

REVIEW ARTICLE

Ethnobotanical, Phytochemical, and Pharmacological Aspects of *Melastoma* sp.

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ABSTRACT

Melastoma is a genus that belongs to the Melastomataceae family and consists of 50–70 species distributed around India, Southeast Asia, Australia and the Pacific Island. Numerous species of this plant show potential therapeutic purposes. This review summarizes the scientific findings on the ethnobotanical uses, phytochemistry and pharmacological activities of *Melastoma* sp. The leaves of *Melastoma* sp. was widely used by Asian as decoction for the remedy of gastrointestinal disorder apart from root, which was consumed as juice for skin diseases, fever and pain. Majority of the scientific studies focused on *M. malabathricum* showing high antimicrobial activity towards selected gram-negative and gram-positive bacteria from different parts of the plant. *In vitro* studies showed that *Melastoma* sp. possessed anti-coagulant, antioxidant, antiproliferative and immunomodulatory activities. Apart from *in vitro*, various *in vivo* studies have been conducted involving methanolic leaf extracts using Sprague Dawley rats for inhibition of anti-ulcer, anti-nociceptive, anti-inflammatory, anti-carcinogenic and anti-diabetic activities. Flavonoids, triterpenes, tannins, saponins and steroids are the main classes of secondary metabolites identified from *Melastoma* sp. Kaempferol derivatives exhibited significant main constituents from the flowers and leaves using various semi polar solvent extracts. Few phytosterols were also isolated from the leaves extract albeit the absence of alkaloids. This review shows that *Melastoma* sp. is an important genus of Melastomataceae family, however, the phytochemical and pharmacological findings of various species in this genus are still limited, indicating a great opportunity to explore new therapeutic activities with novel bioactive constituents.

Keywords: *Melastoma* sp., Melastomataceae, ethnobotanical, phytochemical, pharmacological

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INTRODUCTION

Melastoma sp. belongs to Melastomataceae family with two significant botanical names, namely, *Melastoma candidum* D. Don (magenta in colour) and *Melastoma imbricatum* Wall. Ex triana (white colour) and altogether comprises more than 50 species (1,2). *M. candidum* D. Don is synonymously known as *Melastoma malabathricum* Linn, *Melastoma affine* D. Don, *Melastoma cavaleriei* H. Lev. and Vaniot, *Melastoma esquirolii* H.Lev. or *Melastoma polyanthum* Blume. The local names for *M. candidum* species vary as Senduduk or Keduduk in Malaysia, Senggani in Indonesia, Straits or Singapore Rhododendron in English, Yeh Mu Tan

in China and Malatungaw in Philippines. Two species, namely, *Melastoma magnificum* Bakh.f. and *M. imbricatum* var. laeve Bakh. f., were identified under *M. imbricatum* Wall. Ex triana, whereas the majority of locals recognized this type of *Melastoma* sp. as follows: Senduduk putih, Keduduk putih or Senduduk Ayer in Malaysia; White Rhododendrom in English; and Da Bao Ya Lang, Mo Nim, Nim Fa, Chu Ku Nim or Kai T'au Kwo in Chinese (3). Spanning from the Indo-Malay to the Pacific and India Ocean regions, *M. malabathricum* Linn is the most known species and frequently used for research and ethnobotanical purposes (4). To date, *M. kemamanense* is included to the recent *Melastoma* sp. found in Kemaman, Malaysia (5).

Morphologically, *Melastoma* sp. is a small tree with reddish stem that grows up to 5 m tall and has small scales. The leaves are lance-shape and bristly on the underside with petals coloured in magenta or white. The flowers only last a day. The fruits exhibit irregular shape with many seeds (6). Parts of the plant, such as the fruit, leaves and seeds, are edible and contains medicinal benefits ranging from anticoagulant (7), antioxidant (8),

antibacterial (9), antifungal (10), antiproliferative (11) and immune modulatory activities (12).

This review discloses ethnobotany and exploring scientific evidence (13) on recent phytochemicals, *in vitro* and *in vivo* studies to provide updated information about the properties of *Melastoma* sp., an invasive plant that is traditionally consumed and investigated for its diverse medicinal purposes.

Ethnomedicinal Uses of *Melastoma* sp.

The leaves, roots, bark, stems, fruits and whole parts of *Melastoma* sp. have been used traditionally to treat numerous ailments, such as wounds, diarrhea, skin problems and toothache. Table I summarizes relevant documented ethnomedicinal uses and the tribes and countries where they are being applied. Most ethnomedicinal studies on *Melastoma* sp. focused on one species only, *M. malabathricum* Linn. Ethnomedicinal surveys involving *Melastoma* sp. were conducted for the most part (65%) among the tribal people of India and to a decreased extent in Bangladesh (22%) and other countries such as Philippines, Thailand and Malaysia.

The leaves are the most widely used part of this plant, and the administration route varies depending on the medicinal use. In India, the decoction or juice of *Melastoma* sp. leaves is taken orally as a remedy for diarrhea, dysentery and stomach disorder (14–19), whereas the paste of leaves is applied topically to treat cuts and wounds (18,20,21). In Bangladesh, mouth ulcers are treated by gargling with the leaf juice (22), which is also applied on the skin to treat scabies and abscesses (23).

The roots are the second most frequently used part of *Melastoma* sp. in ethnomedicine. In India, a root preparation is applied topically to treat wounds and skin diseases (24–26) and used as a mouth wash to relieve toothache (15,27). The roots are also used to treat jaundice, small pox and leucorrhea (27). In Bangladesh, root juice is taken orally to treat body pain, diarrhea, dysentery, leucorrhea (23), urinary problem (23,28) and jaundice (29). A root decoction is ingested to treat dysentery and fever in the Philippines (30) and to treat diarrhea in Malaysia (31).

Some surveys have reported the use of *Melastoma* sp. bark by several tribes in India to treat wounds, skin diseases (17,24,25), diarrhea and dysentery (19). In Thailand and India, the fruit has been applied to treat several oral diseases, such as tooth decays, gum diseases, mouth ulcers and geographic tongue (32,33). The Tripura tribe in Bangladesh and the Mizo tribe in India use the whole *Melastoma* sp. plant to treat medical conditions related to the digestive system, such as diarrhea, dysentery (24), vomiting and stomach pain (34).

Extraction Methods

Extraction is necessary to separate and characterise the desired constituents of *Melastoma* sp. plant (37). Improving the analytic extraction and increasing the interaction of the surface of the constituent with the solvent system are necessary (38). Table II shows all the methods, such as the Soxhlet extraction, maceration and ultrasound-assisted extraction, employed for the solvents in the procedures. These techniques are critically influenced by the solvent types (38) (39). The active constituents from various parts and extracts of *Melastoma* sp. have been identified and isolated using chromatographic methods, such as high performance liquid chromatography, liquid chromatography mass spectrometry and thin layer chromatography (40). Table III shows the methods of extraction for *Melastoma* sp.

Phytochemicals from *Melastoma* sp.

Numerous studies have been performed to identify phytochemical constituents in *Melastoma* sp. Table IV summarizes the identified phytochemicals from the herb and their corresponding class of compound/compound name along with the plant part of the herb and types of extract. Phytochemicals such as saponins, flavonoids, triterpenes, flavan-3-ols, anthocyanins, tannins, steroids and phenolics were found to contribute to the numerous pharmacological activities. These pharmacological properties have attracted interest of many researchers to further explore this herb. Furthermore, the plant-derived drugs/medications are increasingly accepted by the public due to the undesirable side effects of chemically synthesized medications. Identifying and isolating various phytochemical groups from *Melastoma* sp. are significantly associated with its ethnomedicinal values (4). Phenolic compounds are the secondary metabolites that can be found ubiquitously in most terrestrial plants. Phenolic acids are easily absorbed by the digestive system and offer numerous anti-aging benefits. Numerous studies have been conducted to identify phenolic compounds with strong antioxidant activity (53). Antioxidants are important protection against various diseases, such as hypersensitivity, diabetes, cardiovascular diseases and cancer (54). Saponins, tannins, flavonoids, triterpenes and steroid were detected in the leaves of *M. malabathricum* L. (Malaysia); however, alkaloids were not found in the respective samples (55). The following year, three compounds were identified from the flower ethyl acetate extract, namely naringenin, kaempferol and kaempferol-3-O-D-glucoside, kaempferol-3-O-(2'',6''-di-O-p-trans-coumaroyl)glucoside and kaempferol-3-O-D-glucoside (methanolic) (8). In 2008, Simanjuntak reported the presence of tannins, saponins, tannins, glycosides, flavonoids and steroid/triterpenoids in the leaves of *Melastoma malabathricum* L. in Sumatra, Indonesia (56). Six compounds, namely, auranamide, patricabratine, α -amyrin, quercitrin, quercetin and

Table 1: Ethnomedicinal practices of *Melastoma* sp.

Botanical name	Vernacular name	Medicinal uses	Plant part used/ Implementation	Tribe/ Country practiced	Refs
<i>Melastoma malabathricum</i>	Kakku phang	Mouth ulcer	Leaves – fresh leaves juice is used for the ulceration of the mouth.	Garo/ Bangladesh	(22)
<i>Melastoma polyanthum</i> B.	Bakhi, batgi	Hypertension, hypercholesterolemia	Stem – cooked with meat and consumed	Kalanguya/ Philippines	(30)
		Dysentery, fever	Roots – decoction		
<i>Melastoma malabathricum</i> L.	Builukham-pa	Wound	Bark, root	Mizo/ India	(24)
		Diarrhoea, dysentery	Whole plant		
<i>Melastoma malabathricum</i> L.	Chumkot	Body ache, breathing difficulty	Leaves	Nicobarese/ Andaman & Nicobar Islands, India	(35)
<i>Melastoma malabathricum</i> L.	Damchui	Dysentery	Leaves – fresh leaves are crushed to get crude juice and taken orally	Chorei/ India	(14)
<i>Melastoma malabathricum</i> L.	Tai-tong	Body pain, diarrhea, dysentery, leucorrhea, urinary problems	Root – juice of root is taken orally	Tripura/ Bangladesh	(23)
		Scabies, abscesses	Leaves – the juice or paste is applied topically		
<i>Melastoma malabathricum</i> L.	Gach putti	Urinary tract infection	Root – the juice obtained from macerated root is taken with yogurt, daily	Tonchongya/ Bangladesh	(28)
<i>Melastoma malabathricum</i> L.	Mogapoti	Vomiting, stomach pain	Whole plant – paste of whole plant is given orally	Tripura/ Bangladesh	(34)
<i>Melastoma malabathricum</i> L.	-	Jaundice, small pox, leucorrhea, toothache	Root, leaves	Kurumba gounder, Sadaya gounder and Ariyan/ India	(27)
<i>Melastoma malabathricum</i> L.	Kechi-Yaying	Dysentery	Fresh leaves	Adi/ India	(15)
		Wound	Leaves		
		Toothache	Roots, leaves – used as mouth wash		
<i>Melastoma malabathricum</i> L.	Yachubi	Skin problems, diarrhea, dysentery and leucorrhea	Leaves, bark	Meitei/ India	(16)
<i>Melastoma malabathricum</i> L.	Senduduk	Diarrhea	Root – decoction is taken orally	Jah Hut/ Malaysia	(31)
<i>Melastoma malabathricum</i> L.	Yachubi	Strengthen teeth, prevent tooth decay and gum disease	Fruit	Maring/ India	(32)
<i>Melastoma malabathricum</i> L.	Karali	Cuts and wounds	Leaves – leaves paste is applied externally	Didayi/ India	(20)
<i>Melastoma malabathricum</i> L.	Koiam-pay-bang	Jaundice	Root – root juice is taken orally	Marma/ Bangladesh	(29)
<i>Melastoma malabathricum</i> L.	Builukham	Wound	Bark	Tribes of Mizoram/ India	(17)
		Diarrhea	Leaves		
		Leucorrhea	Leaves and flower top		
<i>Melastoma malabathricum</i> L.	Mantram chettu	Body swellings	Aerial parts of plant – the powder of aerial parts is taken orally with a cup of water	Kondareddis/ India	(36)
<i>Melastoma malabathricum</i> L.	Longumpu	Cuts, wounds, stomach disorder and fever	Fresh and dry leaves	Naga/ India	(18)
<i>Melastoma malabathricum</i> L.	Chulasi	Wounds and skin disease	Stem, bark and root – the paste is applied externally	Tribes of Darjeeling/ India	(25)
<i>Melastoma malabathricum</i> L.	Khakhuchi	Cuts and wounds	Leaves – the juice is applied externally	Garos/ India	(21)
<i>Melastoma malabathricum</i> L.	Se la play	Mouth ulcer and geographic tongue	Fruit – hold in mouth	Karen/ Thailand	(33)
<i>Melastoma malabathricum</i> L.	Koroli	Skin problem, diarrhea and dysentery	Bark and leaves	-/ India	(19)
<i>Melastoma malabathricum</i> L.	Nakkukaruppan	Wounds	Roots – the paste is applied on wounds	Kuruma/ India	(26)

kaempferol-3-O-(2",6"-di-O-p-trans-coumaroyl)- β -glucoside, were identified and characterised based on the increasing polarities of solvents by Sirat et al. through purification using repeated chromatographic techniques (57). Elucidation was conducted by spectroscopic means and direct comparison with previously reported

data. In 2011, Sharma and Kumar reported the total phenolic content and flavonoids in *M. malabathricum* L. by using Folin Ciocalteu reagent and aluminium chloride method, respectively. The results from this study show that the leaves of the plant are a rich source of phenolic compounds and exhibit antioxidant activity.

Table II. A brief summary of the experimental conditions for various methods of extraction for plants material.

	Soxhlet extraction	UAE/Sonication	Maceration
Common solvent used	Organic solvents	Water, aqueous and nonaqueous solvents	Water, aqueous and nonaqueous solvents
Temperature (°C)	Under heat	Room temperature, or under heat	Room temperature
Pressure applied	Atmospheric	Atmospheric	Atmospheric
Time required	Long (3 – 18 hour)	Short (1 hour)	Long (3 – 4 days)
Volume of solvent required (mL)	Moderate (150 – 200)	Moderate (50 – 100)	Large (Depending on the sample size)
Polarity of natural products extracted	Dependent on extracting solvent	Dependent on extracting solvent	Dependent on extracting solvent

Table III: Methods of extraction for *Melastoma* sp.

Part use	Drying	Extract/Fraction/Isolate	Analysis	Ref
Leaves	n/a	Maceration – methanol (1:20 (w/v))	HPLC	(41)
Leaves	Open air under shade	Maceration – chloroform	HPLC	(42)
Leaves	Air-dried	Maceration – methanol	LC-MS	(43)
Leaves	Air-dried	Maceration – methanol Sonication/UAE – water	GC-MS	(44)
Leaves	Oven (50°C)-dried	Soxhlet extraction – deionised water; ethanol; ethyl acetate; hexane	HPLC	(45)
Leaves	n/a	Maceration – methanol	HPLC	(46)
Leaves		Maceration – methanol (1) Fractionation of methanol – liquid-liquid continuous extraction appliance using n-hexane, chloroform and ethyl acetate solvents in volume ratio of 1: 3. (2)	UV-Vis spectrophotometer	(47)
Fruit	n/a	Maceration – methanol (1) Soxhlet extraction – ethanol (2) Sonication/UAE – ethanol (3)	UPLC-MS/MS	(48)
Leaves	Oven (40°C - 45°C)-dried	Maceration – methanol (1) Fractionation of methanol – liquid-liquid extraction with a solvent n-hexane and water with the aim of separating polar and non-polar compounds. (2)	n/a	(49)
Leaves, flowers and stem	Oven (45°C)-dried	Maceration – methanol	n/a	(50)
Leaves and fruits	Air-dried	Maceration – ethanol	UV-Vis spectrophotometer	(51)
Leaves	Oven (40°C)-dried	Maceration – hexane (1:2 (w/v)) and using ethanol (1:2 (w/v))	UPLC-QTOF/MS	(52)

n/a, not applicable

The total flavonoid content of the plant was 25.27 ± 0.219 mg g⁻¹. Sharma and Kumar reported that the concentration of flavonoid in the leaves is lower than that of phenolic compounds (54). In the following year, Wong et al. reported the chemical constituents of *M. malabathricum* L. from chloroform and ethyl acetate extracts from the leaves and flowers, respectively (58). Ursolic acid, 2 α -hydroxyursolic acid, asiatic acid, β -sitosterol 3-O- β -D-glucopyranoside and the glycolipid glycerol 1,2-dilinolenyl-3-O- β -D-galactopyranoside were identified from the chloroform extract. Kaempferol, kaempferol 3-O- α -L-rhamnopyranoside, kaempferol 3-O- β -D-glucopyranoside, kaempferol 3-O- β -D-galactopyranoside, kaempferol 3-O-(2'',6''-di-O-E-p-coumaryl)- β -D-galactopyranoside, quercetin and ellagic acid were identified from the ethyl acetate extract. Danladi et al. recently conducted phytochemical screening and total phenolic and flavonoid content

analyses of the methanolic extract from different parts of *M. malabathricum* L. (58,59). Phytochemical screening showed that all parts of this plant contain tannins, steroids, phenols and flavonoids. Interestingly, flower extract exhibits the highest total phenolic content, whereas the leaf has the highest flavonoid content, followed by the flower. Diris et al. recently investigated the phytochemicals of *M. malabathricum* and *M. beccarianum* leaf crude extracts. Three compounds, namely, 8,11-octadecadienoic acid methyl ester, stearic acid methyl ester and tocopherol, were detected in *M. malabathricum*; whereas α -tocopherol- β -D-mannoside was only detected in *M. beccarianum* (44).

IN VITRO STUDIES

Anticoagulant Property of *Melastoma* sp.

The hot water leaf extract of *Melastoma* sp. exhibits potent

Table IV: Identified phytochemicals from the *Melastoma* sp. and their corresponding class of compound/compound name along with the plant part of the herb and types of extracts

Class of compound/compound name	Plant part	Types of extract	References
flavonoids, triterpenes, tannins, saponins and steroid	leaves	water	(55)
naringenin, kaempferol and kaempferol-3- <i>O</i> - <i>D</i> -glucoside, and	flowers	ethyl acetate	(8)
kaempferol-3- <i>O</i> -(2'',6''-di- <i>O</i> - <i>p</i> - <i>trans</i> -coumaroyl)glucoside and kaempferol-3- <i>O</i> - <i>D</i> -glucoside	flowers	methanol	(8)
flavonoids, saponins, tannins, glycosides, and steroid/triterpenoids	leaves	-	(56)
auranamide, patriscabratine, α -amyrin, quercitrin, quercetin, and kaempferol-3- <i>O</i> -(2'',6''-di- <i>O</i> - <i>p</i> - <i>trans</i> -coumaroyl)- β -glucoside	leaves	<i>n</i> -hexane, ethyl acetate and methanol	(57)
ursolic acid, 2 α -hydroxyursolic acid, asiatic acid, β -sitosterol 3- <i>O</i> - β - <i>D</i> -glucopyranoside and the glycolipid glycerol 1,2-dilinolenyl-3- <i>O</i> - β - <i>D</i> -galactopyranoside.	leaves and flowers	chloroform	(58)
kaempferol, kaempferol 3- <i>O</i> - α - <i>L</i> -rhamnopyranoside, kaempferol 3- <i>O</i> - β - <i>D</i> -glucopyranoside, kaempferol 3- <i>O</i> - β - <i>D</i> -galactopyranoside, kaempferol 3- <i>O</i> -(2'',6''-di- <i>O</i> - <i>E</i> - <i>p</i> -coumaroyl)- β - <i>D</i> -galactopyranoside, quercetin and ellagic acid.	leaves and flowers	ethyl acetate	(58)
tannins, steroids, phenols and flavonoids	leaves, flowers, fruits and stems	methanol	(59)
8,11-octadecadienoic acid methyl ester, stearic acid methyl ester, tocopherol, and α -tocopherol- β - <i>D</i> -mannoside	leaves	water	(44)

anticoagulant property (7). Mechanisms of *Melastoma* extract associated with intrinsic and common pathways of coagulation were evaluated by activated partial thromboplastin time (aPTT). Prothrombin time (PT) assay was used to monitor the integrity of coagulation proteins, and thrombin time (TT) measures the time consumed for thrombin-mediated fibrinogen conversion to fibrin clot. The anticoagulant activity of the hot water leaf extract of *Melastoma* sp. was significant in aPTT test but insignificant for PT and TT assays. In addition, the anticoagulant effect of *Melastoma* sp. did not vary with gender (7). The hot crude extract of *Melastoma* sp. with isolated cinnamic acid and its derivative also exhibited anticoagulant activities (60). Considering the functional clot-based findings, *Melastoma* sp. can be developed as an herbal-based anticoagulant agent for treating various cardiovascular diseases in the future.

Antioxidant Properties of *Melastoma* sp.

The antioxidant properties of aqueous and ethanol extracts of *Melastoma* sp. were evaluated by measuring the capacity of both extracts in scavenging the free radicals 2,2-diphenyl-2-picrylhydrazyl (DPPH) and 2,2-azinobis (3-ethylbenzothiazoline-6-sulfonic acid (ABTS) (12,61). Based on the IC₅₀ values, the aqueous extract of *Melastoma* sp. exert strong free radical scavenging towards DPPH, whereas the ethanolic extract exhibited increased ABTS free radical scavenging activities (12,62). Ab Rahman and colleagues reported that the DPPH scavenging activity of aqueous extract of *Melastoma* sp. was insignificant compared with that ascorbic acid (control) (63). Additionally, the ferric-reducing antioxidant power of ethanolic extract was better than that of the aqueous extract of *Melastoma* sp. (12).

Antimicrobial Properties of *Melastoma* sp.

Melastoma sp. are traditionally reputed as either antimicrobial agent or a poisonous plant (64). Antibacterial agent is classified as bactericidal or bacteriostatic by killing bacteria via destroying bacterial cell wall or by reducing bacterial growth, respectively (65). The structure of bacterial cell wall (either Gram-positive or Gram-negative) plays a prime role in tolerance or susceptibility of bacteria against antibacterial effect of compounds (66). For example, the crude flower and fruit methanol extracts of *Melastoma* sp. act as bactericidal to both Gram-positive bacteria, such as *Listeria monocytogenes* IMR L55 and *Staphylococcus aureus* compared with Gram-negative bacteria, such as *Escherichia coli* and *Salmonella typhimurium* (67). These findings are in agreement with those of Alnajjar and co-workers (12), who proved that both ethanolic and aqueous extracts of *Melastoma* sp. inhibit Gram-positive bacteria, *S. aureus* and *Streptococcus agalactiae*. By contrast, no antibacterial activity was found against the Gram-negative bacteria *E. coli* and *Klebsilla pneumonia* (12). The acetone, aqueous, chloroform, ethyl, ethyl acetate and hexane extracts of *Melastoma* sp. also showed good antibacterial effects against different clinical wound isolates of *S. aureus*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *E. coli* and *K. pneumonia* (50,68–71). The antibacterial properties of *Melastoma* sp. can also be attributed to the presence of phenols and flavonoid compounds (72). The antibacterial mechanism of *Melastoma* sp. may be related to their ability to target different components and the function of a bacterial cell, such as inactivation of microbial adhesins, enzymes, and cell envelope transports (73). In addition to its bactericidal activity, *Melastoma* sp. possessed bacteriostatic mode of action against both Gram-positive *S. aureus* and Gram-negative *E. coli* (74). Bacteriostatic mode of action of leaf extract of *Melastoma* sp. against both strains were observed after 5 hours of incubation period. This result may also indicate a broad spectrum of antibacterial activity from different parts of *Melastoma* sp. plant. This disparity between the activities of the flower, fruit, leaf

and solvent extraction of *Melastoma* sp. is due to the mixtures of bioactive compounds present in the crude extracts compared with the pure compound contained in the standard antibiotics (75). In an antifungal study, the ethanol leaf extract produced zone of inhibition ranging from 7–18 mm against the following selected fungi: *Helminthosporin oryzae*, *Alternaria alternate*, *Fusarium oxysporum*, *Candida albicans* and *Aspergillus parasiticus* but not effective against *Colletotrichum acutatum* (74). The potential ability of *Melastoma* sp. to kill such an enormous spectrum of pathogens provides scientific basis for the local usage of *Melastoma* sp. in the treatment of various infectious diseases.

Cytotoxic Properties of *Melastoma* sp.

The aqueous extract inhibited the proliferation of Caov-3 and HL-60 cell lines, whereas the chloroform extract exhibited antiproliferative activity against the Caov-3, HL-60 and CEM-SS cell lines. The methanol extract showed antiproliferative activity against MCF-7, HeLa, Caov-3, HL-60, CEM-SS and MDA-MB-231 cancer cell lines (11,76). The n-hexane extracts isolated from flower, leaf and stem parts of *Melastoma* sp. also exhibited anti-proliferative effect against MCF-7 human breast cancer cells in a concentration-dependent manner (76). However, all extracts did not inhibit the proliferation of 3T3 normal cells, thus indicating their non-cytotoxic properties (77,78). Similar finding in *Melastoma* sp. leaf methanol extracts which were harvested from 7 different locations (Kuala Terengganu, Kemaman, Jertih, Tumpat, Bakong Luar, Jeram Perdah and Bachok) also showed potent cytotoxic effect against HepG2 human hepatocellular cancer cell line but not on Chang liver normal cell line (79). The findings described that the sample obtained from Kuala Terengganu exhibit the highest cytotoxic activity based on the IC_{50} value of 1.4 $\mu\text{g/mL}$ compared with the other locations. The methanol extract is the most effective extract of *Melastoma* sp. from the obtained data because it inhibited the proliferation of various cancer cell lines (11,79). *Melastoma* sp. extracts from the leaves and stems exhibited cytotoxic activity in brine shrimp cultures with LC_{50} values of 53.84 and 52.71 $\mu\text{g/mL}$, respectively (64,80).

Immunomodulatory Properties of *Melastoma* sp.

Immunomodulatory study on the effects of *Melastoma* sp. on human peripheral blood mononuclear cells (PBMC) proved that both aqueous and ethanol extracts exhibited strong ability to proliferate the viability of PBMC, the IC_{50} values established were 1.78 ± 1.2 and 6.545 ± 0.93 $\mu\text{g/mL}$, respectively (12). Alnajjar et al. (12) also showed that both extracts were not toxic to normal immune cells, thus suggesting that *Melastoma* sp. can potentially modulate the cellular immune systems. The authors postulated that the presence of quercetin in *Melastoma* sp. (8) has contributed to the immunomodulatory activity. These findings seem to be consistent with other research of Nair et al. (81) that the flavonoid quercetin exhibit the ability to modulate the immune response

and increase the percentage of PBMC. Additionally, compounds isolated from *Melastoma* sp., which include alpha-amyrin, betulinic acid and quercetin, also exert inhibitory effects on platelet activating factor receptor binding with rabbit platelets (82). Table V lists all the *in vitro* activities of *Melastoma* sp.

IN VIVO STUDIES

The use of *Melastoma* sp. as important medicinal plant has been known since antiquity in the treatment of many ailments. Numerous pharmacological studies and clinical practices have reported that this plant possesses numerous biological functions. Table VI provides the updated data and study description of the *in vivo* studies of *Melastoma* sp. All of these studies have focused only on one species, *Melastoma malabathricum*, and most of the plant part used in the studies is the leaf. Several studies conclusively declared that this plant exhibits significant anti-ulcer (83), anti-nociceptive (84), anti-inflammatory (85), anti-carcinogenic (86) and anti-diabetic activity (43) and exhibited appreciable gastroprotective (87) and hepatoprotective (88) activities. *M. malabathricum* also stimulates the male reproductive system (89). The majority of the study extracted the leaves using methanol and the activity was determined by different types of murine with varying doses. Fig. 1 illustrates types of murine used in the *in vivo* studies of *M. malabathricum*. Sprague Dawley rats are most commonly used in the studies followed by albino rats and mice.

CONCLUSION

Melastoma sp. has been attaining interest from people worldwide for its pharmacological effects and medical benefits. The present review study indicates that *Melastoma* sp. particularly *Melastoma malabathricum* Linn has shown promising results in experimental studies, both for *in vitro* and *in vivo* in animals. From ethnobotanical use to laboratory works, *Melastoma malabathricum* Linn regardless of the parts used, was found rich with antioxidants and possessed properties such as anti-microbial, anti-coagulant, immunomodulatory, anti-ulcer, anti-nociceptive, anti-inflammatory, anti-carcinogenic and anti-diabetic activities. Thus, this plant has vast potential to be developed as nutraceuticals.

Despite most studies conducted to elucidate its phytochemicals and medicinal effects, many still take in the form of plant extract to obtain its synergistic effects. The pure bioactive compounds, isolated from the *Melastoma* sp. are not really been sought and thoroughly investigated that could be the limitation of its medicinal potential. In addition, none of the studies has been translated to clinical practice. Therefore, particular attention should be addressed to identify the prominent or new bioactive molecule with better therapeutic efficacy as a future direction for *Melastoma* sp.

Table V: *In vitro* studies on *Melastoma* sp.

Effect/Activity	Species, Part(s) Used, Extraction solvent(s)	Study Design(s)	Result(s)	References
Anticoagulant	<ul style="list-style-type: none"> <i>M. malabathricum</i> leaf aqueous and methanol extracts 	<ul style="list-style-type: none"> Clot-based <i>in vitro</i> screening assays: <ol style="list-style-type: none"> activated partial thromboplastin time (aPTT) prothrombin time (PT) thrombin time (TT) Mixing studies 	<ul style="list-style-type: none"> Hot water of <i>Melastoma</i> leaves extract possessed the most potent anticoagulant properties comparable to heparin (positive control). 	(7,60)
Antioxidant	<ul style="list-style-type: none"> <i>M. malabathricum</i> leaf aqueous, ethanol and methanol extracts 	<ul style="list-style-type: none"> Free radical scavenging assays: <ol style="list-style-type: none"> 2,2-Diphenyl-1-picrylhydrazyl (DPPH) 2,2-azinobis (3-ethylbenzothiazoline-6-sulfonic acid (ABTS) Ferric reducing antioxidant power (FRAP) 	<ul style="list-style-type: none"> Aqueous extract scavenged DPPH and ABTS free radicals, with IC₅₀ values 11 µg/mL and 64 µg/mL, respectively. Ethanol extract scavenged DPPH and ABTS free radicals, with IC₅₀ values 8.5-12 µg/mL and 63 µg/mL, respectively. FRAP of aqueous and ethanol extracts were 28,750±0.03 and 33,590±0.04, respectively. 	(11,12,61–63,74)
Antimicrobial	<ul style="list-style-type: none"> <i>M. decemfidum</i>, <i>M. malabathricum</i> flower, fruit, leaf and stem aqueous, chloroform, ethyl acetate, hexane ethanol and methanol extracts 	<ul style="list-style-type: none"> Disc diffusion methods: <ol style="list-style-type: none"> Minimum inhibitory concentration (MIC) Minimum bactericidal concentration (MBC) 	<ul style="list-style-type: none"> Aqueous and ethanol leaf extracts displayed antibacterial activity against Gram-positive bacteria only: <i>Staphylococcus aureus</i> and <i>Streptococcus agalactiae</i>. Aqueous and ethanol leaf extracts displayed no inhibitory effect against the growth of Gram-negative bacteria <i>Escherichia coli</i> and <i>Klebsilla pneumonia</i>. Flower and fruit methanol extracts demonstrated antibacterial effect against Gram-positive bacteria <i>Listeria monocytogenes</i> IMR L55 and <i>S. aureus</i> IMR S244 compared to Gram-negative bacteria <i>E. coli</i> and <i>Salmonella typhimurium</i> IMR S100. The MIC and MBC of flower and fruit extracts against <i>L. monocytogenes</i> IMR L55 were 12.5 mg/mL and 100 mg/mL, respectively, whilst 100 mg/mL against <i>S. aureus</i>. Ethanol leaf extract was effective in inhibiting the growth of <i>Helminthosporin oryzae</i>, <i>Alternaria alternate</i>, <i>Fusarium oxysporum</i>, <i>Candida albicans</i> and <i>Aspergillus parasiticus</i>, but ineffective against <i>Colletotrichum acutatum</i>. 	(50,67–69,74)
Cytotoxic	<ul style="list-style-type: none"> <i>M. malabathricum</i> leaf and stem methanol extract 	<ul style="list-style-type: none"> 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) cell proliferation assay Brine shrimp lethality bioassay 	<ul style="list-style-type: none"> The aqueous leaf extract exerted cytotoxicity against CaOV3 and HL-60, with IC₅₀ values of 50 µg/mL and 11 µg/mL, respectively. The chloroform leaf extract displayed cytotoxicity against HeLa, CaOV3, HL-60 and CEM-SS, with IC₅₀ values of 96 µg/mL, 34 µg/mL, 30 µg/mL and 22 µg/mL, respectively. The leaf methanol extract demonstrated potent cytotoxic effect against HepG2 cells with IC₅₀ value of less than 10 µg/mL. The leaf methanol extract also exhibited cytotoxic effect against MCF-7, HeLa, CaOV3, HL-60, CEM-SS and MDA-MB-231 cells with IC50 values of 87 µg/mL, 88 µg/mL, 41 µg/mL, 13 µg/mL, 30 µg/mL and 59 µg/mL, respectively. LC₅₀ values of leaves and stem extracts in brine shrimps cultures were 53.84 µg/mL and 52.71 µg/mL, respectively. 	(8,11,64,76,79)
Immunomodulatory	<ul style="list-style-type: none"> <i>M. malabathricum</i> leaf aqueous extract ethanol extract 	<ul style="list-style-type: none"> 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) cell proliferation assay Platelet activating factor (PAF) receptor binding inhibitory assay 	<ul style="list-style-type: none"> Aqueous and ethanol extracts promote the proliferation of human peripheral blood mononuclear cells (PBMC) in a concentration-dependent manner. Compounds isolated from <i>Melastoma</i> sp. which include alpha-amyrin, betulinic acid and quercetin demonstrated inhibitory potential of 67.3%, 64.3% and 57.4%, respectively, on PAF receptor binding with rabbit platelets. 	(12,82)

Table VI: The effect of *Melastoma* sp. through *in vivo* studies

Plant part	Solvent	Test model/doses	Findings	Ref
Leaves	Ethanol	Sprague Dawley rats/ 50, 250 and 500 mg/kg	<ul style="list-style-type: none"> ↓ Ulcer area ↓ Ulcer score 	(83)
Leaves	Methanol	Sprague Dawley rats/ 50, 250, or 500 mg/kg	Hepatoprotective against paracetamol- (PCM;3 g/kg) and carbon tetrachloride (CCl4; 0.15 mL/kg)-induced liver toxicity models	(88)
Leaves	Petroleum ether	Sprague dawley rats Inherited cataract mice/100, 250, and 500 mg/kg	<ul style="list-style-type: none"> ↓ Non-opioid mediated atinociceptive activity capsaicin-induced neurogenic noniception ↓ Glutamate-induced paw licking 	(84)
Leaves	Methanol	Albino mice/ 1.5 to 2 mg/10 g body weigh	↑ Platlet count	(84)
Leaves	Methanol	Sprague dawley rats/ 50, 250, and 500 mg/kg	<ul style="list-style-type: none"> ↓ Volume, acidity of gastric juice, SOD, GTP and GTR ↑ PH, gastrilc wall mucus, CAT, MPO and TBARS 	(87)
Leaves	Ethanol	Albino rats/ 250 and 500mg/kg	↓ Edema volume	(85)
Leaves	Methanol	Albino rats/ 100, 250, and 500 mg/kg	↑ Plasma level of Insulin, Hexokinas Fructose-1-6-bi Phosphatase, glucose-6-phosphate, HDL, LDL cholesterol	(43)
Leaves	Ethanol	Swiss albino mice/ Dalton Ascite Lymphoma (DAL) bearing mice / 20, 150,300 mg/kg	<ul style="list-style-type: none"> ↓ Tumor size (Ascite Lymphoma) ↓ Cell counts 	(86)
Leaves	Ethanol	Winstar albino rats/ 250,500mg/kg	↑ Total sperm, viable sperm, sperm motility and sperm quality	(89)

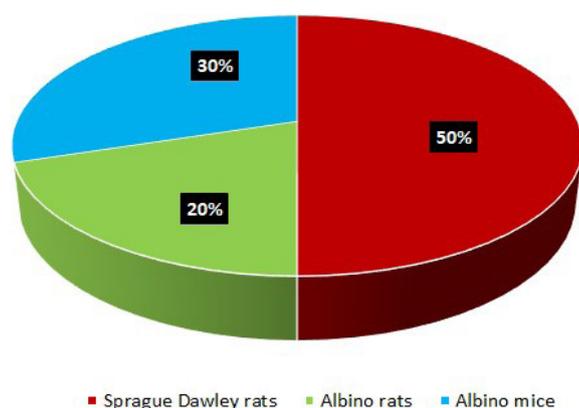


Figure 1: Pie chart illustrating the types of murine used in *Melastoma malabathricum* in vivo studies

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