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Review of Pharmacognostic Features, Phytochemical Constituents and Pharmacological Actions of *Melastoma malabathricum* LINN (Melastomaceae)

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ABSTRACT

Melastoma malabathricum is a medicinal plant found in tropical and temperate Southeast Asian countries. It has been used for a long period in traditional medicine. Moreover, various scientific investigations reported have shown that that the plant is effective against various diseases due its phytochemical constituents. This study aimed to review the studies carried on *Melastoma malabathricum* in order to have comprehensive information on its phytochemical constituents and pharmacological action (therapeutic uses). The data were searched from electronic data bases and some printed materials. The key word used for searching information is *Melastoma malabathricum*. The electronic sources of data include; highwire, googlescholar, sciencedirect and pub med. The review revealed that *Melastoma malabathricum* has potent therapeutic activities such as antidiabetic, antihyperlipidemic, antibacterial, antifungal, antiparasitic, antiviral, antiulcer and antidiarrheal activity. It was also reported to have antioxidant as well as hepatoprotective activity. *Melastoma malabathricum* contains different classes of secondary metabolites such as triterpenoid, alkaloids, amide, flavonoids anthocyanins, hydrolysable tannins and steroidal tannins. Other phytochemical constituents such as alpha –amyrin, patriscabratine, auranamide, quercetin, quercitrin, kaempferol-3-O-(2" , 6" -di-O-p-trans-coumaroyl)-beta-glucoside, rutin, *malabathrin* B, C, and D. 1,2,4,6- tetra-O-galloyl-β-D-glucoside, pterocarinin C, pasuarictin, pedunculagin, 1,4,6-tri-O-galloyl-β-D-glucoside, strictinin, nobotanins B, G, H and J were isolated from *M. malabathricum*

Keywords: *Melastoma malabathricum*, phytochemical, Constituents, Therapeutic Activity

INTRODUCTION

Melastoma malabathricum Linn belonging to the family *Melastomaceae*, is an inhabitant of tropical and temperate Southeast Asian countries and is called Senduduk in Malay (Malaysia), kendudu in Riau (Indonesia) and Ye mu dan by the Chinese. It has three different varieties; dark purple-magenta petal flower, light pink-magenta petals and other rare variety with white petals (Joffry *et al*., 2012). It is a medicinal plant with a height of 12-13 ft., but sometimes it grows higher up to 20 ft. (Burkill, 1966). The berry-like fruits of *Melastoma malabathricum* Linn are rich in anthocyanins (Che Omar *et al*., 2013). *Melastoma malabathricum* is used in Malaysia, India and China as herbal medicine for the treatment of various diseases such as wound, dysentery, hemorrhoids, diarrhoea, leucorrhoea and cut. It is also used for infection during confinement and to prevent scarring of smallpox and piles (Ong & Norzalina 1999, Begum & Nath 2000).

This study is aimed to review the available studies carried out on *Melastoma malabathricum* in order to have comprehensive information on its phytochemical constituents and pharmacological actions (therapeutic uses).

Distribution

M. malabathricum Linn belongs to the family Melastomataceae and it is commonly found in tropical and temperate Southeast Asian countries. The plant spreads from Madagascar and India to Australia. It is very common throughout Malaysia. Other common names are "Straits Rhododendron" in Singapore, "Mang Kre" in Thailand and "Ye mu dan" in Chinese speaking region. It has three different varieties; with different colour of petals; dark purple-magenta , light pink-magenta and the third being the rare variety with white petals (Susanti *et al*., 2007; Rajenderan, 2010; Joffry *et al*., 2012).

Taxonomy

The taxonomic hierarchy of *M. malabathricum* is presented in Table 1.1 (Rajenderan, 2010).

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Table 1.1: Taxonomic hierarchy of *M. malabathricum* L. (Rajenderan, 2010).

Kingdom	**Plantae–Plants**
Subkingdom	Tracheobionta–Vascular plants
Superdivision	Spermatophyta–Seed plants
Division	Magnoliophyta–Flowering plants
Class	Magnoliopsida–Dicotyledons
Subclass	Rosidae
Order	Myrtales
Family	Melastomataceae-Melastome family
Genus	*Melastoma* L.
Species	*Melastoma malabathricum* L.

Morphology of *M. malabathricum*

M. malabathricum is an evergreen tree and it flowers throughout the year. It is commonly 4 m in height, but sometimes, it grows higher up to 6 m. Characteristics of this species are leaves 0.25–2 inch wide, with stalks 0.25–0.5 inch long, flowers 1–3 inch wide, calyx closely set with short chaffy and silky or silvery scale (Burkill, 1966; Susanti *et al*., 2007). The *M. malabathricum* Linn has berries-like fruits (Che Omar *et al*., 2013). Figure 1.0 shows the pictures of a leaf. The flower has dark purple-magenta petals and yellow pistil. The fruits of the plant are purple in colour and oval in shape and when burst reveal sticky dark purple mass with orange seeds. Stem is reddish brown in colour. These findings are similar to the finding of Joffry *et al*. (2012). The colours of dried powdered leaf and fruit are pale green and red respectively whereas the colour of powdered dried stem and flower are brown and purple respectively. The picture of flower and seed of *M. malabathricum* is shown in Figure 2.0, whereas the pictures of a close ups of the plant is shown in Figure 3.0.

Figure 1.0 : Leaf of *M. malabathricum*

Figure 2.0: Flower and fruit of *M. malabathricum*

Figure 3.0: *M. malabathricum* plant

Traditional Use of *M. malabathricum*

M. malabathricum is used in Malaysia, India and China as herbal medicine. The different parts of the plant have been used for the treatment of various ailments. The decoction of leaves and shoots have antiemetic and antispasmodic actions (Sulaiman *et al*., 2004). The crude extracts of the leaves and roots have been used to relieve toothache and are also used externally against different types of inflamed wounds (Sulaiman *et al*., 2004). Susanti *et al*. (2007) reported that *M. malabathricum* plant has been used in traditional Malay medicine as astringent and in post-partum treatment. Furthermore, the white flower variety is considered more valuable due to its miraculous healing properties.

Therapeutic Activity of *M. malabathricum*

Several scientific investigations have been carried out on *M. malabathricum* and it was found out that, the different parts of *M. malabathricum* such as leaves, flowers, roots, stem and fruit pulp have various therapeutic activities (Joffry *et al*., 2012), and are discussed in the following sections.

Antioxidant, Hepatoprotective, Antidiabetic and Antihyperlipidemic Activity of *M. malabathricum*

Several studies have reported that, *M. malabathricum* have potent antioxidant, hepatoprotective, antidiabetic as well as

antihyperlipidemic activities (Alnajar *et al*., 2012, Kumar *et al*., 2013, Nishanthini *et al*., 2013). The details of these activities are provided below;

Antioxidant Activity of *M. malabathricum*

Melastoma malabathricum was reported to have potent antioxidant activity in both *in vitro* and *in vivo* methods (Alnajar *et al*., 2012; Mamat *et al*., 2013). The methanol extract of *M. malabathricum* flower exerted higher free radical scavenging activity than ethyl acetate extract. The higher antioxidant activity in methanol extract is associated with the presence of kaemferol-3-0-(2",6"-di-0-p-trans-coumaroyl) glucoside which was found to have higher antioxidant activity than the other compounds present in the extract. The antioxidant activity of this glucoside is believed to be due to the presence of poly-hydroxyl group which stabilizes DPPH free radicals by donating hydrogen atoms (Susanti *et al*., 2007; Sirat *et al*., 2010).

Quercetin and quercitrin isolated from the leaves of *M. malabathricum* exhibited antioxidant activities higher than vitamin E via the method of ferric thiocyanate. The isolated compounds inhibited the production of peroxides which are toxic to the cells. The quercetin demonstrated the highest DPPH free radical scavenging activity in comparison with other isolated compounds as well as the two standard compounds of vitamin C and E (Susanti *et al.*, 2008). Another antioxidant study of methanol, chloroform and aqueous extracts of *M. malabathricum* using DPPH free radical scavenging activity and superoxide scavenging activity showed that all extracts have potent antioxidant activity and this effect is suggested to be one of the possible mechanisms for the antiproliferative activity of *M. malabathricum* (Zakaria *et al*., 2011; Mamat *et al*., 2013). The aqueous extract of *M. malabathricum* showed better activity than the ethanol extract toward DPPH radicals and ferric reducing antioxidant power. However, the reverse was the case for the ethanol extract which exhibited better ABTS free radicals scavenging activity than the aqueous extract (Alnajar *et al*., 2012). The higher antioxidant activity of methanol extract of *M. malabathricum* is suggested to play a vital role in hepatoprotective and antidiabetic activity (Kumar *et al*., 2013; Mamat *et al*., 2013).

Hepatoprotective Activity of *M. malabathricum*

Some drugs and chemicals such as the high doses of paracetamol and carbon tetrachloride (CCl_4) are associated with the hepatotoxic property that may cause severe hepatic damage and impaired hepatic activity (Olaleye & Rocha, 2008). It has been scientifically demonstrated that *M. malabathricum* has the ability to combat hepatic toxicities by increasing the level of hepatic antioxidants which in turn prevents the peroxidation of toxic free radicals (Nishanthini *et al*., 2013).

Hyperglycemia is one of the predisposing factors for hepatotoxicity. Hyperglycaemia is a metabolic disorder associated with increase in the blood glucose level above the normal range. This condition causes increased lipid production which will leads to decreased production of antioxidant enzymes (superoxide dismutase, catalase and glutathione peroxidase) and increased production of free radical peroxide which ultimately leads to lipid peroxidation of cell membranes (Nishanthini *et al*., 2013). Methanol extract of *M. malabathricum* prevents the oxidative damages of free radical in streptozocin induced diabetic rats by increasing the level of the above antioxidant enzymes. It was reported that the ethanol extract of *M. malabathricum* leaf increases the level of liver antioxidant and decreases the level of free radicals in CCl_4 induced hepatotoxic rats (Nishanthini *et al*., 2013). Moreover, the methanol extract of *M. malabathricum* leaf has been reported to have hepatoprotective effect against paracetamol and CCl_4 induced hepatotoxicity (Kamisan *et al*., 2013). Histological finding indicated that there were no signs of toxicity in hepatic cells after treatment with extract and this was comparable with hepatic cells of control group. Liver antioxidant plays a vital role in the hepatoprotective activity (Kamisan *et al*., 2013; Mamat *et al*., 2013). Therefore, it can be concluded that *M. malabathricum* exerted hepatoprotective protection by increasing the activity of liver enzymes which in turn inhibits the cell damage by free radicals.

Antidiabetic and Antihyperlipidemic Activity of *M. malabathricum*

Both diabetic and hyperlipidemic conditions are metabolic disorders. *M. malabathricum* has been used in traditional medicine for the treatment of these disorders (Joffry *et al*., 2012). Both *in vitro* and *in vivo* methods were used for the determination of antidiabetic and antihyperlipidemic activities. Methanol extract of *M. malabathricum* demonstrated significant reduction in blood sugar level in both pre and post glucose loading and also increases plasma insulin level in streptozocin induced diabetic rat. It was suggested that the plant exerted its action in a similar mode to that of glibenclamide (Kumar *et al*., 2013). Furthermore, the extract decreases the level of elevated blood cholesterol and triglyceride to almost normal level (Kumar *et al*., 2013). Similarly, it was also reported that ethanol extract of the leaves of *M. malabathricum* significantly decreased blood glucose level, lipid profile and some elevated biochemical parameters in alloxan-induced diabetic rat (Balamurugan *et al*., 2014). According to the finding of Ado *et al*. (2013), the

methanol extract of leaves and fruits of *M. malabathricum* inhibited the porcine pancreatic lipase. The inhibitory effects provided by the leaves and fruits were 96.9% and 87.6% respectively. Additionally, the inhibitory effects of these extracts helped in slowing down the digestion of triacylglycerols (TAGs) which in turn prevents the risk of obesity, which itself is one of the risk factors of cardiovascular diseases.

Antimicrobial Activity of *M. malabathricum*

Drug resistance to antibiotics is one of the major challenges in the health care delivery system. Drug resistance affects the health outcome, and it increases the duration and cost of treatment. In traditional medicine, it is believed that herbs play a vital role in the treatment of infections and consequent to this, *M. malabathricum* is used in Malaysia in the treatment of infection and wound (Ong & Norzalina, 1999). This usage is also supported by scientific studies, which have shown that *M. malabathricum* is effective against various microorganisms (Alwash *et al*., 2014).

Antibacterial Activity of *M. malabathricum*

M. malabathricum demonstrated positive activities against various bacterial isolates. The methanol extract of flower and fruit showed positive antibacterial activity against *Listeria monocytogenes* and *Staphylococcus aureus*. However both extracts showed negative effect against *Escherichia coli* and *Salmonella typhimurium* (Che Omar *et al*., 2013). On the contrary, Alnajar et al. (2012) observed a different result on *E. coli* were observed by Alnajar and co-workers (Alnajar *et al*., 2012). They found out there was positive effect against *E. coli* as well as other organisms. The three other organisms are *S. aureus, S. agalactiea* and *Klebsilla pneumonia.* Additionally, the highest antibacterial effect was found to be against gram positive bacteria. Ursolic acid, 2α-hydroxyursolic acid, asiatic acid, β-sitosterol 3-O-β-D-glucopyranoside, kaempferol and quercetin isolated from *M. malabathricum* were found to have antimicrobial activity against *S. aureus* reference strain, M-r *S. aureus* reference strain (MRSA), 11 clinical MRSA isolates, 3 clinical *P. aeruginosa* isolates and *P. aeruginosa* ref. strain (Alwash *et al*., 2013b; Wong *et al*., 2012). Furthermore, methanol extract of *M. malabathricum* was found to have antibacterial activity against Gram-positive and Gram-negative bacteria with largest zones of inhibition diameter against MRSA, *P. aeruginosa, V. parahaemolyticus and S. aureus* (Alwash *et al*., 2014). Similarly, *M. malabathricum* inhibited the growth of different clinical wound isolates of *S. aureus and P. aeruginosa* (Sunilson *et al*., 2008). A study carried out by Choudhury *et al*. (2011), showed that methanol and acetone extracts of *M. malabathricum* leaf exhibited remarkable zone of inhibition against *Staphylococcus aureus, Streptococcus sp. and E. coli*. However, the aqueous extract of the bark and leaves were found to inhibit the growth of *B. brevis* and *V. cholorae.* While the bark extract was found to inhibit the growth of *S. aureus* and leaves extract inhibited the growth of and *B. subtilis* (Thatoi *et al*., 2008). Similarly, the methanol leaf extract of *M. malabathricum* was reported to have higher antibacterial activity against *S. aureus* (MRSA) compared to *S. aureus* (MSSA) and the effect is dose dependent (Chuah *et al*., 2014).

However, the aqueous leaves extract of the plant did not display any significant (p>0.05) antibacterial activity against *Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa and Staphylococcus aureus* (Diris *et al*., 2017). This may be attributed to the differences in the chemical compositions of aqueous and methanol extracts.

Antifungal Activity of *M. malabathricum*

The fungi especially *Candida albican* is one of the major causes of female genital infections. The indiscriminant use of antibiotics in the treatment of the infection has lead to the development of resistance towards antifungal drugs. A study has shown that ethanol extract of the root of *M. malabathricum* exhibited positive effect against *Candida albican* (Napisah *et al*., 2011). However, in the study carried out by Cavin *et al*., (1999), methanolic extract of the leaf of *M. malabathricum* did not inhibit either *C. albican* or *Cladosporium cucumerinum;* another plant fungi. The reasons for the difference could be the type of extract or the source of the plant, one of which was Malaysian whereas the other was Indonesian. In addition to these extracts the antifungal activity was also shown by aqueous leaf extract which inhibited the growth of *C. krusei* (Thatoi *et al*., 2008). These findings have shown that *M. malabathricum* can be a source of antifungal drug and may serve as a better alternative medicine.

Antiparasitic Activity of *M. malabathricum*

Several studies have shown that *M. malabathricum* has various antiparasitic activities as follows;

The aqueous, ethanol and chloroform extracts of the leaves of *M. malabathricum* significantly inhibited the hatching of *Haemonchus contortus* egg *in vitro.* All extracts demonstrated *larvicidal* activity in a dose dependent manner. The aqueous extract exhibited complete inhibition of motility on an adult worm after an 8hrs of treatment. The crude aqueous extract of *M. malabathricum* was found to cause immotility of about 62.25% within 2 h after exposure as well as complete inhibition of the motility of adult worms after an 8 h exposure. The higher doses of the extracts may cause inhibition of motility earlier (Suteky & Dwatmadji, 2011). On

the other hand, the study carried out by Basripuzi *et al*. (2013), was found to be contrary to the above finding as it reported that, *M. malabathricum* is ineffective or failed to eliminate *H. contortus* at the concentration used. Moreover, it demonstrated negative fecal egg count reduction test (FECRT) and mean fecal egg count (FEC) pattern (Basripuzi *et al*., 2013). The variations between these two findings may be as a result of variation in experimental conditions therefore similar conditions should be followed in order to confirm the finding of Suteky & Dwatmadj (2011). Thus, the anthelmintic activity of *Melastoma malabathricum* cannot be confirmed because of the insufficient data. Therefore, there is need to carry out more scientific investigations using different extracts on different worms at different stage of development in both *in vitro* and *in vivo* studies.

Antiviral Activity of *M. malabathricum*

A study shows that, the methanol extract of leaves of *M. malabathricum* demonstrated antiviral activity at the early stage replication of herpes simplex virus type 1 (HSV-1) and measles viruses. This activity is associated with the presence of several chemical compounds in the plant. Although, the extract protected the cell when inoculated simultaneously, but it failed to exert prophylactic action against these viruses (Nazlina *et al*., 2008). Similarly, the methanol extract of the aerial part has demonstrated antiviral effect against HSV-1 virus (Lohézic-Le *et al*., 2002). This shows that, *M. malabathricum* contains a potent antiviral agent that can be used as an alternative for the treatment of viral infections.

Antiulcer Activity of *M. malabathricum*

The aqueous leaf extract of *M. malabathricum* has been reported to have significant protection against ethanol-induced gastric ulcers in the rats (Hussain *et al*., 2008; Zainulddin *et al*., 2016). Similarly, methanol extract demonstrated significant antiulcer activity in the ethanol induced gastric ulcer (Halim *et al*., 2017; Zabidi *et al*., 2012). However, it failed to show positive effect against indomethacin-induced gastric ulcer, and even aggravated the ulceretic effect of indomethacin (Zabidi *et al*., 2012; Zainulddin *et al*., 2016). In contrast, the finding of Balamurugan *et al*. (2013c), showed that the ethanol extract possessed significant antiulcer activity in both ethanol and indomethacin induced ulcer in a dose dependent manner. Nevertheless, the gastric mucosal protection is higher in ethanol than indomethacin induced ulcer. A mixture of the chloroform extracts of *M. malabathricum* and *Muntingia calabura* have also been demonstrated to possess gastroprotective effect (Zakaria *et al*., 2016).

Therefore, it can be seen from these findings that aqueous, methanol and ethanol extracts possessed prophylactic effect against gastric ulcer and the beneficial effects were due to the compounds in the extracts and their antioxidant, wound healing and anti-inflammatory nature.

Antidiarrheal Activity of *M. malabathricum*

M. malabathricum has positive antidiarrheal activities as reported by various findings. It has been reported that both aqueous and ethanol extracts exhibited positive effects on various parameters used to measure the antidiarrheal activity (Sunilson *et al*., 2009; Balamurugan *et al*., 2013b). The extracts significantly decreased the faecal output in castor oil induced diarrhoea in laboratory animals and decreased intestinal secretions induced by magnesium sulphate. In fact, it was mentioned that the antidiarrheal activity of *M. malabathricum* was comparable to loperamide, which is the standard antidiarrheal agent (Sunilson *et al*., 2009; Balamurugan *et al*., 2013b).

Stimulatory Effect of *M. malabathricum* on the Reproductive System

The ethanol extract of *M. malabathricum* was found to increase the weight of reproductive organ in male albino rats. Additionally, there was a significant increase in total sperm count and viability of sperms. Moreover, there is an increase in the number of female's impregnation, increase in the number of implantations and increase in the number of viable fetuses. The overall result gives an indication that *M. malabathricum* has a positive effect on both the male and female reproductive organs which in turn increases fertility (Balamurugan *et al*., 2013d).

Effect of *M. malabathricum* on Blood and Blood Components

M. malabathricum was found to have various effects on blood and blood components. The effects are as follows:

a) Immunomodulatory Activity of *M. malabathricum*

M. malabathricum has the ability to increase the proliferation of white blood cells. It has been reported that both ethanol and aqueous extracts increased the viability of human peripheral blood mononuclear cell (Alnajar *et al*., 2012). The ability of this plant extracts to increase the white blood cells is important because it can be used to improve the immune system in an immune compromised patient. However, there is a need to carry out more investigations because there is likelihood that it can used as an adjunct in the treatment of various diseases associated with low immune system such as AIDS.

b) Anticoagulant Activity of *M. malabathricum*

M. malabathricum has been reported to have potent anticoagulant activity. According to the finding of some researchers (Manicam *et al*., 2010) the aqueous extract of *M. malabathricum* leaf causes deficiency of clotting factors which, in turn affects the intrinsic pathway of the coagulation cascade.

Moreover, the hexuronic acids, polysaccharides, and polyphenolics fractions of *M. malabathricum* were found to prolong the blood clotting intrinsic pathway (Khoo *et al*., 2014).

c) *M. malabathricum* Effect on Platelet Count

The methanol extract of *M. malabathricum* leaf increases the thrombocyte count in mice. Therefore, the extract may be used for the treatment of thrombocytopenia (Karupiah & Ismail, 2014).

Antinociceptive, Antipyretic, Anti-Inflammatory and Wound Healing Activity of *M. malabathricum*

The ethanol extract of *M. malabathricum* leaf demonstrated antinociceptive activity at both peripheral and central nervous system in laboratory animal (Sulaiman *et al*., 2004). The antinociceptive effect of the methanol extract of the leaves of the plant via non-opioid mechanism has also been reported (Jaios *et al*., 2016). The chloroform extract also possessed antipyretic activity (Zakaria *et al*., 2006a; Zakaria *et al*., 2006b). The antinociceptive effect was later reported in chloroform and aqueous extracts and furthermore, the chloroform extract was reported to posses antipyretic effect (Zakaria *et al*., 2006a; Zakaria *et al*., 2006b; Balamurugan *et al*., 2012). In addition, all the three extracts demonstrated strong anti-inflammatory effect, and Susanti *et al*., (2008) has attributed the anti-inflammatory effect of *M. malabathricum* to the flavonoids compounds it contains. It is clear that tissue inflammation delays wound healing and agents that have anti-inflammatory activity would help in wound healing. A study on the effect of the methanol extracts of the plant on arthritis showed that the extract prevented the development of Complete Freund's Adjuvant-induced arthritis in rats in a dose dependent manner (Kumar *et al*., 2016).

Additionally, it has been reported that *M. malabathricum* is used in traditional medicine in the treatment of wound (Joffry *et al*., 2012). Various studies have been carried out on wound healing property of *M. malabathricum*, where it proved to be effective. The methanol extract of *M. malabathricum* used topically as an ointment provided positive and significant wound healing property in both excision and incision wound in the rat. Furthermore, it regenerated original tissue in a wound more than the both the negative and positive control (Sunilson *et al*., 2008). It was also reported that application of aqueous extract to the wound surface for about five days provides significant improvement of the wound contraction in treated group. However, the scar showed no form of lesion with less inflammation after 15 days of the application of aqueous extract to the wound surface (Nurdiana & Marziana, 2013). These studies have shown that *M. malabathricum* has a good wound healing property and both aqueous and ethanol extract of the *M. malabathricum* contained compounds that improve wound healing which can be related to its antibacterial and anti-inflammatory activity. It is suggested that kaempferol-3-O-(2" , 6" -di-O-p-trans-coumaroyl)-beta-glucoside may be responsible for wound healing property of *M. malabathricum* (Susanti *et al*., 2008; Alwash *et al*., 2013a).

Cytotoxic and Antiproliferation (Anticancer) of *M. malabathricum*

Cytotoxicity study is carried out to determine the toxic effect of substance or compound on a particular cell. Moreover, cytotoxicity is carried out to determine and establish cellular toxicity of a substance and to assess the ability of a compound to inhibit the growth and proliferation of cancerous cells. Several studies have shown that *M. malabathricum* is an active cytotoxic and antiproliferative medicinal plant. According to study carried out by Susanti *et al.* (2007), ethyl acetate extract of *M. malabathricum* and two compounds isolated from the flower of *M. malabathricum*; naringerin and kaemferol-3-0-(2",6"-di-0-p-trans-coumaroyl) glucoside demonstrated changes in the structure of MCF-7 cancer cells. The two isolated compounds exerted anticancer activity against MCF-7 by inhibiting the multiplication and growth of MCF-7 with kaemferol-3-0-(2",6"-di-0-p-trans-coumaroyl) glucoside having the highest anticancer activity (Susanti *et al*., 2007). It has been reported that methanol extract inhibited the proliferation of MCF-7, Hela, Caov-3, HL-60, CEM-SS, MDA-MB-231 cancer cell lines, whereas chloroform extract inhibited the proliferation of Caov-3, HL-60 and CEM-SS cell lines. The number of cell lines inhibited by the aqueous extract was even lesser with only Caov-3 and HL-60 being affected. Another important point was that all three extracts failed to inhibit the growth of 3T3 cells (normal cells) (Zakaria *et al*., 2011). In contrast, methanol extract of *M. malabathricum* demonstrated no cytotoxic effect against Vero and L929 cells (Nazlina *et al*., 2008; Alwash *et al*., 2014). It can be proposed that *M. malabathricum* exhibited anticancer activity via several mechanisms, which include antioxidant activity via scavenging of free radicals and inhibiting the lipid peroxidation of free radical such as peroxide (Nishanthini *et al*., 2013).

Verma *et al.* (2016) studied the effect of *M. malabathricum* extract on diethylnitrosamine (DEN) and ferric nitrilotriacetate (Fe-NTA)-induced renal carcinogenesis, renal hyperproliferation, and oxidative stress in rats. The extract demonstrated potent chemoproctective effect by suppressing renal tumour incidence, which was confirmed by the macroscopic and histopathological observation.

Toxicity Studies of *M. malabathricum*

Both acute and sub-acute toxicity studies of *M. malabathricum* have been carried out. The different doses of methanol leaves extracts were found to be safe, and it demonstrated no toxic reactions up to the end of the study. This showed that *M. malabathricum* is safe in acute toxicity study (Kumar *et al*., 2013). Moreover, the ethanol extract of leaves showed that LD_{50} is 2000 mg/kg (Balamurugan *et al*., 2012). From these finding, we can see that it has a wide therapeutic index which confirmed its safety. Zahi *et al*. (2017) also reported the safety of ethanol extract of the plant on skin as well its safety on liver, spleen and kidneys.

Despite, the safety of *M. malabathricum* extracts in acute toxicity studies, sub-acute studies showed effects on liver enzymes. It was found out that the aqueous extract of the leaves given to laboratory animal orally for 28 days increased the liver enzymes (alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase). Additionally, histopathological findings showed that, there are toxic changes in both liver and kidney. However, there were no treatment-related mortality or morbidity up to the end of the study (Manicam *et al*., 2013).

Stability of Anthocyanins of *M. malabathricum*

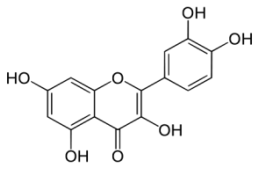
The *M. malabathricum* was found to have highest color density at pH 2.5 and 3.0 compared to pH greater than 3.5. The anthocyanins of *M. malabathricum* were susceptible to degradation at higher pH than 3.5 and its degradation index was found to increase up to 78% at pH than 3.5. In general the stability of anthocyanins in *M. malabathricum* extract was not significantly affected by the pH range between 2.0 to 4.5 (Aishah *et al*., 2013).

Phytochemical Studies

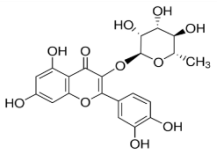
Preliminary phytochemical screening of methanol extract of *M. malabathricum* leaf revealed the presence of flavonoids, phenolic compounds, tannins, triterpenes and steroids, whereas saponins and glycoside were absent (Zakaria *et al*., 2011; Kumar *et al*., 2013). However, the ethanol extract of *M. malabathricum* leaf was found to contain saponins, glycoside and carbohydrate (Sheela *et al*., 2012; Nishanthini *et al*., 2013; Balamurugan *et al*., 2013c). The aerial part of *M. malabathricum* was reported to contain tannins whereas steroid was absent (Lohézic-Le Dévéhat *et al*., 2002). Additionally *M. malabathricum* contained high total phenolic content (Khoo *et al*., 2014; Mamat *et al*., 2013) and flavonoid content (Mamat *et al*., 2013).

Chemical Compounds Isolated from Different Parts of *Melastoma malabathricum*

Various chemical constituents were isolated from different parts of *M. malabathricum* as shown in Table 2.2 and the structures of certain compounds are shown in Figure 2.1



quercetin



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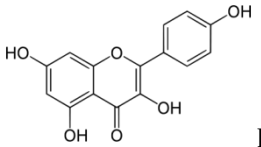
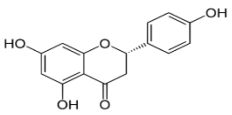
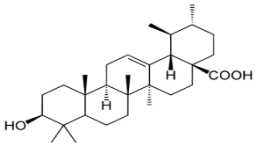


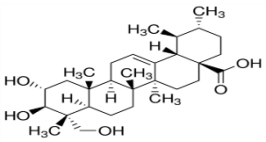
kaemferol



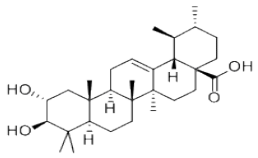
Naringerin



Ursolic acid



Asiatic acid



2α-hydroxyursolic acid

Figure 2.1: Chemical structures of some compounds isolated from *M. malabathricum*

Table 2.2: Phytochemical constituents isolated from *Melastoma malabathricum*

Plant parts	Secondary Metabolites	Phyto-constituents	Author
Leaves	Triterpenoid,	Alpha –amyrin.	Susanti *et al*., (2008), Sirat *et al*., (2010), Nazlina *et al*., (2008)
	Alkaloids	Patriscabratine.	
	Amide	Auranamide.	
	Flavonoids	Quercetin.	
	Flavonoids	Quercitrin.	
	Flavonoids	Kaempferol-3-O-(2" , 6" -di-O-p-trans-coumaroyl)-beta-	
	Flavonoids	Glucoside Rutin.	
Leaves	Hydrolysable tannins	*Malabathrin* B, C, and D. 1,2,4,6- tetra-O-galloyl-β-D-glucoside, pterocarinin C. Pasuarictin, Pedunculagin, Nobotanin D. 1,4,6-tri-O-galloyl-β-D-glucoside, Strictinin nobotanins B, G, H and J.	Yoshida *et al*., (1992).
Fruits	Anthocyanins	Cyanidin dihexoside. Cyanidin hexoside. Delphinidin hexoside.	Anuar *et al*., (2013)
Flower	triterpene acid	Ursolic acid.	Wong *et al*., (2012)
	Triterpene acid	2α-hydroxyursolic acid.	
	Triterpenes	Asiatic acid.	
	Steroidal glycoside	β-sitosterol -3-*O*-β-*D*-*glucopyranoside*.	
	Glycoside	Glycolipid glycerol 1,2-dilinolenyl-3-*O*-β-*D*-galactopyanoside. Ellagic acid.	
	Hydrolysable tannins (ellagitannins)	Kaempferol -3-*O*-α-*L*-rhamnopyranoside. Kaempferol -3-*O*-β-*D*-glucopyranoside.	
	Flavonoids	Kaempferol- 3-*O*-β-*D*-galactopyranoside. Kaempferol 3-*O*-(2″,6″-di-*O*-*E*-*p*-coumaryl)-β-*D*- galactopyranoside. Naringerin Quercetin. Kaempferol. Kaempferol-3-0-D-glucoside. Kaempferol-3-0-(2",6"-di-0-p-trans coumaroyl) glucoside.	Susanti *et al*., (2007), Wong *et al*., (2012).
	Flavonoids Flavanone	Kaempferol.	
	Flavonoids	Kaempferol-3-O-(2",6"-di-O-p-trans-coumaroyl)-β- glucopyranoside.	
	Flavanols		
Leaves	Flavonoid		Alwash *et al*., (2013a) Alwash *et al*., (2013b).

CONCLUSION

It has been demonstrated that different parts of *Melastoma malabathricum* have therapeutic value against various disease conditions which justified the reasons for the use of the plant in herbal traditional medicine. Many of these findings confirmed the claims regarding the traditional use of plant. Antidiarrheal effect of the plant justified the traditional belief of Malaysians and Indians for the use of the plant in the treatment of diarrhoea. The antipyretic and anti-inflammatory effect of this plant may the reason why the plant is used for toothache traditionally. The antibacterial, antifungal and antiviral effect of the plant may be the reasons why it is effective traditionally for treatment of skin diseases and infection during confinement. Moreover this plant was found to be safe according to the various studies. The excellent therapeutic effect of *Melastoma malabathricum* against various pathologic conditions is attributed to its various chemical constituents. Therefore, there is need to use the therapeutic effects of this plant maximally as it provided in this studies. More studies are required to isolate and characterized

each active constituents and to determine their therapeutic effect against more disease conditions like hypertension and renal stone. Since medicinal plant serve as agent for drug development also there is need to carry out long term toxicity study of the plant to know the safety and toxicity associated with this plant when used for long period of time.

CONFLICT OF INTEREST: No conflict of interest

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