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Review Article

MEMECYLON SPECIES: A REVIEW OF TRADITIONAL INFORMATION AND TAXONOMIC DESCRIPTION

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ABSTRACT

The present review is to avail the comprehensive information on taxonomy, phytochemistry and pharmacology of Indian *Memecylon* species. *Memecylon* is one of the complex genus of flowering plants and it is an important source of traditional medicine. Owing to complexity in morphological characters, identification of *Memecylon* species has become very difficult. Nomenclature status of most of the Indian *Memecylon* species is not clear. Phylogenetic studies report on this genus are also very few. *Memecylon* species reported having potential pharmacological activities. This background made us present a review on Indian *Memecylon* species. Information on this plant genus was searched using various electronic databases in reference to the terms Indian *Memecylon* species taxonomy, phylogeny, pharmacological activities and phytoconstituents along with Indian classical texts, journals, etc. There is a confusion regarding the taxonomic status of *Memecylon malabaricum, M. amplexicaule, M. depressum*, *M. wightii. M. umbellatum* and *M. edule*. Several chemical constituents like memecylaene, umbelactone, amyrin, sitosterol, tartaric acid, malicacid, oleanolicacid, ursolicacid and tannins, triterpenes, and flavonoids have been identified in this genus. The plant extracts of this genus have been demonstrated to have potential pharmacological activities. Some of the phytoconstituents are attributed to the pharmacological potential of this genus. Further, there is a need to validate its taxonomic status and pharmacological properties by using modern biological techniques. If future studies throw a light on these aspects, definitely it will help in developing a potential biopharmaceutical product.

Keywords: Biological activities, Taxonomy, *Memecylon* species, Phylogeny

INTRODUCTION

The genus *Memecylon* L. belongs to family *Melastomataceae,* which is used for medicinal purposes in Asia-Pacific regions [1]. It consists of more than 300 species, mainly in the Old World tropics. In India, the genus is represented by about 40 species (table 1) out of which 21 are endemics [2]. The Western Ghats is the major centre of *Memecylon* diversity with 27 species, including 20 endemics confined to this biodiversity 'hotspot' [3]. The genus *Memecylon* is associated closely to *Syzygium* R. Br [4]. In Ayurveda and Siddha, several *Memecylon* species are reported to be used by tribals in the treatment of skin disorders, stomach disorders, herpes, chickenpox, leucorrhoea, polyuria, menorrhagia, dysentery and also in the treatment of bacterial infections and inflammation [5]. *M. umbellatum* leaves are used to treat a snake bite, given orally or in the form of infusion [6]. Ethnomedically fruit of *M. malabaricum* is used to control sterility in men [7], and the leaf juice of *M. capitellatum* is taken internally for a month to treat diabetes [8]. The leaves of other *Memecylon* species namely *M. lushingtonii* are effective in the post-citoal contraceptive. The bark of *M. angustifolium* is used as a tonic and refrigerant [9]. Apart from medicinal uses, *Memecylon* species are used as ornamentals, decorative plant work, walking sticks, light axe handles, combs, [10] timbers, yellow dye and in combination with myrobalans and sappan wood produces bright red tinge, astringent ripe berries are eaten at the time of famine worldwide [11] and also as a mordant in silk dyeing industries.

Information on this plant genus was searched using various electronic databases in reference to the terms Indian *Memecylon* species taxonomy, phylogeny, pharmacological activities and phyto-constituents along with Indian classical texts, journals. *Memecylon* species taxonomical data was searched using various floras of India and also taxonomy journals. Independent search was conducted using search terms such as genus *Memecylon* or *Memecylon* species taxonomy, phytochemistry, pharmacology, molecular studies in Indian *Memecylon* species in google scholar and Pubmed central website. The included articles were then grouped qualitatively under the effect of *Memecylon* species explaining taxonomy, phylogeny, pharmacology and phytochemistry and their mechanisms of action. Published literature concerning mechanisms of action of various diseases including inflammation, diabetes, antioxidant, anticancer, antihelminthic, emphasizing pharmacological potential was retrieved from PubMed and PubMed central. Those studies which explained the pharmacological potential, phytochemistry, phylogeny of Indian *Memecylon* species is included and rest were excluded from giving the comprehensive review on only Indian *Memecylon* species.

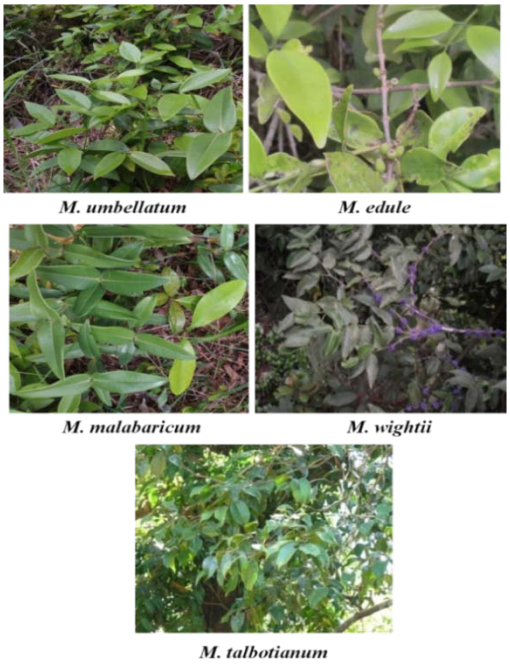

Fig. 1: Leafy branches of different species of *Memecylon* (Source: photos captured during field visit to Western Ghats region by Bharathi T. R.)

Table 1: List of Indian *Memecylon* species recorded in the plant list and their distribution along with red list category

S. No.	*Memecylon* species	Distribution in India	Vernacular names	Red list category
1	*M. angustifolium* Wight	Karnataka, Kerala, Tamil Nadu	Attukanala (Ma), Aattukanala (Ma) Vellaikkaya (Ta)	NE
2	*M. agastyamalaianum* Santhosh *et al.,*	Kerala	----------	NE
3	*M. bremeri* Viswanathan	Tamil Nadu	----------	CE
4	*M. capitellatum* L.	Tamil Nadu	----------	NE
5	*M. clarkeanum* Cogn.	Kerala, Tamil Nadu	----------	Vu
6	*M. deccanense* Clarke	Kerala	----------	Vu
7	*M. depressum* Benth.	Karnataka, Kerala, Tamil Nadu	Kaikkathetti (Ma)	NE
8	*M. edule* Roxb.	Throughout India	Kaayam(Ma), bangas (Gr), delekair, miat (En), and nemaaru (Or)	En
9	*M. flavescens* Gamble	Kerala, Tamil Nadu	----------	En
10	*M. gracile* Bedd.	Karnataka, Kerala	Elimaram (Ma), Uchikkaca (Ta)	NE
11	*M. grande* Retz.	Throughout India	Palluvirisa (Ma)	NE
12	*M. heyneanum* Benth.	Karnataka, Maharashtra, Kerala, Tamil Nadu	Kannavu, Kanalai, Kaya (Ot)	NE
13	*M. lawsonii* Gamble	Kerala	----------	En
14	*M. lushingtonii* Gamble	Throughout India	----------	En
15	*M. malabaricum* Clarke	Karnataka, Western Ghats	Gandu, Kepala, Lokundi, Volle Kodi (Ka)	NE
16	*M. manickamii* Murugan *et al.*	Tamil Nadu	----------	NE
17	*M. mundanthuraianum* Viswanathan & Manickm	Tamil Nadu	----------	NE
18	*M. parvifolium* Thw.	Western Ghats	Gisian, Malabahi (Ot)	NE
19	*M. procerum* Thw.	Western Ghats	----------	NE
20	*M. rivulare* Bremer	Kerala		NE
21	*M. royenii* Blume	Kerala, Tamil Nadu, Karnataka	----------	En
22	*M. sisparense* Gamble	Tamil Nadu	----------	CE
23	*M. sivadasanii* Mohanan *et al.*	Kerala	--------	NE
24	*M. sylvaticum* Thw.	Kerala	----------	NE
25	*M. talbotianum* Brandis	Karnataka, Tamil Nadu	Chappalu (Ka), Kancan (Ta)	NE
26	*M. terminale* Dalzell	Karnataka	Smallest Indian *Memecylon* (En)	NE
27	*M. tirunelvelicum* Murugan *et al.*	Tamil Nadu.	----------	NE
28	*M. umbellatum* Burm.	Kerala, Maharashtra, Karnataka	Huli Soppu (Ka), Ironwood tree (En), Kaya (Hi), Anjan (Hi).	En
29	*M. wightii* Thw.	Karnataka, Kerala	----------	NE
30	*M. subramanii Henry*	Kerala	----------	CE
31	*M. sessile Benth.*	Western Ghats	Nedum-schetti (Ma)	NE
32	*M. gracillimum* Alston	Tamil Nadu		Th
33	*M. molestum Cogn.*	Kerala, Tamil Nadu	----------	Th
34	*M. varians Thw.*	Tamil Nadu	----------	NE
35	*M. macrocarpum Thw.*	Tamil Nadu	Maha Kuratiya (Ta)	Th
36	*M. jadhavi Reddy et al.,*	Andra pradesh	----------	NE
37	*M. wightianum Triana*	Kerala	----------	Th
38	*M. rostratum Thw.*	Tamil Nadu	---------	Th
39	*M. madgolense* Gamble	Andra pradesh	----------	NE
40	*M. leucanthemum* Thw.	Tamil Nadu	----------	NE

According to the Plant List [29]. Vernacular names-Ma-Malayalam, Ta-Tamil, Or-Oriya, Gr-Greek, En-English, Hi-Hindi, Ot-others, Red list category-NE-Not evaluated, Th-Threatened, CE-Critically endangered, En-Endangered, Vu-vulnerable.

Taxonomy of *Memecylon* species

Taxonomically, *Memecylon* is one of the most difficult genera and the delimitation of species is mainly by such traditional characters such as shape and size of leaves, position and nature of inflorescence, the length of pedicels, shape and nature of cohesion of the calyx, and the presence or absence of disc rays [12].

Identification of *Memecylon* species is difficult because of closely resembling morphological features. For example, *Memecylon* species determination in Madagascan is based on both morphological and ecogeographic factors have been taken into account because Madagascan is the island where the genus *Memecylon* is radiated extensively throughout Madagascar. Floral morphology is strongly conserved, but leaf morphology and inflorescence positions are quite variable and often diagnostic at the species level. In several cases, different species have converged on similar vegetative morphologies, leading to taxonomic confusion. Comprehensive taxonomic revisions in species-rich groups like *Memecylon* are a prerequisite for further study of the mechanisms of species diversification [13].

In India, Gamble assigns *M. amplexicaule* var. *malabarica* Clark partly to *M. malabaricum* Cogn. and partly to *M. depressum* Benth., the former is confined to higher elevations and the latter to elevations up to 365 m.[14] Even Hooker in Flora of British India

treats *M. depressum* as the synonym of *M. amplexicaule.*[15] Brandis[16] mentioned *M. malabaricum* Cogn. was the accepted name for *M. amplexicaule.* Hence, there is a confusion regarding the taxonomic status of *M. malabaricum, M. amplexicaule* and *M. depressum*. Another species *M. wightii* Thw. also resembles *M. amplexicaule* var. *malabarica* Clarke [17] and Triana united it with *M. amplexicaule*. Based on this ambiguity Saldanha [18] stressed on the need for clarification regarding the relationship between *M. amplexicaule* var. *malabarica* and *M. wightii.*

M. umbellatum Burm. f. embraces a number of varieties, some of which have been raised to specific rank by different authors [14]. Some taxonomists treated *M. umbellatum* and *M. edule* Roxb. as separate species [19]. However, Brandis, [16] Quisumbing, [20] Neginhal [21] and Pullaiah [22] treated *M. umbellatum* as a synonym of *M. edule.* Bhat [23] mentioned that *M. umbellatum* and *M. edule* as conspecific in some of the regional floras, [24-27] Bremer, [28] however, considered them as distinct species. He indicated that *M. umbellatum* is a species of the dry zone and also doubts about its occurrence in India. *M. ovatum* Sm., another species belongs to this complex has been reported from Dakshina Kannada. This species, however, may not be specifically distinct from *M. edule* and at the most may represent a variety of the species. Pullaiah [22] considered *M. molestum* Cogn. and *M. edule* Roxb. var. *molesta* Clarke are similar species.

Nomenclature status of the majority of Indian *Memecylon* species listed in Plant list is under unresolved category [29]. According to IUCN Red list [30] *M. bremeri*, *M. lawsoni*, *M. sisparense* and *M. subramanii* are critically endangered species. *M. clarkeanum*, *M. deccanense*, *M. edule*, *M. flavescens*, *M. lawsonii*, *M. lushingtonii*, *M. royenii* and *M. umbellatum* are under the endangered category. *M. gracillimum*, *M. variens, M. macrocarpum, M. wightianum and M. rostratum are threatened* species (table 1). Two recently identified *Memecylon* species from South India *viz., M. kollimalayana* and *M. ponmudianum* are critically endangered [31]. Therefore, from both the taxonomic and conservation point, the genus *Memecylon* should get proper attention.

Molecular studies

Maximum-likelihood analyses of both internal and external transcribed spacers of nuclear ribosomal DNA sequences in 167 samples of African *Memecylon* species and 22 samples of related genera namely *Lijndenia*, *Mouriri*, *Spathandra*, *Votomita* and *Warneckea* were carried out [32]. Monophyly of *Memecylon* is strongly supported in most of the analyses except 5.8S. It is a sister-group relationship between a small species-group from Western and Central Africa (*Memecylon* subg. *Mouririoidea*, ovary 4-loculed) and the remaining taxa (*M.* subg. *Memecylon*, ovary unilocular). In the combined analysis, series of monophyletic groups of large subgenus namely, *M.* subg. *Memecylon* representing different parts of the widespread paleotropical distribution that includes three distinct groups in Indo-Malaysia apart from African and Madagascan. Based on this analysis three East African species (*M. fragrans*, *M. greenwayi*, *M. semseii*) are returned to *Memecylon* after being erroneously transferred to *Lijndenia* by Borhidi. Further, a key is provided to the two subgenera and twelve sections currently recognized in African *Memecylon*. They emphasized that further study is warranted towards a sectional classification of Indo-Malesian *Memecylon* and for revision of the seven Madagascan sections recognized by Jacques-Félix [32]. However identification of four Indian *Memecylon* species viz., *M. umbellatum*, *M. malabaricum*, *M. wightii*, *M. talbotianium* was done based on ITS sequences (ITS 1, 5.8S and ITS2). The sequences were blasted in NCBI GeneBank for species identification. Genotyping among these species were reduced through the help of phylograms generated from their ITS sequences. Generated rDNA sequence successfully distinguished these species from other closely related *Memecylon* spp [33].

Phytochemistry

Phytochemical analysis of chloroform and ethyl acetate seed extracts of *M. edule* revealed the presence of Alkaloids, triterpenes, flavonoids and saponin [10]. The tannin content was found highest in bark than in leaves, roots and stem of *M. umbellatum* and lowest amount was present in inflorescence and no significant variation was found in fresh and in samples stored up to three years [34]. The phytochemical screening of *M. umbellatum* was carried out and analysis revealed the presence of various phytoconstituents such as phytosterols, terpenoids, glycosides, tannins and flavonoids amino acids, carbohydrates, gum, resins, proteins and other phenolic groups. The extracts were subjected to chromatography in methanol: chloroform (1:9) v/v, which shows better separation of compounds and it is most distinct and clear in iodine vapour and UV light. This study provides promising results for the utilization of this plant as a formulation for the drug to treat diabetes after testing for clinical trials and further analysis [35-37]. *M. terminale* plant extracts revealed the presence of significant levels of alkaloids and flavonoids, and moderate amounts of steroids, tannins, and phenols. Among the extracts, the methanolic extract of the plant contained a good percentage of phenolics [38]. The methanolic extracts of leaves of 32 *Memecylon* species collected from the Western Ghats were evaluated for phytochemicals and pharmacological potential. Results showed that phenolic contents of the methanol extracts were comparatively low in *M. gracile* and *M. depressum* and flavonoid content was high in *M. grande* and lowest in *M. talbotianum* [39].

Anthocyanins reported from *Memecylon* species are Cy-3, 5-diglucoside from *M. amplexicaule* and Mv-3, 5-diglucoside from *M. caeruleum* [40]. Phytochemical constituents from the aerial parts of *M. umbelletum* included β-amyrin, sitosterol, oleanic acid, ursolic acid, sitosterol-β-D glucoside umbe lactone [41]. Joshi *et al.* [42] elucidated the structures of fatty acids such as octocosonoic acid, cerotic acid, ethyl palmitate, palmitic acid and butyric acid based on spectral data from the n-hexane extract of the roots of *M. umbellatum.*

The chemical constituents identified from different species of the genus *Memecylon* are listed in table 2 and fig. 2. The compounds which have been isolated from *Memecylon* species are known to possess several biological properties such as anti-inflammatory, antimicrobial, antidiabetic, antioxidant, anthelmintic anticancer, antiviral and multiple sclerosis properties which is used against several diseases which are listed in table 2.

Different solvent extracts of *M. umbellatum* stem were evaluated to determine the chemical constituents using GC-MS (Gas chromatography-Mass spectrophotometry) analysis. Totally, 20 different compounds from chloroform extract, 11 from petroleum ether extract and 10 from ethanol extract were identified [62]. *M. umbellatum* leaf extract treated with green synthesized silver and gold nanoparticles and the effect of the phytochemicals present in *M. umbellatum*, including saponins, phenolic compounds, phytosterols, and quinones, on the formation of stable silver and gold nanoparticles was investigated by Fourier-transform infrared spectroscopy. The morphology and crystalline phase of the nanoparticles were determined by transmission electron microscopy and energy-dispersive x-ray spectroscopy. The results indicate that the saponins, phytosterols, and phenolic compounds present in the plant extract play a major role in the formation of silver and gold nanoparticles in their respective ions in solution. The characteristics of the nanoparticles formed suggest application of silver and gold nanoparticles as chemical sensors in the future [63].

The methanol extract of *M. edule* contained squalene, palmitic acid, and fatty acid as evident from GC-MS analysis and the related functional group was identified using FT-IR spectra [62]. The GC-MS profile of ethyl acetate extract of *M. edule* showed 26 major compounds with different parentage of peak values. Among them, steric acid was the predominant (20.19%) constituent [64]. The metabolite profiling of methanol extracts of *M. talbotianum* was subjected to UPLC-PDA-ESI/HDMS. Eighteen metabolites were identified, of which synapoyl-hexose-formic acid; kaempferol 3-*O*-feruloylhexosyl rhamnoside; 6-C-arabinosyl-8-C-glucosyl-apigenin and isorhamnetin-3-O-glycoside-7-O-glycoside were the main constituents [49].

In HPLC analysis, rutin, quercetin and protocatechuic acid were found to be the major components present in *M. talbotianum*. The presence of these compounds in this plant species is reported for the first time, and they could be responsible for the antidiabetic activity of *M. talbotianum* [58].

Table 2: Chemical constituents of *Memecylon* species and their mechanism of action

S. No.	Plant name	Part used	Chemical group	Compound name	Pharmacological activity	Mechanism of action	References
1	*M. umbellatum*	Leaf	Ketone	Umbelactone	Antioxidant, radical scavenging, antibacterial, antimutagen, and anticarcinogen	----------	[42] [36]
			Triterpenes	Amyrin, ursolic acid	Inflammation, viral infections, cancer, and diabetes	Inhibition of NF-κB and CREB activation. Ursolic acid is been shown to inhibit JNK expression and IL-2 activation of JURKAT leukemic T cells leading to the reduction in proliferation and T cell activation.	[42] [43] [44]
			Lipid	Sitosterol	Heart diseases, cancer, HIV, rheumatoid arthritis, psoriasis, allergies	Inhibit the production of carcinogens, cancer-cell growth, invasion, and metastasis, and promote apoptosis of cancerous cells (Meric *et al.*2006).	[45] [42]
			Fatty acids	octacosanoic acid, cerotic acid, ethyl palmitate, palmitic acid and butyric acid	multiple sclerosis, diabetes, fibromyalgia, myocardial ischemia	Suppress the transfer of glucose from the stomach to the small intestine and by inhibiting glucose transport at the brush border of the small intestine. Inhibition of proinflammatory cytokines and chemokines, and stimulation of anti-inflammatory ones.	[46] [42] [47]
2	*M. talbotianum*	Leaf	Flavonoids	Apigenin Luteolin Quercetin Kaemferol Rutin Isorhamnetin	Cancer, **inflammation,** diabetes	Increase the intracellular concentration of glutathione, enhancing the endogenous defense against oxidative stress. Strong inhibitor of ornithine decarboxylase, an enzyme that plays a major role in tumor promotion.	[48] [49]
			Phenolics	Gallic acid, Protocatechuic acid, feruloyl quinic acid, Catechins	Neurodegenerative diseases, Diabetic complication, inflammation, helminthic and skin diseases.	By modifying the properties of alpha-synuclein, a protein associated with neurodegenerative diseases. By decreasing the expression of proapoptotic genes (*bax, bad*, *caspase-1* and cyclin-dependent kinase inhibitor). Improve activity of catalase and SOD.	[50] [51] [52] [53] [54] [49]
			Organic acids	Cinnamic acid, Sinapic acid, Ferulic acid.	Chagas' disease, cancer, atherosclerosis, liver and kidney disorders and diabetes	Sinapic acid has been described as chain-breaking antioxidants that probably act as radical scavengers. This function is related to their hydrogen atom donating ability and their ability to stabilize the resulting phenoxyl radicals via the conjugated system comprising the arene and the alkenyl carboxylate side chain. Decrease lipid peroxidation and enhance the level of glutathione and antioxidant enzyme levels.	[55] [56] [57] [58]
3	*M. caeruleum* *M. amplexicaule*	------	Anthocyanin	Mv-3,5-diglucoside Cy-3,5-diglucoside	Cardiovascular disorders	Inhibitory effects on proapoptotic and cardioregulatory genes. Modulating apoptotic regulatory bcl-XL, p53 and c-myc genes.	[40]
4	*M. malabaricum*	Leaf		4,9,14,19-Tetramethyl-1,6,11,16-tetraoxacycloeicos-3,8,13,19-tetraene (Memecylaene)	Inflammation and allergic disorders	unknown	[59] [60]
5	*M. edule*	Leaf	Triterpenes, tannins, and flavonoids	unknown	unknown	unknown	[61]

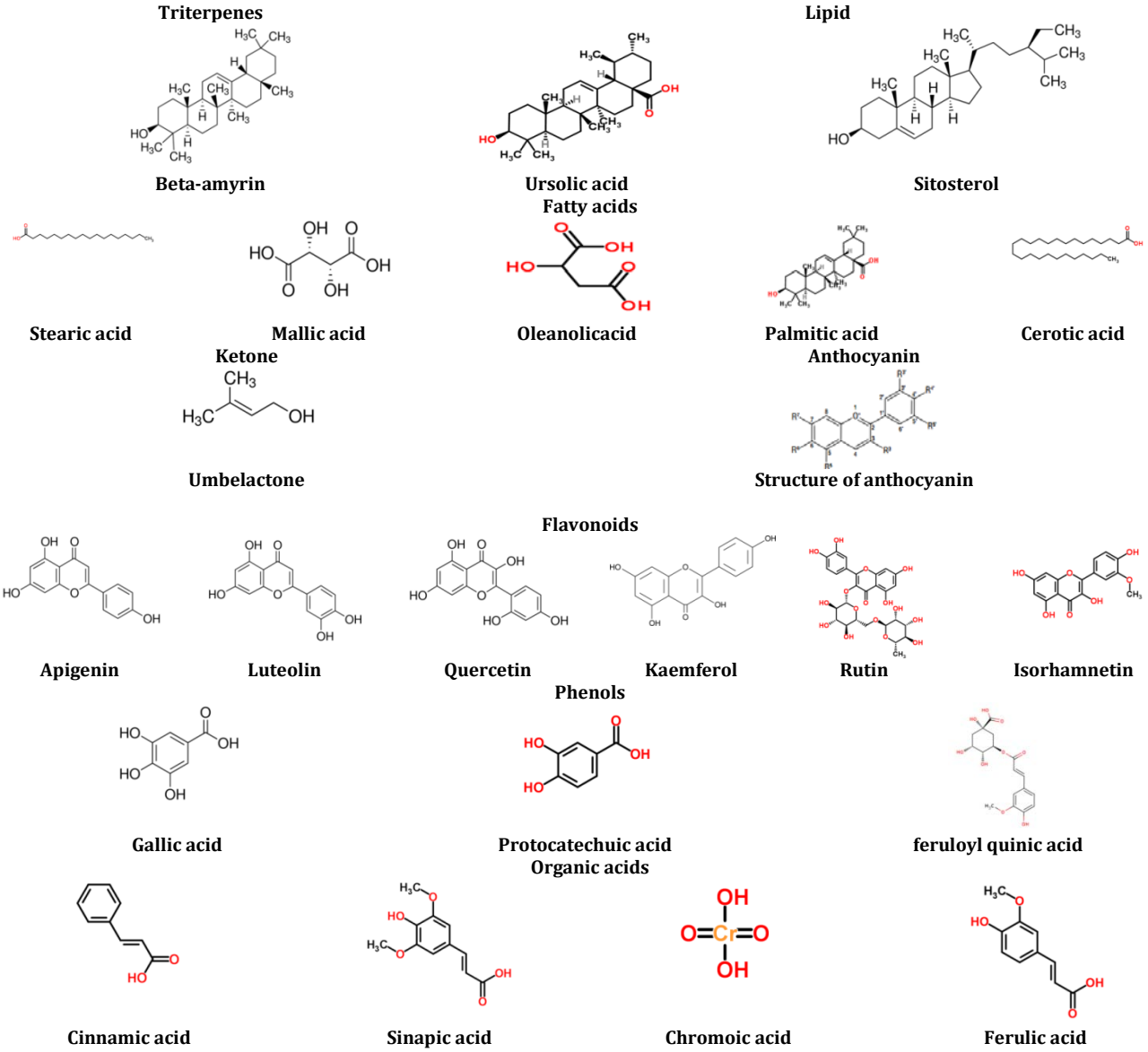

Fig. 2: Structures of chemical constituents reported from *Memecylon* species

Pharmacological potential of *Memecylon* species

Antidiabetic activity

The oral administration of alcoholic extracts of the leaves of *M. umbellatum* led to a significant lowering of serum glucose level in normal and alloxan-induced diabetic mice. The result indicated the *M. umbellatum* has interesting possibilities as a source of oral hypoglycemic agent. Methanolic extract of *M. malabaricum* also showed a similar effect when compared to standard reference gliclazide [65, 59]. The acute toxicity studies of *M. umbellatum* revealed no side effect on the liver and kidney as evident by the significant reduction in urea and creatinine level as compared to diabetic control. The chronic studies confirmed a gain in body weight of the extract administered rats [66]. Antidiabetic and anti-hyperglycemic potential of *M. umbellatum* were analysed for different solvent extracts like hexane, ethyl acetate, and methanol. Inhibition of α-amylase, nonenzymatic glycosylation of hemoglobin, the glucose diffusion assay and the glucose uptake by the yeast cells were used to evaluate antidiabetic potential. Methanol extracts showed higher antidiabetic activity. In glucose diffusion assay significant inhibition of glucose movement at various time intervals was observed when compared to control [37].

The administration of oral doses of *M. talbotianum* leaf methanol extract (MTLME) decreases the glucose level after four weeks in diabetic animals in MTLME treated animals along with controlling the levels of TG in diabetic and in treated animals and endogenous antioxidants including SOD, Catalase and GSH. Histopathological and immunohistological studies of the pancreas showed the protective effect of MTLME extract on intraoral administration [58].

Anti-inflammatory activity

The alcoholic leaf extract of *M. umbellatum* was examined for wound healing potential in the form of ointment (0.5, 1.0 and 2% w/w), the excision and the incision wound model in rats. The extract induced a significant response in both the wound models as compared to the standard drug nitrofurazone ointment (0.2%w/w) [67]. The ethanolic extract of *M. umbellatum* was evaluated for anti-inflammatory activity using acute rat model by carrageenan induced rat paw edema and a sub-acute rat model by cotton pellet induced granuloma. The extract showed significant anti-inflammatory activity in both the animal models and the weight of adrenal glands were also found to be significantly increased in extract treated animals. The results show the dose-dependent anti-inflammatory activity [68].

The anti-inflammatory activities of the leaves of *M. edule* were determined for different solvent extracts such as hexane, ethyl acetate, methanol, and ethanol. The most active fraction was further tested *in vivo* for its anti-inflammatory activity using the ethyl phenyl propiolate (EPP)-induced mouse ear edema and the writhing test in mice administrated orally 200 mg/kg of ethyl acetate (EtOAc) caused a significant inhibition of the writhing response by 56.6% [69].

Memecylaene, a novel compound isolated from *M. malabaricum* and this compound was tested for anti-inflammatory activity in albino rats in acute and sub-acute animal models. Analysis of biochemical parameters, such as antioxidant enzyme activities from granuloma, lipid peroxidation inhibition in the liver of granuloma induced rats, as well as mucopolysaccharides from the granuloma was carried out. Memecylaene treatment significantly increased the antioxidant enzyme activities (CAT, SOD and GPx ($P<0.05$). Inhibition of lipid peroxides in liver and mucopolysaccharides in granuloma tissue. The anti-inflammatory activity of Memecylaene showed in both the models of inflammation which is attributed to their antioxidant and phospholipase A2 inhibitory activities. Thus, the study validated the scientific rationale of ethnomedicinal use of *M. malabaricum* to inflammatory associated diseases and unveils its mechanism of action [60].

Different solvent extracts of *M. talbotianum* were evaluated for anti-inflammatory properties. Methanol extract exhibited highest inhibition for xanthine oxidase (IC50 12.56 mg/ml) and 15-lipoxygenase (IC50 1 mg/ml) [70]. *In vitro* antispasmodic activity was evaluated using ethanol plant extract of the *M. umbellatum* using rat ileum. The extract at a concentration of 50, 100, and 200 mg exhibited inhibition respectively, against acetylcholine-induced contraction in isolated rat ileum preparation. The antispasmodic activity may be due to its cholinergic system blockade. This study reveals that the extract antagonizes the contraction in ileum stimulated by acetylcholine, indicates that the extract shows atropine-like action [71]. Dhar *et al.* [72] reported that the crude plant extract of *M. umbellatum* had anti-amphetamine and spasmolytic activity against Ranikhet disease virus.

Antioxidant activity

The methanol extract of *M. umbellatum* leaf was evaluated for *in vitro* antioxidant activity and *in vivo* antinociceptive effect in acetic acid induced writhing model in Swiss albino mice. The plant extract was also subjected for brine shrimp lethality bioassay to evaluate its cytotoxic property. The results revealed the antioxidant property as compared with the ascorbic acid used as standard and a dose-dependent (250 and 500 mg/kg) analgesic effect. The investigation also showed that it has strong lethality (LC50 1.178 µg/ml) against brine shrimp nauplii compared with vincristine sulphate used as positive control. The antioxidant, antinociceptive and cytotoxic properties support the traditional uses of *M. umbellatum* [73].

The antioxidant activities of the solvent extract of the leaves of *M. edule* were determined by different solvent extracts such as hexane, ethyl acetate, methanol and ethanol of the dry leaves were tested *in vitro* for their interleukin-10 production. At 200 mg/kg orally, the EtOAc caused a significant inhibition of the writhing response by 56.6% which was like indomethacin at 10 mg/kg. EtOAc, MeOH and MeOH50 exhibited radical scavenging activity [69].

Different solvent extracts of *M. talbotianum* was evaluated for antioxidant properties. Methanol extract exhibited with greater reactive oxygen species scavenging activity, DPPH, ABTS, superoxide radical scavenging activity (SRSA) and reducing power properties reported [74].

M. terminale plant extracts were screened for antioxidant properties. The methanol extract showed a dose-dependent antioxidant activity [38]. The methanolic extracts of leaves of 32 *Memecylon* species collected from the Western Ghats were evaluated for pharmacological evaluation. The highest antioxidant activity was observed for *M. heyneanum* [39].

Hepatoprotective activity

The hepatoprotective effect of *M. umbellatum* roots against acetaminophen induced hepatotoxicity in rats was evaluated. An oral dose of 200 or 400 mg/kg produced significant hepatoprotection by reducing elevated levels of serum enzymes and restored normal histological features of the liver, when compared to the control group [75]. The leaf extracts of *M. umbellatum* also showed significant hepatoprotective activity [76]. Pretreatment of rats with the root extract exhibited marked protection against carbon tetrachloride hepatotoxicity. The results showed that the extracts decreased the level of SGOT, SGPT, ALP, γ-GT and bilirubin at the dose of 400 mg/kg, comparable to standard drug silymarin. The result also showed that the ethanolic extract treated groups have significantly shorten the thiopental sleeping time in rats as compared to animals receiving CCl4 alone [75].

Nephroprotective activity

Ethanol extract of *M. umbellatum* root was investigated for nephroprotective activity against cisplatin-induced acute renal damage in rats. The extracts at 100 to 400 mg/kg body weight showed a dose-dependent reduction in elevated blood urea, serum creatinine and also normalized the histopathological changes in the curative regimen. These findings suggest that the apparent system of nephro protection by *M. umbellatum* [77].

Analgesic activity

The ethanol extract of *M. umbellatum* root was evaluated for its central and peripheral analgesic activity in tail-flick, hot plate and acetic acid induced writhing models. The plant extract showed more prominent peripheral effect than the central effect [78]. The analgesic activities of the solvent leaf extract of *M. edule* was determined by the ethanol extract showed interleukin-10 production [69]. *M. terminale* plant extracts were screened for analgesic and RBC protective activity. The results showed a dose dependent activity [38]. The ethanol extract of *M. umbellatum* was evaluated for anti-pyretic activity in yeast induced pyrexia model in rats. A dose dependent reduction in yeast induced hyperpyrexia was observed in rats when compared to the standard drug paracetamol [78].

Antihelmintic activity

Aqueous and ethanol leaf extracts of *M. malabaricum* were evaluated for their antihelmintic activity against *Pheritima posthuma* which involved the determination of time of paralysis and time of death of the worms. Both the extracts exhibited highly significant antihelmintic activity at the highest concentration of 60 mg/ml. Piperazine citrate was included as the standard reference and normal saline as control [79].

Anticancer activity

Apoptogenic and anti-proliferative activity of ethyl acetate extract of *M. edule* leaves (EtAc-LME) in gastric cancer cell lines and non-cancerous gastric mucous cells, and the mechanism of EtAc-LME induced apoptosis was determined by analysing the activation of pro-caspases, PARP cleavage, expression of cytochrome-c (Cyt-c) by western blotting, mRNA expression of Bcl-2, Bax by RT-PCR, loss of mitochondrial potential using DiOC6 dye, annexin binding assay and its influence on cell cycle arrest by flow cytometry. The results showed that EtAc-LME inhibited the gastric cancer cell growth in dose-dependent manner and cytotoxicity was more towards the gastric cancer cells (NUGC and MKN-74) compared to normal gastric cells (GES-1), suggesting more specific cytotoxicity to the malignant cells. Over expression of Cyt-c and subsequent activation of caspases-3 and down regulation of Bcl-2 and loss in mitochondrial potential in EtAc-LME treated MKN-74 and NUGC cells suggested that EtAc-LME induced apoptosis by mitochondrial dependent pathway. Hence the study suggests that ethyl acetate extract of *M. edule* induces apoptosis selectively in gastric cancer cells emphasizing the importance of this traditional medicine in the treatment of gastric cancer [80].

Antimicrobial activity

Alcoholic extract of *M. umbellatum* was evaluated for its antimicrobial activity, and the study showed maximum antibacterial activity against *Staphylococcus aureus* (Gram positive) and it also showed antibacterial activity against Gram-negative bacteria, and also alcoholic extract alone showed slight antifungal activity [81-82].

Different solvent extracts were screened for antimicrobial activity using both polar and nonpolar solvents among all the extracts ethyl acetate, and methanol extracts of seed and leaves have shown activities when compared to other extracts. [34, 83] The petroleum ether, chloroform, and ethanol leaf extract showed concentration-dependent activity against all the tested bacteria with zone of inhibition at various concentrations [35-36].

Memecylon edule methanol extracts were investigated against Gram-positive (*Staphylococcus aureus, Staphylococcus epidermidis*, *Micrococcus luteus* and *Bacillus cereus*) and Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *Kelebsiella pneumonia*) and fungi such as *Aspergillus niger*, *A. fumigatus* and *Candida albicans* by disc diffusion method. Antimicrobial studies revealed that both the extracts have significant activity against gram-positive, gram-negative bacteria and fungus [82]. Chloroform and ethyl acetate seed extracts showed moderate antibacterial activity and secondary metabolites of this plant used for wound healing property and other forms of bacterial infections [10]. Ethyl acetate extract showed antibacterial and antifungal activity against *Salmonella typhimurium* and *S. pneumonia* [64, 85, 86] and Vivek [84] reported the antimicrobial activity of methanol extracts of *M. malabaricum*, *M. talbotianum*, *M. edule*, *M. umbellatum* and *M. wightii* leaves against both Gram-positive and Gram-negative bacteria and fungi.

The antibacterial activity of *M. talbotianum* was determined against human pathogens through disc diffusion, (MIC), (MBIC) test as visualized by Alamar blue and confocal laser scanning microscopy. (MIC for Gram-positive bacteria 54 µg/ml). The bacterial cells were lysed at 24 h incubation resulting in nearly a 4 log10 CFU/ml drop in cell viability at 1.6 X MIC for the methanol plant extract. The extract at two-fold MIC inhibited the bacterial biofilm formation and at 8 fold MIC eradicated the biofilm. The extract was less effective on Gram-negative bacteria [49].

Memecylon terminale plant extracts were screened for antibacterial activity; results showed a dose-dependent antibacterial activity against different Gram-positive and Gram-negative bacterial strains [38]. The methanolic extracts of leaves of 32 *Memecylon* species were evaluated for antibacterial activity, and a broad spectrum of antibacterial activity was observed in *M. clarkeanum* and *M. sessile* [39].

Genotoxic studies

The antigenicity studies of *M. umbellatum* alcoholic leaf extracts were carried out against cyclophosphamide-induced chromosomal aberration and micronucleus formation. The results showed that these extracts had prevented the genotoxicity of cyclophosphamide. The frequency of chromosomal aberration and micronucleus (MN) although not significant statistically, the percentage aberration and MN formation appeared to be dose and time dependent. There was a slight depression in the mitotic index compared to negative controls. Thus, the extracts were found to be non-mutagenic on bone marrow cells of mice. The antigenocity studies are directly related to the protective role of the extracts on the genetic material [76].

Tissue engineering studies

Electrospinning studies were carried out for skin tissue engineering in four different plant extracts namely *Indigofera aspalathoides*, *Azadirachta indica*, *Memecylon edule (ME)* and *Myristica andamanica* along with a biodegradable polymer, polycaprolactone (PCL). The ability of human dermal fibroblasts (HDF) to proliferate on the electrospun nanofibrous scaffolds was evaluated via cell proliferation assay. HDF proliferation on PCL/ME nanofibers was found the highest among all the other electrospun nanofibrous scaffolds, and it was 31% higher than the proliferation on PCL nanofibers after 9 d of cell culture. The interaction of HDF with the electrospun scaffold was studied by F-actin and collagen staining studies. The results confirmed that PCL/ME had the least cytotoxicity among the different plant extract containing scaffolds studied here. Early and intermediate epidermal differentiation of adipose derived stem cells was performed on PCL/ME scaffolds. The study demonstrated the potential of electrospun PCL/ME nanofibers as substrates for skin tissue engineering [87].

CONCLUSION

In India the genus *Memecylon* is represented by about 40 species, out of which 21 species are endemics. Taxonomic status of the Indian *Memecylon* species is not clear owing to complexity in their morphology. Molecular biology offers different techniques to solve taxonomical confusions. However, molecular work has not been conducted on Indian *Memecylon* species. Therefore, molecular studies should be conducted on Indian *Memecylon* species to resolve their taxonomical and nomenclatural problems. *Memecylon* species have shown potential pharmacological activities such as anti-inflammatory, antidiabetic, antiviral, hepatoprotective, antimicrobial and antioxidant activity. Few studies have revealed the compounds responsible for these bioactivities. However, exact mechanism of action of bioactive compounds from *Memecylon* species is not known. If future studies throw a light on these aspects, definitely it will help in developing a potential biopharmaceutical product. In addition *Memecylon* species show great promise in developing a drug to cure herpes and other skin ailments.

CONFLICT OF INTERESTS

Authors do not have any conflict of interest

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