An up-to-date review on phytochemical constituents and pharmacological activities of *Melastoma malabathricum*

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Abstract: *Melastoma malabathricum* is well known traditional medicinal herb of South East Asia, India and China having many medicinal properties such as anti-diabetic, antihyperlipidemic, antioxidant, liver protective activity, anticoagulant activities, antiulcer activity, wound healing activity, gastroprotective, anti-microbial, antipyretic, anti-diarrheal, fertility enhancement effect, anti-cancer, anti-inflammatory, anti-nociceptive, chemomodulatory activity, anti-obesity and anti-venome activity. It contains many class of bioactive compounds such as flavonoids (Quercetin, Kaempferol), phenolic compounds (gallic acid, benzoic acid, epicatechin), steroidal class of compounds (β-sitosterol), tannin (Malabathrin, Casuarictin) and anthocyanins. This review article covers complete phytochemical and pharmacological activities of *Melastoma malabathricum* after 2011 till now.

Keywords: *Melastoma malabathricum*; Ethnopharmacology; Phytopharmacology; Phytochemistry

Introduction:

Life cannot be possible without plants and they are the vial source of Medicine also known as ethnomedicine (Aslam & Ahmad, 2016)(Azwanida, 2015). There are many medicinal plants that have been used for thousands of years (Alsarhan, Sultana, Al-Khatib, Rafiq, & Kadir, 2014). *Melastoma malabathricum* is well known ornamental plant that had pink and white flowers and belongs to family Melastomataceae. It is distributed in Asia especially in South East Asia (Figure 1), commonly known by different names in different part of World and mentioned in figure 2 (Joffry et al., 2012). It had many medicinal properties such as antibacterial (Khatun et al., 2014) (Nurhadis et al., 2012), anti-viral (Nazlina, Norha, Noor Zarina, & Ahmad, 2008), anti-oxidant (Mamat et al., 2013)(Alnajar, Abdulla, Ali, Alshawsh, & Hadi, 2012), anti-diabetic (Kumar, Ahmed, Gupta, Anwar, & Mujeeb, 2013), anti-inflammatory (Balamurugan, Sakthidevi, & Mohan, 2012), anti-nociceptive (Z. A. Zakaria et al., 2016)(Zainul Amiruddin Zakaria, Sodri, Hassan, Anuar, & Abdullah, 2012), gastroprotective (Zainul Amiruddin Zakaria, Zainol, et al., 2015)(Zabidi et al., 2012). Anti-ulcer (Zabidi et al., 2012), anti-coagulant (Khoo, Abas, Abdullah, Mohd Tohit, & Hamid, 2014), anti-cancer (Balamurugan, Nishanthini, & Mohan, 2013), anti-obesity (Karupiah & Ismail, 2014) and wound healing (Ab Rahman, Abdul Razak, & Mohd Bakri, 2014)(Nurdiana & Marziana, 2013). It possess many important bioactive compounds responsible for pharmacological activities such as flavonoids (Wong, Hag Ali, & Boey, 2012), tannin (Yoshida, Nakata, Hosotani, Nitta, & Okudat, 1992)(Joffry et al., 2012), anthocyanin (Anuar, Mohd Adnan, Saat, Aziz, & Mat Taha, 2013) and phenolic compounds. List of bioactive compounds and pharmacological activities after year 2011 were mentioned in table 1 and 2 resepectively.

(a)

(b)

(c)

Figure 1: *Melastoma malabathricum* (a) White flowers (b) Purple flowers (c) Fruits (Autumn Belle, 2017)(Cooper, 2017)

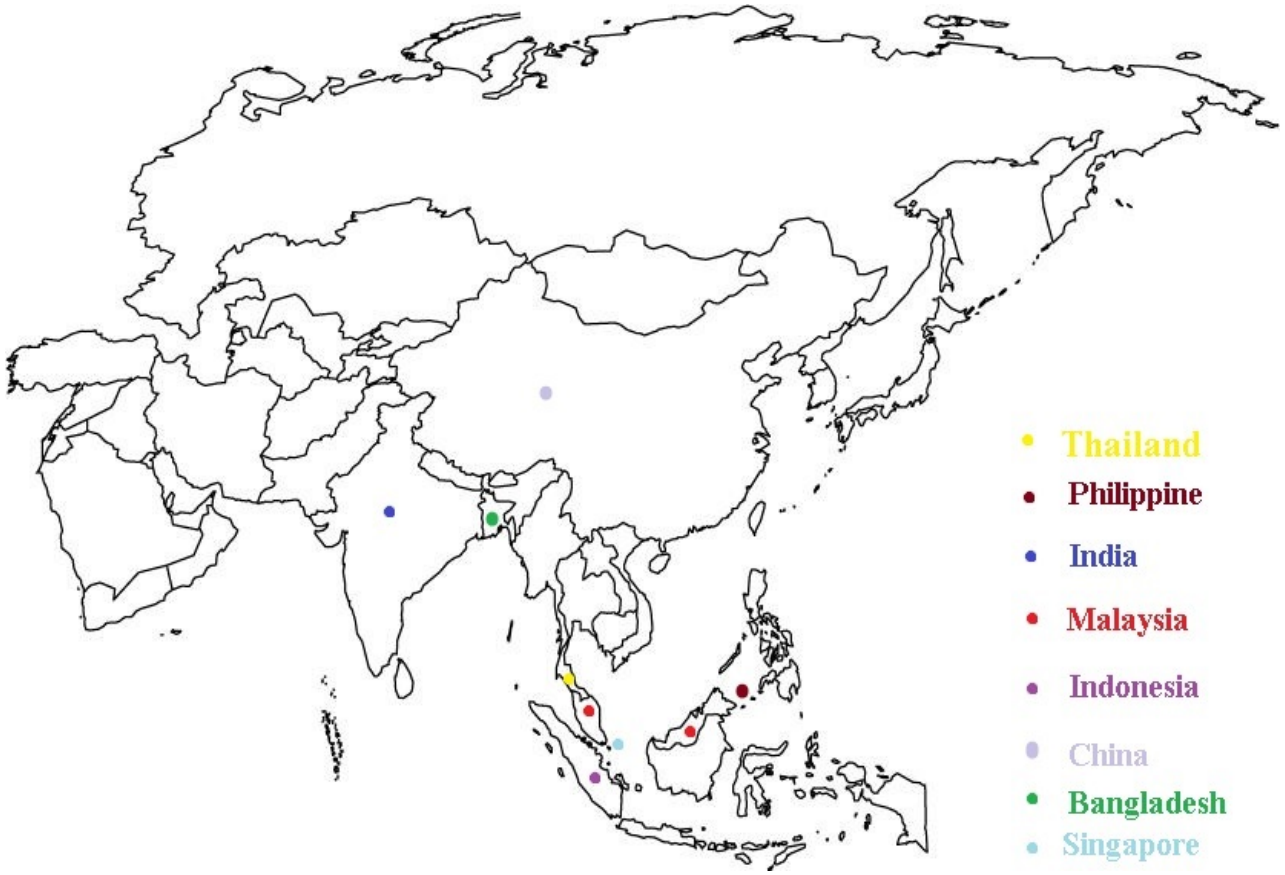


Figure 2: Distribution of *Melastoma malabathricum* (Joffry et al., 2012)

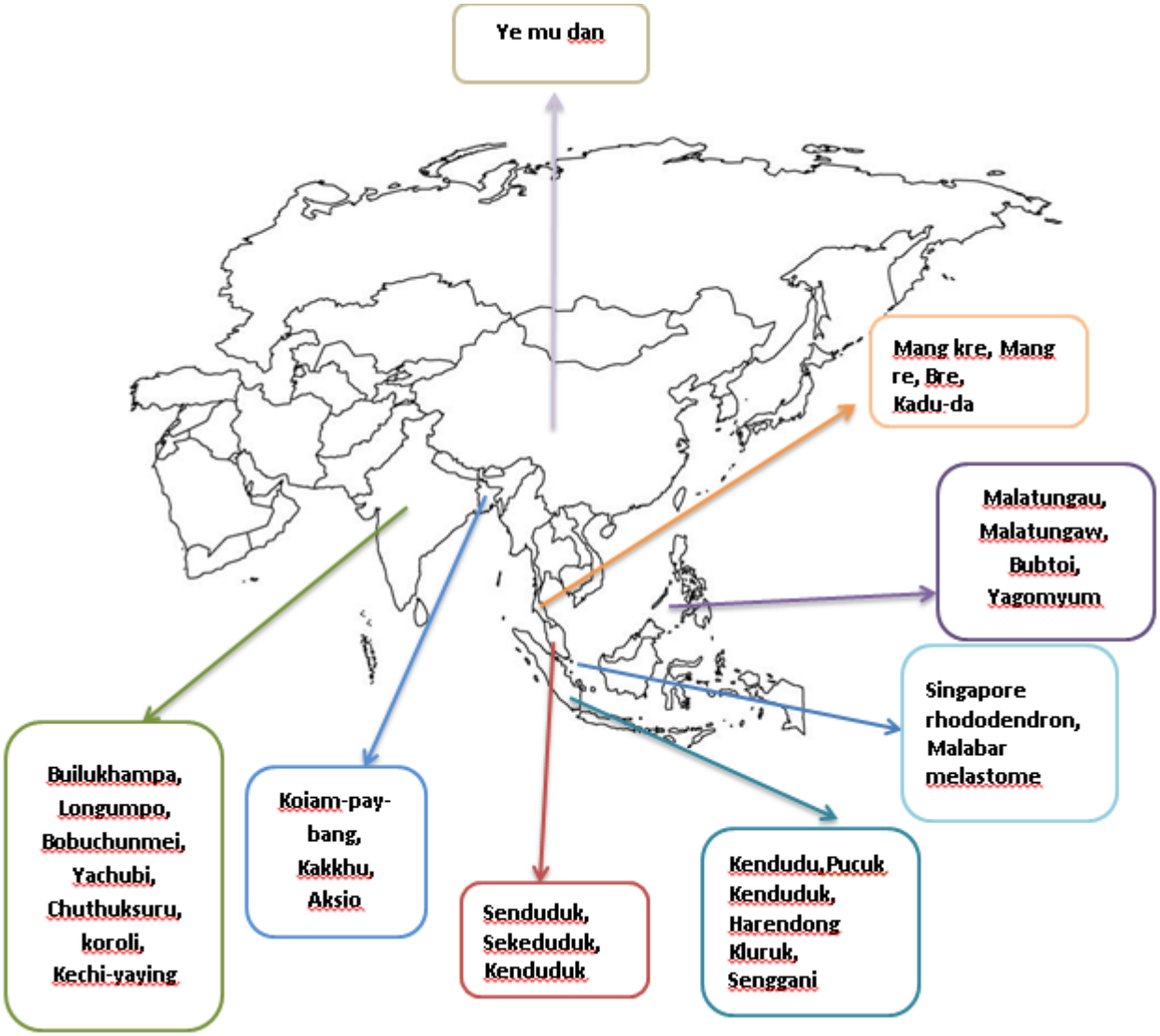


Figure 3: Common names of *Melastoma malabathricum* (Joffry et al., 2012)

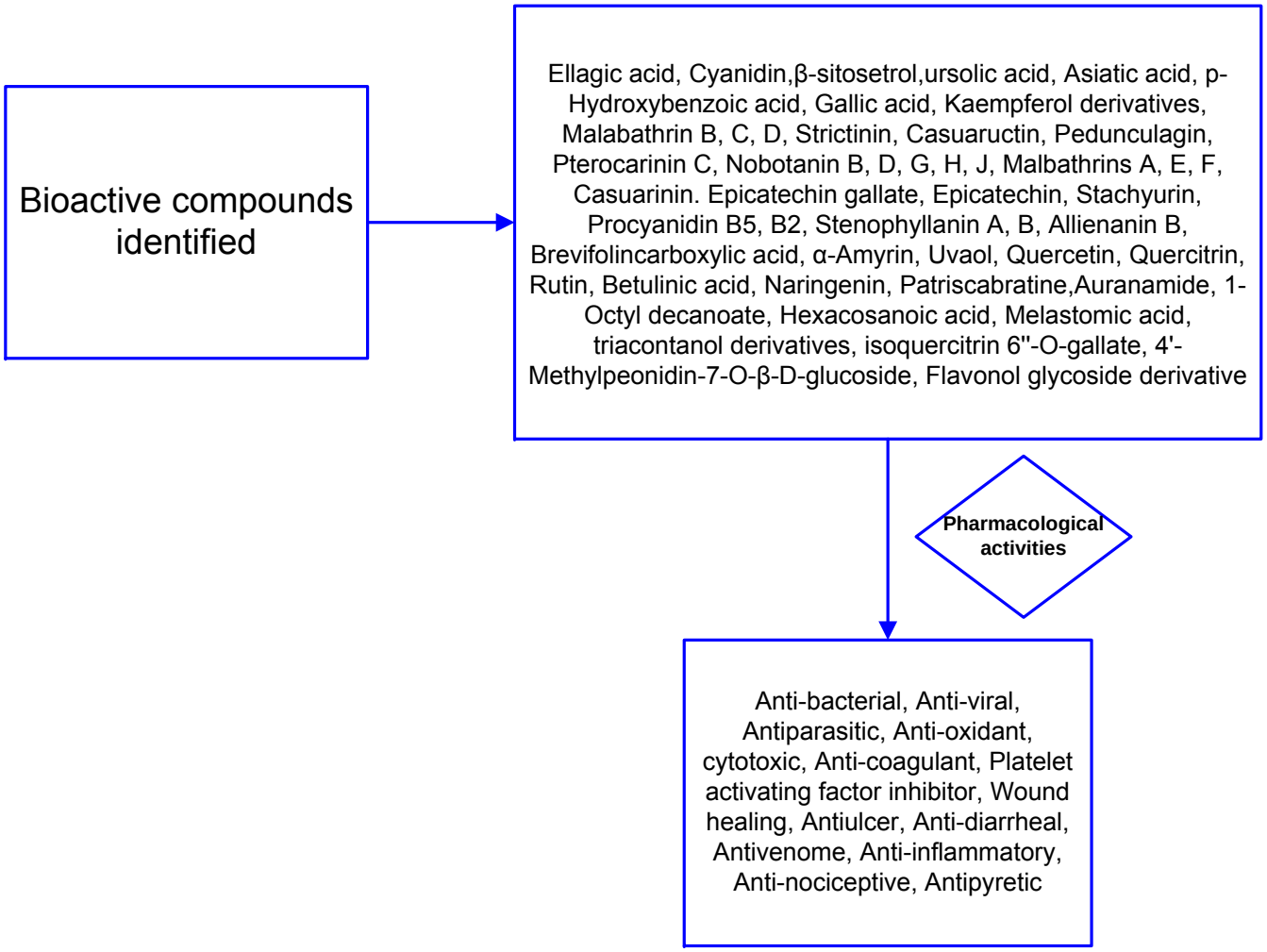


Figure 4: Literature review available before 2012 (Joffry et al., 2012)

Table 1: Chemical constituents reported

Chemical Constituents	**Part use**	**Pharmacological activity**	**Reference**
Ursolic acid **(1)**, 2 -hydroxyursolic acid, asiatic acid **(2)**, β-sitosterol-3-O-D-glucopyranoside **(3)** glycolipid glycerol 1,2-dilinolenyl-3-O-D-galactopyanoside **(4)**	Leaves	Antibacterial activity	(Wong et al., 2012)
Kaempferol **(5)**, kaempferol 3-O-L-rhamnopyranoside, kaempferol 3-O- D-glucopyranoside, kaempferol 3-O- D-galactopyranoside, ellagic acid **(6)**, quercetin **(7)**	Flower	Antibacterial activity	(Wong et al., 2012)
Acidic polysaccharides (rhamnogalacturonan, homogalacturonan, and rhamnose hexose-pectic type polysaccharide) and polyphenolics	leaves	Anticoagulant Activity	(Khoo et al., 2014)
Anthocyanins revealed the presence of cyanidin dihexoside, cyanidin hexoside, and delphinidin hexoside	Fruit	n.a	(Anuar et al., 2013)
3,4-Dehydroproline amide **(8)**, Mefloquine **(9)** and 2-(3,5- +Diphenyl-pyrazol-1-yl)benzothiazole	Leaves	Anti-microbial and anti-malarial	(Balamurugan, Nishanthini, & Mohan, 2012)
Kaempferol-3-O-(2",6"-di-O-trans-p-coumaroyl)-β-D-glucopyranoside	Leaves	Anti-microbial	(Alwash, Ibrahim, & Ahmad, 2013)
Kaempferol, quercetin	Leaves	Antioxidant	(Karupiah & Ismail, 2013)
Cinnamic acid **(10)**, para-hydroxycinnamic acid	Leaves	Anticagulant activity	(Khoo, Abdullah, Abas, Tohit, & Hamid, 2015)

Table 2: Pharmacological activities reported

Pharmacological activity	**Part use**	**Drying**	**Extract/Fraction/Isolate**	**Dose/ Testing method**	**Animals/Cell line culture**	**Experimental model (In Vivo / In Vitro)**	**Results**	**Reference**
Anti-diabetic, antihyperlipidemic and antioxidant	Leaves	Open air under shade	Extracted with methanol in a Soxhlet apparatus for 3 days.	100 mg/kg 250 mg/kg 500 mg/kg	Healthy albino rats (Wistar strain)	In-vivo	A	(Kumar et al., 2013)
Antioxidant and liver protective activity	Leaves	Open air under shade	40 g of powder leaves were macerated in 800 ml of methanol for 72 hours in the ratio of 1:20 (w/v).	50 mg/kg 250 mg/kg 500 mg/kg	Male Sprague Dawley rats	In-vivo	B	(Mamat et al., 2013)
Anticoagulant activities	Leaves	Open air under shade	Hot and cold water extraction; Methanol extract	100 - 1000 µg/ml	n.a	In-vitro	C	(Manicam et al., 2010)
Antiulcer Activity	Leaves	n.a	The ground dried leaves (40 g)were soaked in methanol 1: 20 (w/v) three times at room temperature for 24 h	50–500 mg/kg	Male Sprague Dawley rats	ethanol- and indomethacin-induced gastric ulcer models	D	(Zabidi et al., 2012)
Antioxidant	n.a	n.a	100 g was soaked in 1,000 mL of 95% ethanol for three days. Second extract was soaking 100 g of MM in 2,000 mL of distilled water then shaking for four hours in a water bath	DPPH Method, ABTS Method, FRAP Method	n.a	Invitro	E	(Alnajar et al., 2012)
Antibacterial	n.a	n.a	Same as above	Disc Diffusion Method	n.a	Invitro	E	(Alnajar et al., 2012)
Wound healing activity	leaves	n.a	Decoction	Cell Proliferative Activity	n.p	invitro	F	(Ab Rahman et al., 2014)

Table 2: (Continue)

Pharmacological activity	**Part use**	**Drying**	**Extract/Fraction/Isolate**	**Dose/ Testing method**	**Animals/Cell line culture**	**Experimental model (In Vivo / In Vitro)**	**Results**	**Reference**
Fertility enhancement effect	Leaves	Open air under shade	Soxhlet apparatus using ethanol.	250 mg/kg 500 mg/kg	Male albino rats	In-vivo	G	(Balamuruga n, Sakthidevi, & Mohan, 2013)
Gastroprotective activity	Leaves	n.a	Macerated in methanol in the ratio of 1:20 (w/v)	50, 250, 500 mg/kg	Pylorus-ligature rat	Pylorus-ligation in rat model	H	(Zainul Amiruddin Zakaria, Balan, et al., 2015)
Gastroprotective activity	Leaves	n.a	Fractions of methanol extract	50, 250, or 500mg/kg	Pylorus-ligature rat	ethanol-induced gastric ulcer model	I	(Wahida et al., 2017)
Wound healing activity	Leaves	Oven at 50C°	Soaked in distilled water for 24 hours.	n.p	Sprague dawley rat	Excision wound model	J	(Nurdiana & Marziana, 2013)
Hepatoprotective Activity	Leaves	n.a	Soaked three times at room temperature for 24 hours with methanol in a 1:20 (w/v) ratio	50, 250, and 500 mg/kg	Sprague dawley rat	In-vivo Hepatoprotective assay	K	(Kamisan et al., 2013)

Table 2: (Continue)

Pharmacological activity	**Part use**	**Drying**	**Extract/Fraction/Isolate**	**Dose/ Testing method**	**Animals/Cell line culture**	**Experimental model (In Vivo / In Vitro)**	**Results**	**Reference**
Cytotoxicity	Leaves and stem	Open air under shade	Soaked in methanol	Brine shrimp lethality bioassay	n.p	In-vitro	L	(Khatun et al., 2014)
Gastroprotective activity	Leaves	Open air under shade	Soaked in Chloroform	50, 250, and 500 mg/kg	Sprague–Dawley rats	Pylorus ligation induced ulceration model	M	(Zainul Amiruddin Zakaria, Zainol, et al., 2015)
Cytotoxicity	Leaves, stem and flower	Drying cabnit	n-hexane, chloroform and methanol	In-vitro cytotoxicity assay	MCF-7 cell lines	In-vitro	N	(Roslen, Alewi, Ahamada, & Rasad, 2014)
Anti-cancer	Leaves	n.a	Soxhlet extraction with ethanol	150 and 300mg/kg	Swiss Albino mice	In-vivo	O	(Balamuruga n, Nishanthini, et al., 2013)
Anti-inflammatory activity	Leaves	Open air under shade	Soxhlet extraction with ethanol	200-2000mg/kg	Adult Wistar albino rats	In-vivo	P	(Balamuruga n, Sakthidevi, et al., 2012)

Table 2: (Continue)

Pharmacological activity	**Part use**	**Drying**	**Extract/Fraction/Isolate**	**Dose/ In-vitroTesting method**	**Animals/Cell line culture**	**Experimental model (In Vivo / In Vitro)**	**Results**	**Reference**
Chemomodulatory effect	Leaves	Air dried	Soaked in methanol	100-500 mg/kg	Swiss albino	In-vivo	Q	(Verma et al., 2016)
Anti-microbial	Flower and fruits	n.p	Soaked in methanol	Disc Diffusion Method	n.a	In-vitro	R	(Nurhadis et al., 2012)
antinociceptive activity	Leaves	Oven dried	Mixed with distilled water in the ratio of 1:20 (w/v)	300, 500, and 1000 mg/kg	male Balb-C mice	In-vivo	S	(Zainul Amiruddin Zakaria et al., 2012)
Antioxidant and antimicrobial	Leaves	Shade dried	Extracted with ethanol	Disc diffusion method; DPPH	n.a	In-vitro	T	(Sarbadhikary , Bhowmik, Datta, Mandal, & Thakur, 2015)
Antinociceptive activity	Leaves	Air-dried	Ethylacetate, petroleum ether and and aqueous fractions	100, 250, and 500 mg/kg.	Male Sprague Dawley (SD) rats	In-vivo	U	(Z. A. Zakaria et al., 2016)
Anti-Obesity Effects	Leaves	n.a	Methanolic extract	n.a	Male Sprague–Dawley rats	In-vivo	V	(Karupiah & Ismail, 2014)

A= Thus, our findings demonstrate that different doses of MM leaves extract has an antidiabetic, antihyperlipidemic and antioxidant effects, which is evidenced by decreased level of blood glucose, glycated hemoglobin, glucose-6-phasphate, fructose-1-6-phasphate, total cholesterol, triglyceride, LDL cholesterol, VLDL cholesterol, SOD, CAT, GPx, and increased level of HDL Cholesterol, plasma insulin, hexokinase, MDA,. Oral glucose tolerance test shown that MM leaves extract having better glucose utilization capacity.

B= The MEMM exhibited hepatoprotection against paracetamol induced liver injury model, which could be, partly, attributed to its antioxidant activity and, linked to the presence and synergistic action of flavonoids, tannins and saponins

C= This study highlights that the anticoagulant activity of M. malabathricum aqueous leaf extract affects the intrinsic pathway of the coagulation cascade by causing clotting factor(s) deficiency

D= It exhibited significant antiulcer activity in the ethanol induced gastric ulcer model.
E= Popular folk remedy in treatment of different illness
F= It possess moderate activity compared with Nigella sativa
G=The epididymal sperm count, motility and sperm abnormality were increased significantly in treated rats.
H= It possess gastroprotective activity due partly to the presence of quercitrin
I= Ethyl acetate fraction of methanolic extract possesses the highest activity
J= Flavonoid and tannin plays an important role in healing wound
K= Hepatoprotective against PCM- and CCl4-induced liver toxicity
L= Moderate cytotoxicity compared to other medicinal plants when compared (*Baccaurea ramiflora bark , Baccaurea ramiflora leaves , Cnicus arvensis aerial part, Commelina benghalensis aerial part , Hoya parasitica stem , Hygrophila spinosa seed , Litsea glutinosa leaves Malpighia coccigera , Pseudelephantopus spicatus aerial part , Thuja occidentalis bark , Thuja occidentalis leaves , Viscum orientale aerial part)*
M= *Melastoma malabathricum* demonstrates gastroprotective effect plausibly via non-antioxidant, anti-inflammatory actions, and also by increasing the gastric mucosa defense.
N= Leaves and flower of *Melastoma malabathricum* possess more cytotoxicity than stem.
O= *Melastoma malabathricum* exhibited significant antitumor activity on Dalton Ascites Lymphoma (DAL) bearing mice.
P= *Melastoma malabathricum* at doses of 250 and 500mg/kg caused significant inhibition of paw edema
Q= Pretreatment with *Melastoma malabathricum* inhibits diethylnitrosamine (DEN) and ferric nitrilotriacetate (Fe-NTA) induced renal carcinogenesis
R= This study shows that the crude flower and fruit extracts exhibit interesting antimicrobial properties.
S= It involved the activation of several pain pathways.
T= *Melastoma malabathricum* were found to be mot effect when compared with *Phlogocanthus thyrsiflorus*, *Cissampelos pareira*, *Smilax zeylanica*, *Hydnocarpus kurzii*
U= Petroleum ether fraction exerted a non-opioid-mediated antinociceptive activity at the central and peripheral levels via the inhibition of vanilloid receptors and glutamatergic system, and the activation of NO-mediated/cGMP-independent pathway.
V= *Melastoma malabathricum* in high-fat diet tends to reduce body weight, blood lipids, and body fat weight

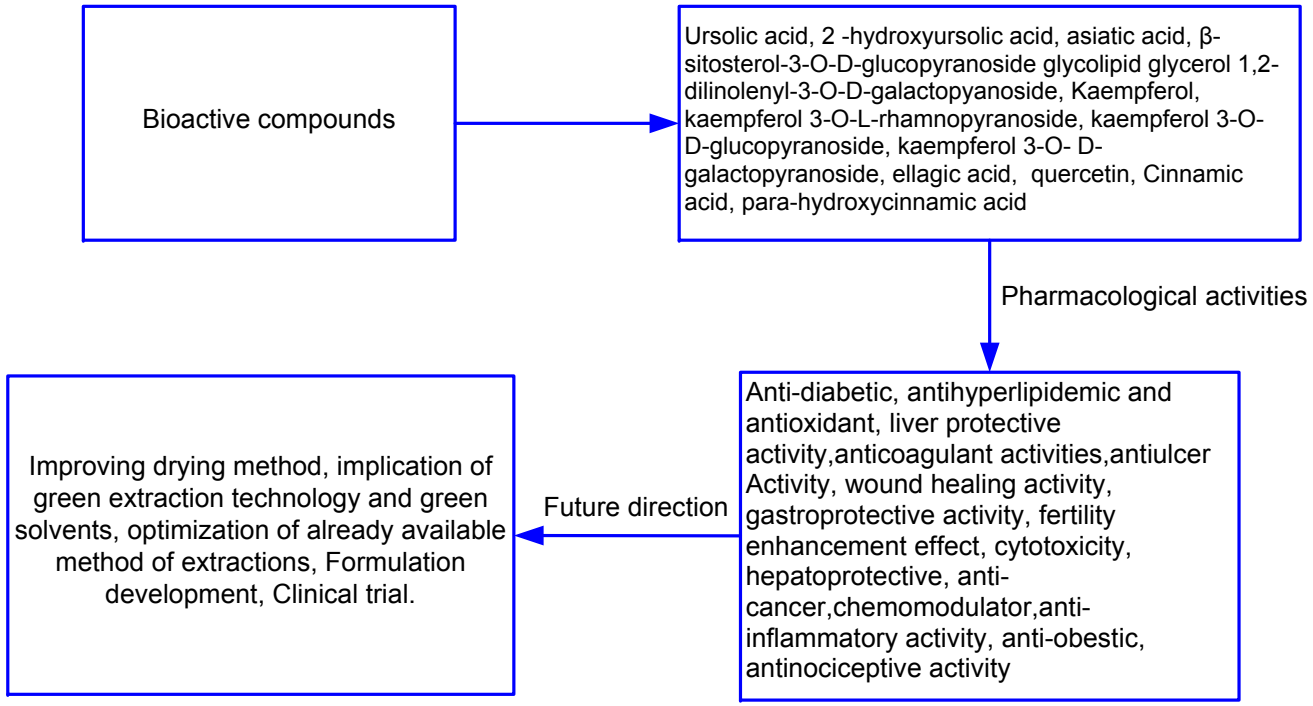


Figure 5: Research after 2011 till now and proposed future directions

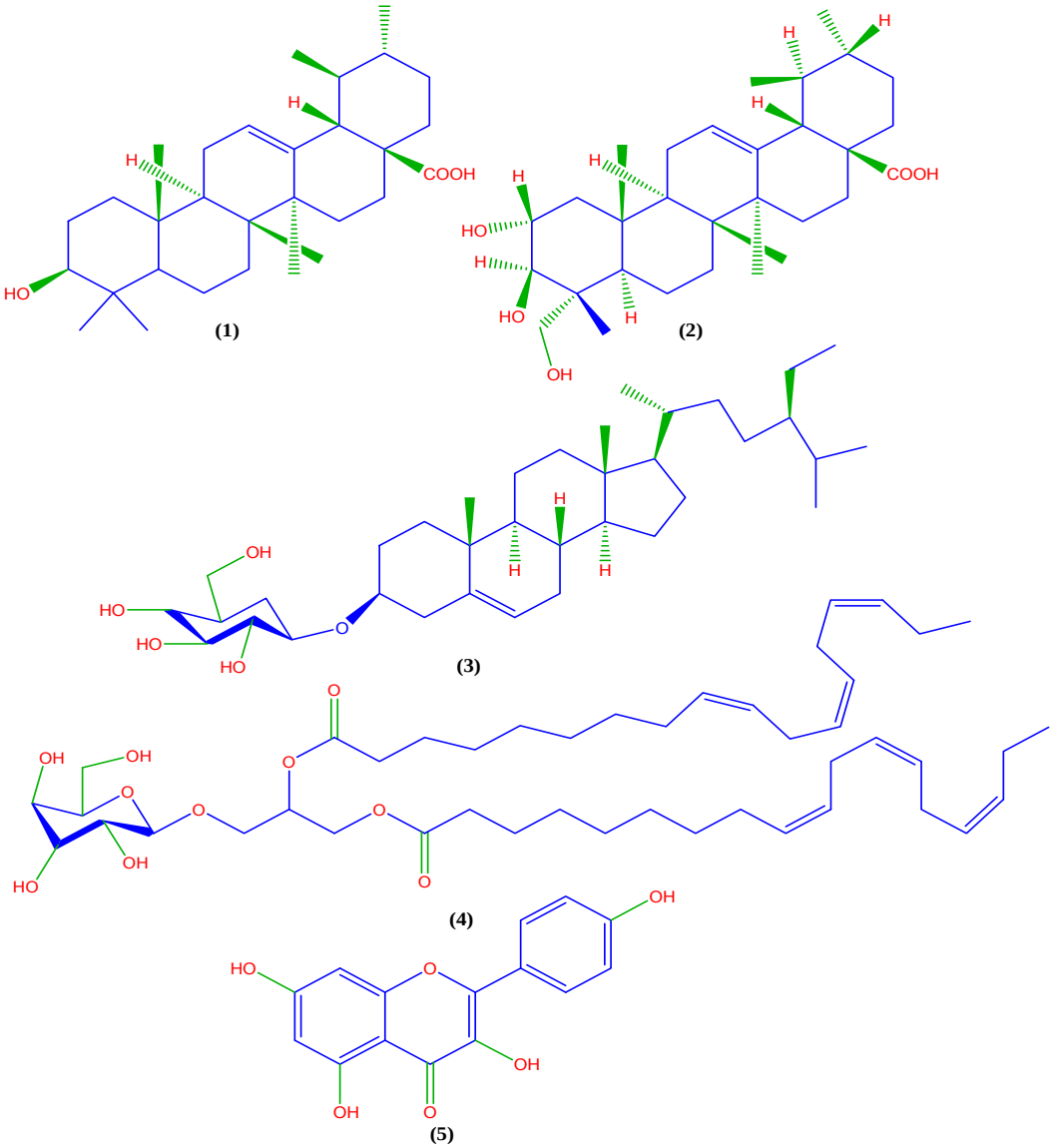
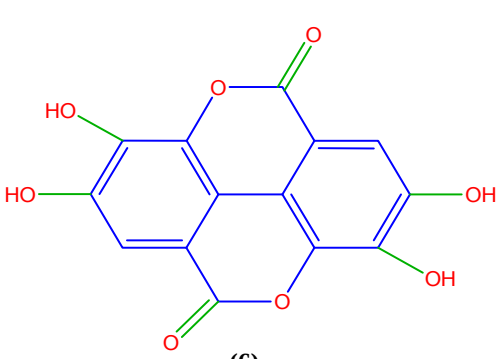


Figure 6: Chemical structures of *Melastoma malabathricum*



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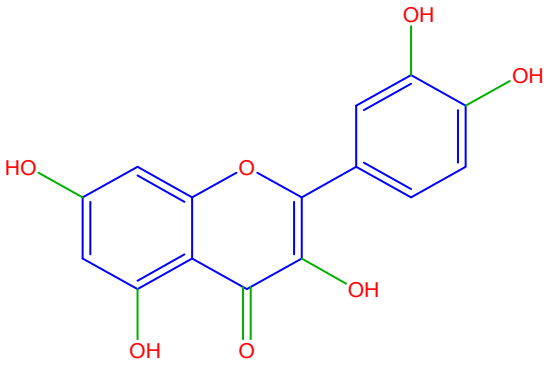

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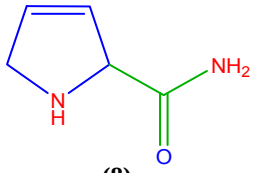

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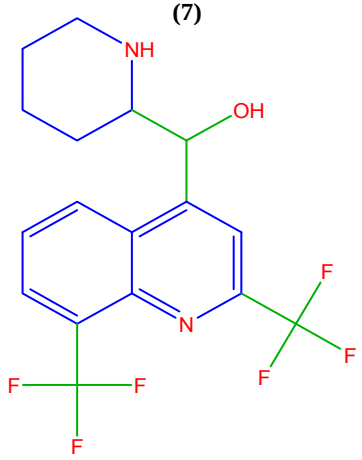

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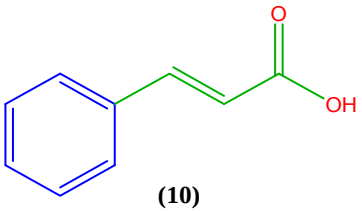

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Figure 6: (Continue)

Conclusion:

Melastoma malabathricum is used as traditional medicinal herb in different parts of India, China, Malaysia, Indonesia, Thailand and other South East Asian countries. There is still need lot of research to optimize the traditional extraction method to improve the extraction yield, pharmacological activities and transforming these extract into different formulations. Many research identified different pharmacological activities in different in-vivo animal models (pre-clinical trial) but none of these activity actually tested on clinical trial to find the effectiveness of medicinal herbs. Moreover, lack of formulation development and stability studies was found.

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