, *Labisia pumila*, *Orthosiphon stamineus*, *Phyllanthus niruri*, *Piper betle* and *Uncaria gambir*. All the plants mentioned in this study have therapeutic properties such as antioxidation, antidiabetics, antiinflammation, which explains and validates their uses in traditional and modern medicine.

Key words: Antioxidant activity, medicinal plants, antimalarial, *Ficus deltoidea*, anti-inflammation

INTRODUCTION

Malaysia is one of the 12 mega-diverse countries identified by the United Nations Environment Programme (UNEP) as harbouring the majority of the earth's species, which may have immense benefits for future generations. It well-endowed with natural resources in agriculture, forestry and minerals has become intention to the local and overseas researcher. Since folk ages, nature has been a medicinal source in traditional medicine and are isolated for the modern drug (Alsarhan *et al.*, 2014). Folklore has used medicinal plant for treating gout, high blood pressure, diarrhoea and skin infection (Shafaei *et al.*, 2014). Recently studies have indicated that the sources of antioxidant in medicinal plant have medicinal properties that give beneficial impact on health.

Halliwell and Gutteridge (1995) have defined antioxidant as "Any substance that when present at low concentration compared with those of an oxidizable substrate, significantly delays or prevents oxidation of that substrate" and Halliwell (2007) has precise the definition of antioxidant as "Any substance that delays, prevent or removes oxidative damage to

a target molecule". Oxidation is a chemical reaction that transfers electrons or hydrogen from a substance to an oxidizing. Antioxidant works to maintain the oxidant at optimum level and reduce free radical by stopping it forming before it can disrupt living cell in our body (Asad *et al.*, 2012). There are two type of antioxidant; synthetic antioxidant and natural antioxidant. Artificial antioxidant is a product from laboratories for food and pharmaceutical industries. It was added to food in order to prolong product shelf life and it used to enhance the stability of therapeutic against that are susceptible to chemical degradation by oxidation in pharmaceutical (Shebis *et al.*, 2013). Synthetic antioxidant such as Butylated Hydroxyl Anisole (BHA), Butylated Hydroxyl Toluene (BHT), Propyl Gallate (PG) and Tertiary Butyl Hydroquinone (TBHQ) has been discouraged use because of their toxicity and carcinogenicity and it has been restricted as they may cause liver swelling and influence liver enzyme activities (Anwar *et al.*, 2006; Tavasalkar *et al.*, 2012).

Natural antioxidant is a product that can be taken directly from organic sources such as fruit, vegetables, grains and meat. There are two types of natural antioxidant, which is endogenous antioxidant and dietary antioxidant. Endogenous

antioxidant is produce from our own bodies such as bilirubin, glutathione, lipoic acid, N-acetyl cysteine, NADPH and NADH, ubiquinone (coenzyme Q10), uric acid and enzymes. while dietary antioxidant also known as exogenous antioxidant can be taken as supplement from plant and microalgae such as vitamin C, vitamin E, β -carotene and others carotenoids, oxycarotenoids and polyphenols (Percival, 1998). Several type of plant material such as vegetables, fruits, leaves, oil seed, cereal crops, barks and roots, spices, herbs and crude plant drugs have been reported to have potential source of antioxidant compound like polyphenols, flavonoids and phenolic compounds (Kahkonen *et al.*, 1999; Khalaf *et al.*, 2008; Proestos *et al.*, 2013). Free radicals are electrical charged molecule by means that they have an unpaired electron, which causes then to seek out and capture electron from other substance in order to neutralize themself (Percival, 1998). The production of the radical occurs continuously in all cells as part of normal cellular function. But, excess of the production of free radical play an important role in degenerative disease like cancer, cataract, immune system weakness and brain problem. It also induces nutrition medicines deterioration (Namjooyan *et al.*, 2010; Young and Woodside, 2001). One of the sources of free radical in the body come from environmental sources, which are from cigarette smoke, pollutants, UV light, ionising radiation and venobiotics.

Polyphenols are the most abundant antioxidants in our diet and are widespread constituents of fruits, vegetables, cereals, olive, dry legumes, chocolate and beverages, such as tea, coffee and wine (Manach *et al.*, 2004). Current studies have shown that polyphenolic mostly constituents in plant have more effective antioxidants *in vitro* than vitamins E or C and it might contribute significantly to the protective effects *in vivo* (El Gharras, 2009), because they comprise a wide variety of molecules that have a polyphenols structure (Han *et al.*, 2007) (i.e., several hydroxyl groups on aromatic rings) but also molecules with one phenol ring, such as phenolic acids. Polyphenols are divided into several classes according to the number of phenol rings. Studies show that diets high in antioxidant reduce cancer death rates, cold and flu Infections and protect against atherosclerosis, heart disease and cataracts. it possess diverse biological properties such as antioxidant, anti-aging, anti-carcinogen, anti-inflammation, anti-atherosclerosis,

cardiovascular protection, improvement of the endothelial function as well as inhibition of angiogenesis and cell proliferation activity sources and significance (Bravo, 1998; Han *et al.*, 2007; Manach *et al.*, 2005). The current consensus stated that, there is evidence that phenolic substance as antioxidants by preventing LDL-lipoprotein, platelet aggregation and damage of red blood cells (El Gharras, 2009) but mostly the evidence base on the experimental (D'Archivio *et al.*, 2007). This study discuss on the overview of antioxidant and it present in the some Malaysian medicinal plants with the research study on their pharmaceutical properties. The objective of this study is to introduce the Malaysian medicinal plant that gives benefits in the pharmaceutical industries.

MEDICAL PLANTS HAVING ANTIOXIDANT PROPERTIES

***Andrographis paniculata*:** *Andrographis paniculata* (Burn. f.) Nees (Acanthaceae) commonly known as 'King of bitters' (Cui *et al.*, 2009) is a native plant to Taiwan, Mainland China and India (Chao and Lin, 2010) (Fig. 1a). According to study from Raina *et al.* (2013), *A. paniculata* is distributed in tropical countries Sri lanka, India, Thailand and Peninsular Malaysia to Indonesia (Raina *et al.*, 2013). *Andrographis paniculata* also known as Hempedu Bumi in Malaysia, herbaceous plant of family Acanthaceae and it is widely cultivated in Southern Asia. The whole plant has variety of therapeutic value and it is use traditionally as an immune system booster to treat infection in gastrointestinal tract and upper respiratory tract, in treatment of wounds, ulcers, leprosy, fever, herpes, sole throat and hypertension (Wasman *et al.*, 2011). Now a days, this plant is used extensively as anti-typhoid, anti-fungal activity, antithrombotic, imunostimulant, antimalarial, anti-hyperglycemic, anti HIV, anti-fertility, cardioprotective, hepatoprotective, antioxidants, anti-inflammatory, anti-snake venom and antipyretic properties (Akbar, 2011; Anju *et al.*, 2012; Ghosh *et al.*, 2012; Ojha *et al.*, 2009; Sivaraj *et al.*, 2011). There were different approaches for determination of pharmaceutical properties of *A. paniculata* (Table 1).

Diterpenoids, polyphenols and flavoids are the main chemical constituents of *A. paniculata* which believe to be

Table 1: Pharmaceutical properties of *A. paniculata*

Pharmaceutical properties	References
Antimicrobial: (<i>Staphylococcus aureus</i> ATCC 25923, <i>Escherichia coli</i> wild type) and fungi (<i>Candida tropicalis</i> ATCC 750, <i>Candida albicans</i> ATCC 10231)	Chakraborty <i>et al.</i> (2011)
Immunomodulation: Anaphylactoid potential	Hu <i>et al.</i> (2015)
Antitoxicity: CYP6AA3- and CYP6P7- expressing <i>Spodoptera frugiperda</i> (Sf9) cells to cypermethrin toxicity	Kotewong <i>et al.</i> (2014)
Antiinflammation: Inhibitory effect on the release of Tumor Necrosis Factor alpha (TNF- α) in the human monocytic cell line THP-1	Low <i>et al.</i> (2015)
Anticancer: Action mechanisms of a purified polysaccharide (APWP) suppress the proliferation of HepG2 cells via inducing apoptosis	Zou <i>et al.</i> (2015)
Antioxidation: Antioxidant action of <i>Andrographis paniculata</i> on lymphoma	Verma and Vinayak (2008)
Antistress activity: Effects of the treatments on stress-induced alterations in body weight, gastric ulcer, adrenal and spleen weights, depressive state and sexual behavior in male rats	Thakur <i>et al.</i> (2014)

responsible for the most biological activities (Sharma and Joshi, 2011). Three main diterpenoid lactones identified in the *paniculata* leaves were andrographolide, neodrographolide and deoyandrographolide which are active ingredients for medicinal value of this plant (Chakraborty *et al.*, 2011; Das and Srivastav, 2014). Among the single compound, andrographolide is the major in terms of bioactive properties (Chao and Lin, 2010). While, flavonoids mainly exist in the root but also isolated from the leaves and the aerial parts of the plant contain alkanes, ketones and aldehydes (Subramaniam *et al.*, 2015).

Cosmos caudatus: *Cosmos caudatus* (Fig. 1b) is locally known as ulam raja in Malaysia is belonging to the family Asteraceae and traditional used for improving blood circulation, reducing body heat, as anti-aging agent, promoting fresh breath, treating infections associated with pathogenic microorganisms and to strengthen muscles and bones (Amna *et al.*, 2013; Mohamed *et al.*, 2013). It generally consumed freshly as salad or cooked by boiling with other spices. *Cosmos caudatus* have pharmaceutical properties (Table 2) such as antioxidant effects (Nurul *et al.*, 2010), exhibits anti-mutagenics, anti-inflammatory, anti-microbial (Rasdi *et al.*, 2010; Salehan *et al.*, 2013), anti-fungal properties several study have indicated that it has been implicated in reduction of risk for chronic diseases such as stroke, cardiovascular disease and some cancer it due to it flavonoids content (Mediani *et al.*, 2013). In addition, *Cosmos caudatus* showed that the antioxidant activity more than 70% and it has been found to contain phenolic, anthocyanins, ascorbic acid, β -carotene, flavoids, flavones and flavanones (Mediani *et al.*, 2013; Mohamed *et al.*, 2013). It is believed that phenolic compound are the main contributor of antioxidant activity in plant extract (Bunawan *et al.*, 2014). It also rich in mineral such as calcium, phosphorus, iron, magnesium and potassium (Mohamed *et al.*, 2013).

Eurycoma longifolia: *Eurycoma longifolia* (Fig. 1c), Ali's walking stick is a small tree that grows along the hilly slopes of the rainforests of Southeast Asia, including Indonesia, Malaysia, Thailand, Laos, Cambodia and Vietnam. It commercially known as Tongkat Ali and "Malaysia ginseng"

in Malaysia (Simaroubaceae) and the root is popular as traditional medicinal plant for anti-aging (Purwantiningsih *et al.*, 2011) and as an alternative for enhance libido, energy, sport performance and weight loss (Talbot *et al.*, 2013), it is due to *E. longifolia* stimulate release of free testosterone but it prohibited to use in sport as it enhance athletic performance. A study by George *et al.* (2013) have indicated that *E. longifolia* do not have doping effect. It also as health supplement for hypertension, diarrhoea, aches, persistent fever, dysentery and glandular swelling and it have demonstrate to possess medicinal values (Table 3) such as the antibacterial (Danial *et al.*, 2013), anti-inflammatory (Varghese *et al.*, 2013) anticoagulant for complications during child birth, aphrodisiac, anti-plasmodial activity, cytotoxic effects, antipyretic, antidiabetic activity, antimalarial, hepatoprotective activity, anticancer, anxiolytic and antiulcer (Mokhtar *et al.*, 2014; Panjaitan *et al.*, 2013; Yusuf *et al.*, 2013). It was popular for its aphrodisiac property due to its ability to stimulate the production or action of androgen hormones, especially testosterone. Chemical compound that have been isolated from the of *E. longifolia* include eurycomanone, eurycomanol, eurycomalactone, canthine-6-one alkaloid, 9-hydroxycanthine-6-one, 14.15 β -hydroxyklaineaneone, phenolic components, tannins, quannisoids and triterpenes (Chen *et al.*, 2014). It have been reported to be antioxidative due to its high concentration of superoxide dismutase (Effendy *et al.*, 2012).

Ficus deltoidea: As an herbal tree, almost all of the parts of *Ficus deltoidea* (Fig. 1d) plant including the roots, bark, stems, leaves and fruits are believed to have medicinal properties (Table 4), which is useful for health purposes in various ailments in the Malay Archipelago (Akhir *et al.*, 2011; Kalman *et al.*, 2013). Traditionally, has been used in treating

Table 2: Pharmaceutical properties of *C. caudatus*

Pharmaceutical properties	References
Antioxidation: The impact of tropical seasons (dry and wet) and growth stages (8, 10 and 12 weeks) of <i>Cosmos caudatus</i> on the antioxidant activity and Total Phenolic Content (TPC)	Mediani <i>et al.</i> (2012)
Preventing osteoporosis: Effects of <i>Cosmos caudatus</i> (ulam raja) on dynamic and cellular bone histomorphometry in ovariectomized rats	Mohamed <i>et al.</i> (2013)

Table 3: Pharmaceutical properties of *E. longifolia*

Pharmaceutical properties	References
Anticancer: Induce apoptosis in HepG2 cells via up regulation of p53	Zakaria <i>et al.</i> (2009)
Antioxidation: Effects on cytochrome P450 (CYP) isoforms CYP1A2, CYP2A6, CYP2C8, CYP2C9, CYP2C19, CYP2E1 and CYP3A4 using <i>in vitro</i> assays	Pan <i>et al.</i> (2014)
Antiparasite activity: Anti- <i>T. gondii</i> activity of crude extract (TACME) and four fractions (TAF 273, TAF 355, TAF 191 and TAF 401) from <i>E. longifolia</i>	Kavitha <i>et al.</i> (2012)
Antistress activity: Improves stress hormone profile and certain mood state parameters	Talbot <i>et al.</i> (2013)
Stimulate androgen hormones: Effects of EL extract on serum testosterone levels, bone biomarkers, biomechanical strength and gene expression of Receptor Activator of Nuclear Factor kappa-B ligand (RANKL), Osteoprotegerin (OPG) and Macrophage Colony Stimulating Factor (MCSF) in orchidectomised rats	Shuid <i>et al.</i> (2012)

Table 4: Pharmaceutical properties of *F. deltoidea*

Pharmaceutical properties	References
Antimelanogenic Activity: Preventing tyrosinase activity <i>in vitro</i> and by suppressing tyrosinase gene expression in B16F1 melanoma cells	Oh <i>et al.</i> (2011)
Antidiabetic activity: <i>Ficus deltoidea</i> stimulates insulin secretion and blocks hepatic glucose production by regulating the expression of glucose-metabolic genes in streptozotocin-induced diabetic rats	Farsi <i>et al.</i> (2014)
Assessments pre- diabetic by fasting plasma glucose, insulin, OGTT and HOMA-IR; body weight and waist circumference; vital signs, comprehensive metabolic and lipid panels	Kalman <i>et al.</i> (2013)
Antidiabetic activities assessed based on the ability of the samples to inhibit yeast and mammalian α -glucosidase as well as α -amylase	Misbah <i>et al.</i> (2013) and Olaokun <i>et al.</i> (2013)
Antioxidation: Measuring the ability of the samples to reduce ferric ions and to scavenge DPPH, superoxide anion, ABTS and nitric oxide radicals	Misbah <i>et al.</i> (2013)
Antiaging: Illustrate the efficacy of the <i>F. deltoidea</i> extract towards alleviating UVB-induced photo- ageing and inflammation in the skin by modulating the expression of pro-inflammatory cytokines, COX-2, MMP-1 and type 1 pro-collagen	Hasham <i>et al.</i> (2013)
Antidiapogenic effect: Extracts of <i>Ficus deltoidea</i> var. <i>deltoidea</i> and var. <i>angustifolia</i> on 3T3-L1 adipocytes	Woon <i>et al.</i> (2014)

Table 5: Pharmaceutical properties of *G. procumbens*

Pharmaceutical properties	References
Antiinflammation: Croton oil-induced mouse ear inflammation	Iskander <i>et al.</i> (2002)
Lowering blood pressure: <i>G. procumbens</i> causes vasodilatory effects by blocking calcium channels	Ng <i>et al.</i> (2013)

gout, high blood pressure, pneumonia, diarrhoea, skin infections and diabetes and to improve blood circulation (Shafaei *et al.*, 2014). *Ficus deltoidea* contain at least 25 flavonoids being identified with the major constituents being flavan-3-ol monomers, proanthocyanidins and C-linked flavone glycosides. and study has found that female leaves of the plant are better than male leaves in term of antioxidant potential (Azemin *et al.*, 2014; Hakimian and Maziah, 2009). Another view from Aris *et al.* (2009) is that the fruit of *F. deltoidea* var. *angustifolia* sp., is a good source of antioxidant. *Ficus deltoidea* also help in wound healing by significantly accelerate the rate of wound healing (Abdulla *et al.*, 2010a) and it has reported that the plant have antidiabetic properties (Misbah *et al.*, 2013). The study on cytotoxicity of aqueous and ethanolic extract of ficus deltoidea on human ovarian carcinoma cell line indicated that the aqueous extract of the plant prompted to promote cell detachment, whereas the ethanolic extract tried to stop cell from proliferation (Akhir *et al.*, 2011). The leaf extract were found to enhance insulin-stimulated glucose uptake.

Gyanura procumbens: *Gynura procumbens* (Fig. 1e) is a medicinal plant belonging to the family Asteraceae locally known in Malaysia as Sambung Nyawa. It widely found in Borneo, Java, the Philippines and peninsular Malaysia. Usually leaves of the *G. procumbens* has been used for treatment various ailment such as fever, kidney disease, inflammation, diabetes, lowering blood pressure (Hoe *et al.*, 2011; Ng *et al.*, 2013). In the present study, *G. procumbens* (Table 5) were identified as anti-hyperglycaemic, anti-inflammatory, anti-plasmodial, anti-cancer, anti-ulcerogenic (Mahmood *et al.*, 2010; Nisa *et al.*, 2012; Vejanan *et al.*, 2012). A study has indicated that the leaf extract of *G. procumbens* have potential in treating wound (Zahra *et al.*, 2011). Bioactive compound

found in the plant concoction including flavoids, saponins, tannins, terpenoids and sterol glycosides.

Labisia pumila: *Labisia pumila* (Fig. 1f) is a small sub-herbaceous plant from the genus of the Labisia that belongs to the family Myrsinaceae L. It is most popular traditionally used by malay woman to maintain healthy female reproductive function and as postpartum medicine (Abdullah *et al.*, 2013). This plant is popular as effective in curing many ailments such as postpartum treatment, anti-flatulence, dysentery, dysmenorrhea, gonorrhoea, rheumatism and preventing osteoporosis caused by post menopause (Al-Wahaibi *et al.*, 2008; Sanusi *et al.*, 2013). The values of this species as protection again disease are largely influenced by its phytoestrogen, anti-inflammatory and antioxidant properties. some studied indicated that *L. pumila* has possible application (Table 6) as anti-inflammatory activity, cytotoxic agent, immunomodulatory, antioxidant, lypolytic and aphrodisiac affects (George *et al.*, 2014; Karimi *et al.*, 2013a). Natural bioactive compound such as resorcinols, flavonoids, saponins and phenolic acid are found in the *L. pumila* (Karimi and Jaafar, 2011; Hussain and Kadir, 2013). Other studied has indicated that isoflavonoids, benzoquinones, alkenyl resoronol, triterpenoids as one of the bioactive compound in *L. pumila* (George *et al.*, 2014). The mechanism of anti-inflammation of *L. pumila* might be related with the bioactive compounds and phytochemicals present in plant (Karimi *et al.*, 2013b). Among three varieties of *L. pumila*, var. *alata* had higher total antioxidant activity compared to the var. *pumila* (Norhaiza *et al.*, 2009).

Orthosiphon stamineus: *Orthosiphon stamineus* (Fig. 1g) or locally known as misai kucing is one of the well-known traditional medicinal plants in several countries of Southeast Asia (particularly in Malaysia, Indonesia, Thailand, Vietnam and Myanmar) which belong to Lamiaceae family (Adnyana *et al.*, 2013). It widely applied (Table 7) to cure cardiovascular, metabolism disorder, rheumatism, edema, jaundice, diuretic, fever, hepatitis, gall stones, eruptive, hypertension, diabetes and epilepsy (Pang *et al.*, 2013; Ramesh *et al.*, 2014). This plant works as antioxidant,



Fig. 1(a-j): Medicinal plant, (a) *Andrographis paniculata*, (b) *Cosmos caudatus* (c) *Eurycoma longifolia*, (d) *Ficus deltoidea*, (e) *Gyanura procumbens*, (f) *Labisia pumila*, (g) *Orthosiphon stamineus*, (h) *Phyllanthus niruri*, (i) *Piper betle* and (j) *Uncaria gambir*

Table 6: Pharmaceutical properties of *L. pumila*

Pharmaceutical properties	References
Preventing osteoporosis: <i>Labisia Pumila</i> var. <i>alata</i> (LPva) protect bone against estrogen deficiency-induced changes by regulating the Receptor Activator of Nuclear Factor kappa-B Ligand (RANKL), Osteoprotegerin (OPG) and Bone Morphogenetic Protein-2 (BMP-2) gene expressions	Fathilah <i>et al.</i> (2013)
Time and dose-dependent effects of <i>Labisia pumila</i> on the bone strength of postmenopausal osteoporosis rat model	Effendy <i>et al.</i> (2015)
Antibacterial activity: Antibacterial activities against eight bacteria (four Gram-positive and four Gram-negative bacteria)	Karimi <i>et al.</i> (2015)
Antioxidation: Comparison between three varieties of <i>Labisia pumila</i>	Karimi <i>et al.</i> (2015)
Antifungal activity: Plant extracts were characterized against <i>Fusarium</i> sp., <i>Candida</i> sp. and <i>Mucor</i> using the agar diffusion disc	Karimi <i>et al.</i> (2013a)
Anti-inflammatory: Using NO production by macrophage RAW 264.7 cell lines induced by LPS/IFN-g	Karimi <i>et al.</i> (2013a)

antimicrobial, antibacterial, antifungal, antitumor, antiulcer, antiviral and anti-inflammatory (Ameer *et al.*, 2012;

Amin *et al.*, 2012; Kannappan *et al.*, 2010). This plant consists of several active chemical compounds such as steroids,

Table 7: Pharmaceutical properties of *O. stamineus*

Pharmaceutical properties	References
Antimicrobial activity: The effect of host extract in the culture medium on anti-candidal activity of <i>Phomopsis</i> sp. ED2	Yenn <i>et al.</i> (2012)
Anti-inflammatory: The anti-pyretic activity of a standardized metha- nol/water (50/50) extract of <i>Orthosiphon stamineus</i> Benth	Yam <i>et al.</i> (2009)
Antidiabetics: Potent α -glucosidase and α -amylase inhibitory activities of standardized 50% ethanolic extracts and sinensetin from <i>Orthosiphon stamineus</i> Benth	Mohamed <i>et al.</i> (2012)

Table 8: Pharmaceutical properties of *P. niruri*

Pharmaceutical properties	References
Antidengue activity: <i>Phyllanthus niruri</i> -mediated synthesis of silver nanoparticles and their mosquitocidal properties against the dengue vector <i>Aedes aegypti</i> (Diptera: Culicidae)	Suresh <i>et al.</i> (2015)
Effects of cocktail of four local Malaysian medicinal plants (<i>Phyllanthus</i> spp.) against dengue virus 2	Lee <i>et al.</i> (2013a)
Anticancer activity: Inhibition of Raf-MEK-ERK and Hypoxia pathways by <i>Phyllanthus</i> prevents metastasis in human lung (A549) cancer cell line	Lee <i>et al.</i> (2013b)
Hepatoprotective activity: The hepatoprotective activity of <i>Phyllanthus niruri</i> (PN) was evaluated against liver cirrhosis induced by thioacetamide (TAA) in male Sprague Dawley rats	Amin <i>et al.</i> (2013)

Table 9: Pharmaceutical properties of *P. betle*

Pharmaceutical properties	References
Antioxidation: Treatment of MCF-7 cells with the plant extract increased activities of catalase and superoxide dismutase	Abraham <i>et al.</i> (2012)
Effect of <i>Piper betle</i> (PB) leaves extract in Nrf2 signaling pathway by using 2 types of cells; mouse embryonic fibroblasts (MEFs) derived from wild-type (WT) and Nrf2 knockout (N0) mice	Wan Hasan <i>et al.</i> (2014)
Antifungal activity: The use of leaf extract against 124 strains of selected fungi	Ali <i>et al.</i> (2010)
Antistress activity: Herbal formulation LI10903F containing <i>Dolichos biflorus</i> and <i>Piper betle</i> extracts on weight management	Sengupta <i>et al.</i> (2012)

oleanolic acid, polyphenols, terpenoids and inositol. Among these various bioactive compound present in *O. stamineus*, phenolic compounds is the most important (Abdelwahab *et al.*, 2011). Twenty phenolic compounds have been isolated from this medicinal plants, including 9 lipophilic flavones, 2 flavonol glycosides and 9 caffeic acid deriavaties (Chew *et al.*, 2011). Other studies indicated that a wide range of flavonoids were detected in various tissues of *O. stamineus* such as rosmarinic acid, quercetin, eupatorin and sinensetin (Almatar *et al.*, 2014).

***Phyllanthus niruri* (Linn.):** *Phyllanthus* (Fig. 1h) species locally known as dukung anak. It has been traditionally used for treating kidney and gallbladder stones (Giribabu *et al.*, 2014), dysentery, influenza, vaginitis, tumours, diabetes, jaundice, liver related diseases and viral infection (Njoroge *et al.*, 2012) and it have been confirmed by a number of biochemical, pharmacological and clinical studies (Venugopalan and Geetha, 2010). These plants also known to have diverse biological activities (Table 8) such as hypoglycemic, anticarcinogenic, hypolipidemic, hepatoprotective, antiplasmodial hypotensis, diuretic, antioxidative (Abdulla *et al.*, 2010b) and anti-inflammatory (Amin *et al.*, 2012; Giribabu *et al.*, 2014). *Phyllanthus* plant has considered as newly discovered of natural product as it has antioxidant sources which is useful for human consumption. Among three species *Phyllanthus niruri*, *Phyllanthus urinaria* and *Phyllanthus amarus*, *P. niruri* shows highest antioxidant activity (Poh-Hwa *et al.*, 2011). More than 50 compound of active phytochemicals (Boim *et al.*, 2010) such as flavoids, alkaloids, terpenoids, lignin, coumarin and saponins have been indentified from various part of *P. niruri* and extract of this plant have been proven to have therapeutic value (Bagalkotkar *et al.*, 2006). Other studies indicate that the

protective role of *P. niruri* against nimesulide-induced hepatic damage is probably because it has antioxidant property (Chatterjee and Sil, 2006). Experiment in animal models and human have shown the plant extract to possess inhibitory activity against hepatitis B-virus (Manjrekar *et al.*, 2008) and it also demonstrate that oral administration of *P. niruri* extract could significantly protect the gastric mucosa from ulcer induction (Abdulla *et al.*, 2010a, b).

Piper betle: *Piper betle* (Fig. 1i) is a tropical plant from family Piperaceae closely related to the common pepper. It is extensively grown in Sri Lanka, India, Malaysia, Thailand, Taiwan and other Southeast Asian countries. It is locally known as Sirih in Malaysia (Pradhan *et al.*, 2013) . It believed that chewing betel quid could reduce stress, strengthen teeth and maintain oral hygiene, it have been practised by old villagers for centuries chewed with slice of betel nut and lime (Haider *et al.*, 2013; Sazwi *et al.*, 2013). The leaves of sirih are used for treating cough, foul smelling in mouth, ozoena, bronchitis, clear throat, vulnery and styptic. Several researchers have reported that this plant has potential (Table 9) as antioxidant, antiplague, antidiabetic, anti-inflammatory, antiulcer, antiplatelet aggregation, antifertility, cardiotionic, respiratory depressant, antihelminthic, cytoprotective, anti-hyperglycemic, antidermatophytic, antinceptive, radioprotective, antimicrobial, antiproliferative (Abraham *et al.*, 2012; Datta *et al.*, 2011; Sripradha, 2014). Bioactive compound major in *P. betle* are polyphenols, alkaloids, steroids, saponins and tannins (Chakraborty and Shah, 2011).

Uncaria gambir: *Uncaria gambir* (Fig. 1j) belongs to family Rubiaceae is a native plant Southeast Asia region particularly in Malaysia and Indonesia. The plant is mainly used for the

treatment of wound, ulcers, asthma, headaches, gastrointestinal illness, bacterial/fungal infections, spongy gums, tooth aches, cancer, cirrhosis, fevers, gastritis, diabetes, rheumatism, dysentery and inflammation of urinary tract (Andre *et al.*, 2013). Usually leaves and young twigs are extracted to produce gambir. The activity of gambir as antioxidant has been studied with some type of mechanism and notable importance as that the antioxidant in gambir is safe. Some studies reported that this plant contains tannins namely, catechutannic acid, acacia catechin, catechu red, catechin, epicatechin and flavonoids (Isnawati *et al.*, 2012). About 76% of gambir is catechin. polyphenol compound with flavonoid structure (Andasuryani *et al.*, 2013). Phytochemical study showed that the major antioxidant compound contained in this plant are flavoids and pharmacological studies showed that gambir extract demonstrated some activities in preventing some damage that cause by free radical-mediated process (Ningsih *et al.*, 2014). Previous study indicated that catechin was identified as the major bioactive compound in gambir (Angraini *et al.*, 2011) and is the main compound determinants of gambir quality (Kassim *et al.*, 2011; Taniguchi *et al.*, 2007).

CONCLUSION

In conclusion, a lot of herbal plant has given emphasis by the government because of it values and origin in Malaysia. Recently, *Ficus deltoidea* have been identified to meet the requirements of the market. By comparing with others medicinal plant, *F. deltoidea* shows a lot of beneficial values and to further study need to be done for public health purpose.

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