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Review

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Phytochemical and Pharmacological potential of *Flemingia* Roxb. ex W.T.Aiton (Fabaceae)

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Abstract

The *Flemingia* genus is an important source of medicinal natural products, particularly Flavonoids and steroids. The collected information is an attempt to cover the more recent developments in the ethnobotany, pharmacology and phytochemistry of this genus. The review includes 39 references on the genus *Flemingia*, and comprises ethnopharmacology, morphology, phytoconstituents, pharmacological reports, clinical study and adverse effects of the prominent species of *Flemingia*. A few species of this genus have medicinal value, among these, *F.strobilifera ,F.macrophylla, F.chappar* (Fabaceae) have been traditionally used in the treatment of epilepsy, insomnia, ulcer, pain ,swelling. Despite a long tradition of use of some species, the genus has not been explored properly. In the concluding part, the future scope of *Flemingia* species has been emphasized with a view to establish their multifarious biological activities and mode of action. The information summarized here is intended to serve as a reference tool to practitioners in the fields of ethnopharmacology and natural products chemistry.

Keywords: *Flemingia strobilifera*, *F. macrophylla*, *F.chappar*, Fabaceae, Flavonoids

Introduction

Many infectious diseases are known to be treated with herbal remedies throughout the history of mankind. Herbs are widely exploited in the traditional medicine and their curative potentials are well documented. In many developing countries traditional medicine is one of the primary health care systems. India is a varietal emporium of medicinal plants and is one of the richest countries in the world in regard to genetic resources of medicinal plants. The agro-climatic are favourable for introducing new exotic plant. In India, Herbal medicines have been the basis of treatment and cure for various diseases. About 1500 plants are systematically used in indigenous system of medicine, like Ayurveda, Unani and Siddha. However, the ethno pharmacologists, botanists, microbiologists and natural-product chemists world over today are constantly in search of medicinal efficacy of plants and their photochemical [1]. A well known objective for studying medicinal plants is the discovery of new bioactive components, in the search for promising drugs. The *Flemingia* genus has been instrumental in the discovery of medicinal natural Products. This review emphasizes the traditional uses and clinical potential of *Flemingia* species. Through this review, authors hope to attract the attention of natural product researchers through out the world to focus on the unexplored potential

of *Flemingia* species. This genus needs to be investigated systematically so that potential species can be exploited as therapeutic agents. This review has been compiled using references from major databases as Chemical Abstracts, Medicinal and Aromatic Plants Abstracts, Pubmed, King's American Dispensatory, Henriette's Herbal Homepage, Duke's Phytochemical and Ethnobotany. The available information on *Flemingia* has been divided into four sections, i.e., ethnopharmacology, morphology, phytoconstituents, pharmacological reports. The reports in which *Flemingia* species have been used as a domestic remedy by common men without any prescription for the treatment of various ailments have been discussed under ethnopharmacology.

The genus Flemingia

Flemingia is a genus of flowering plants in the legume family, Fabaceae. It belongs to the sub family Faboideae (Papilionaceae) and is the major group of Angiosperms**.** native of the tropical and subtropical regions of the old world. About 15 species occur in India. [2]

Scientific Classification

Kingdom : Plantae
Division : Magnoliophyta
Class : Magnoliopsida
Order : Fabales
Family : Fabaceae
Subfamily : Faboideae
Genus : *Flemingia (Flemingia* Roxb. ex W.T.Aiton)
Species : *F. chappar - F. faginea - F. grahamiana -F. lineata - F. macrophylla -F. philippinensis -F. procumbens -F. prostrata -F. semialata -F. strobilifera- F.vestita*.[3]

The *Flemingia* Roxb. ex Ait. was founded in 1812. There are about 39 species. They are grouped into five sections. There are 16 species and one variety in China. They are situated in southwestern part of this country at between latitude 18°to 30°N. and longitude 98°to 121°E. China is very rich in species of *Flemingia* as compared with neighboring countries such as India 15 species, Burma 16 species, Thailand 11 species, Laos 10 species, Vietnam 8 species, Bhutan 1 species, Bangladesh 3 species, Cambodge 3 species and Nepal 5 species.[4]

Genus Flemingia has been described as Shrubs or subshrubs, rarely herbs, erect or trailing. Leaves digitately, 3-foliolate or simple; stipules persistent or caduceus; stipels absent; leaflets usually with sessile glands abaxially. Inflorescence axillary or terminal, racemose or compound racemose, rarely paniculate or capitate. Bracts 2-columned; bracteoles absent. Calyx 5-lobed; lobes narrow and long, lower one longest; tube short. Corolla longer than calyx or included; standard oblong or elliptic, base clawed, with auricles; wings very narrow, auriculate. Stamens diadelphous; vexillary stamen free; anthers uniform. Ovary subsessile; ovules 2; style filiform, glabrous or slightly hairy; stigma small, capitate. Legume elliptic, dehiscent, inflated, not septate. Seeds 1 or 2, almost orbicular, without strophiole. [5]

Ethnopharmacology

Traditional uses

In wealth of India it has been reported that roots of *Flemingia chappar* and *F.strobilifera* are used by santals in epilepsy, hysteria, insomnia and to relieve pain. [2] Traditional healers of Jashpur region of chhattisgarh uses roots of *Flemingia chappar* (salpan) in the treatment of epilepsy, insomnia, acidity and stomach disorders.[6] In Bihar the people of santhal tribes use 1 to 2 drops of juice extracted from pressed seeds put in the eyes as a remedy in eye troubles and to remove cataract. In Madhya Pradesh the *Flemingia chappar* Ham. is known as 'Galphule', in Gamharia (Raigarh) of Madhya Pradesh, the leaf juice mixed with seven drops of mustard oil and a little amount of jaggery is used in eye pain by the tribal people.[7] In Burma the roots of *F.strobilifera* are used to treat epilepsy[8]. The Assamese take a small portion of the root of *F.strobilifera* in order to induce sleep and, it is said, even under great pain heavy sleep is brought on according to the quantity of root taken. There are no ill effects [9]. The leaves of *F.strobilifera*

are reported to be used in Java as vermifuge for children [2]. Dried bracts are used for stuffing pillows and cushions. In Malay Peninsula a decoction of it is administered as a post partum protective medicine and as a lotion to treat rheumatism. In the Philippines a decoction/infusion of the leaves and flowers is prescribed by "curanderose" against tuberculosis [8]. In India, root paste applied externally to body swellings. In Nepal, Root juice (fresh roots crushed in cup of water by mortar and pestle) is taken twice daily for 7 days for diarrhea and dysentery.

In Trinidad and Tobago, it is used for kidney problems [10].

In Gamharia (Raigarh) of Madhya Pradesh, the root decoction of *Flemingia macrophylla* (Mahadeokama) 50 ml. is administered orally three times daily in spermatorrhoea by the tribal people [7]. The roots of *F.macrophylla* are used by santals as an external application to ulcers and swellings, mainly of the neck [9]. The pods of *F.macrophylla* and *F.grahamiana* yield Warrus. Warrus is a dull purplish resinous powder somewhat similar to "kamala" powder (from *Mallotus philippensis* Muell.Arg.) and is obtained from the dried pods of the plants by gentle shaking and rubbing to denude them of their outer hairy covering. It is used in dyeing silk and to a lesser extent wool. In Arabia warrus is employed as a cosmetic, anthelmintic and a remedy for cough and chills [2]. *F.grahamiana* is used externally for skin disease and internally as a purgative and specific for cold [2]. The tuber and roots of *F.tuberosa* are sweet, astringent, useful in dysentery and vagianal discharges (leucorrhoea) [9]. The roots of *F.nana* are used in ulcers and swellings [8]. A decoction of the tubers of *F.vestita* is used as a vermifuge. The outer skin of the tubers is used as an anthelmintic and fish poison [12]. *F.lineata* Roxb. is an undershrub occurring throughout India at lower elevations. It has been tried as a green manure plant. The ash of this plant is made into paste with coconut oil and applied over the affected part in skin diseases [2].

Morphology

F.chappar Ham.ex Benth (synonym: *Moghania chappar*), is a shrub 0.9-1.2m high, the branches terete, apprised tawny pubescent. Leaves 1-foliolate, cordate-orbicular, on a 3.8cm long petiole. Flowers small, yellowish, very shortly pedicelled, forming a small rusty pubescent cluster perfectly enclosed in the complicate large floral bracts and forming axillary and terminal large bracted racemes. In Hindi it is known as Salpan [2].

F.strobilifera R.Br. commonly known as kusrunt in Hindi is an erect much branched shrub 1.2-3m high, branches slender, terete, pubscent towards the pith. Leaves 1-foliolate, ovate lanceolate, petioles 0.6-2.5cm long, pubescent, flowers white or pinkish, covered by large folded bracts, pods oblong, densely hairy, containing one or two seeds [1, 11, 12]

F.grahamiana is a low erect shrub, with tomentose young shoots. Petiole 1.3-2.5 cm., spikes dense ,oblong,2.5-5cm long , often fascicled , bracts under 1.3 cm long ,erect – patent,subpersistent. Calyx 1 cm, teeth plumose. Pods oblong, 1 cm long, finely pubescent, and often covered with red viscous glands [9].

F.tuberosa Dalz is a perennial trailing herb or undershrub with tuberous roots, edible, 5 cm long. Stems 2-3 ft long, copiously branched, pubescent, leaves trifoliolate with oblong lanceolate leaflets. Flowers lilac, pods oblong, glabrous, 1-2 seeded [9].

F.nana Roxb. is about 15-20cm high, stem scarcely any, about 2.5 cm above ground ,woody perennial ,branches few, short, subherbaceous.Leaves 3-foliolate, petioles 2.5-7.5 cm long ,winged. Flowers numerous, in axillary elongate slender racemes 7.5-10cm long. Calyx 4mm long, pubescent and covered with ferruginous glands. Pods 8.4 mm long, oblong, turgid, clothed with a greenish grey tomentum and covered with viscid reddish glands. Seeds2, round [9].

F.vestita Benth.is a much branched trailing herb with tuberous roots, found throughout the Himalayas and Khasi hills. Stems 1-3ft long, hirsute, wiry, leaves trifoliolate with obovate –

cuneate leaflets, flowers bright red, pods subcylindrical, hairy, 1 seeded [2,9].

F.macrophylla (willd.) Kuntze is commonly known as Barasalpan in Hindi. It is an erect shrub, 4-6 ft in height, with sulcate silky young branches, occurring at lower elevations throughout India and in Andman Islands. Leaves digitately trifoliolate, flowers in racemes purple, pods oblong, tomentose 2 seeded [2, 8].

F.strobilifera

F.macrophylla

F.chappar

Phytoconstituents

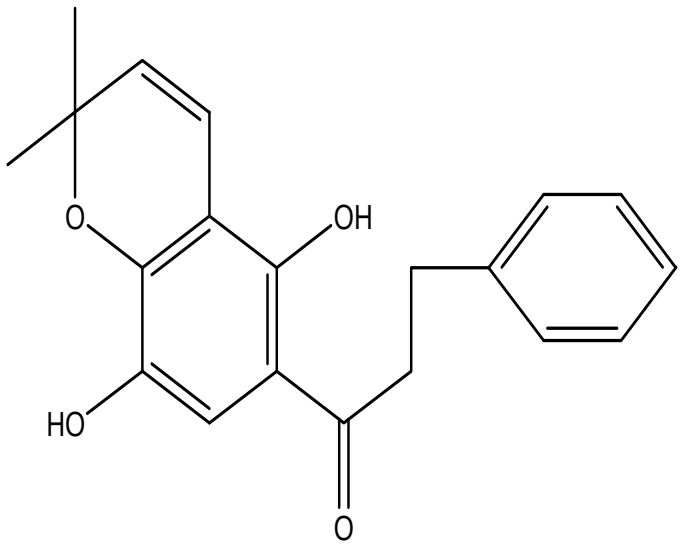
The available literature on phytochemical reports of the genus Flemingia reveals that the *Flemingia* species comprise mainly flavonoids. Table 1 summarizes phytoconstituents reported from various species of *Flemingia.*

Pharmacological reports

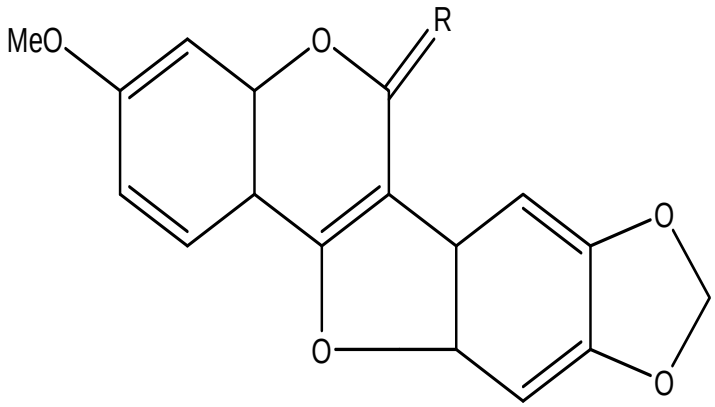
Ethanolic extract (50%) of aerial parts of *F.chappar* has been reported as anticancer. Root pounded or powdered is given orally in filarial. Flemichapparins isolated from *F.chappar* possess antifungal activity. Pounded root of *F.strobilifera* was used for fever. Leaf decoction is used as tonic for sick animals [31]. The methanolic extract of F. strobilifera root and leaf posseses good antioxidant activity, which might be helpful in preventing the progress of various oxidative stresses [32]. Flemingiaflavanone isolated from *F.strobilifera* showed significant antimicrobial activity against Gram-positive (S.aureus, S. epidermidis, MRSA), Gram-negative bacteria (Ps. aeruginosa, E. coli) and fungi (C.albicans)[27]. Anil kumar KV reported the anti-ulcer effect of chloroform extract of *F.strobilifera* root. Anti-ulcer effect was evaluated by water immersion induced ulcer in rats. Pretreatment with Chloroform extract of *Flemingia strobilifera* root at a dose of 15 and 30 mg/kg body wt. increased the gastric mucosal glutathione level, total protein content

Table: 1 Phytoconstituents of various species of *Flemingia.*

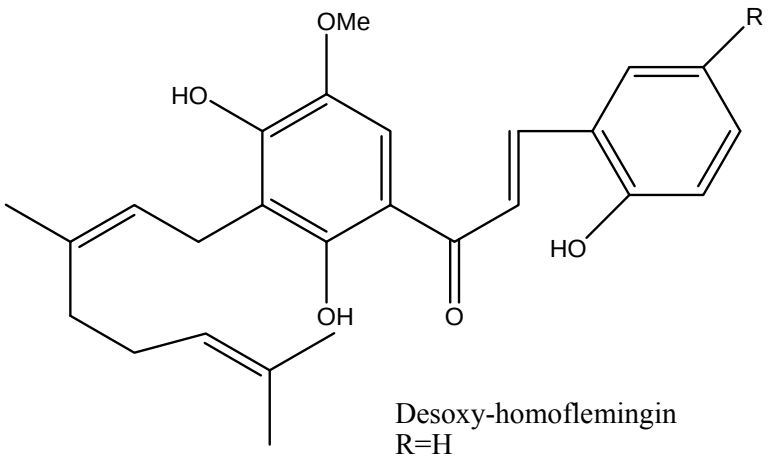
F.chappar	Flemichapparin A, B and C, anthocyanin, β-sitosterol, 7-hyrdoxyflavanon, 2', 4' –di- OH-5'MeO-chalcone. 2', 4' –di- OH & 2'4'4-tri-OH chalcones [13,14,15]
F.macrophylla (willd) Merr.	Flavanones, flemiflavanone A-D, narigenin, genistin, genistein, 5,7,2,4-tetrahydroxyisoflavone, flemichinA,B,C and D FleminginsA,B and C,D , homoflemingin, chalcone, Myricitrin,robinin, homoflemingin , flemiwallichin C and flemistricainsD, E and F, Lupeol, α-amyrin, sitosterol, procyanidin, mix. of dialkyl ph ,fleminone,flemiphyllin[16,17,18,19,20,21,22].
F.strobilifera R.Br.	Quercitin, rutin, quercimeritin.leptosidin,leptosin,phloridzin and naringin, chalcones, n-triacontane, sitosterol, 3,6,dihydroxy2,4,5,4tetramethoxychalcone[23,24,25,26].
F.vestita Benth.	Isoflavanoids, genistein, formononetin, pseudobaptigenin and daidzein [27,28].
F.grahamiana wight & Am.	Flemingins A-C, desoxy and homoflemingins [2, 29].
Flemingia philippinensis	5,7,3',4'-tetrahydroxy-6,8-diprenylsilflavone, flemichin D, beta-sitosterol, lupeol, flemiphilippinin C, flemiphilippinin D, flemiphilippinins E and F [30].



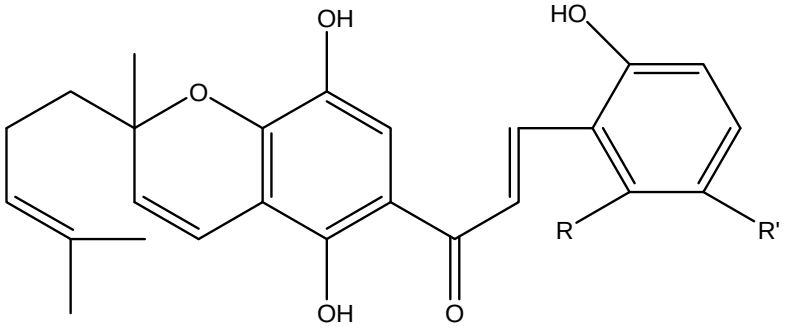
Flemichapparin A



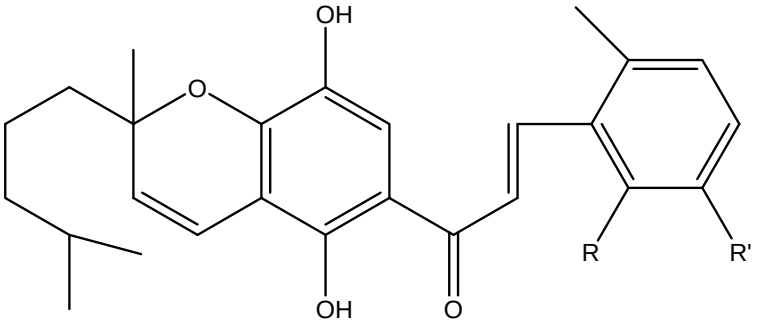
FiemichapparinB
R=H,H
FlemichapparinC
R=O



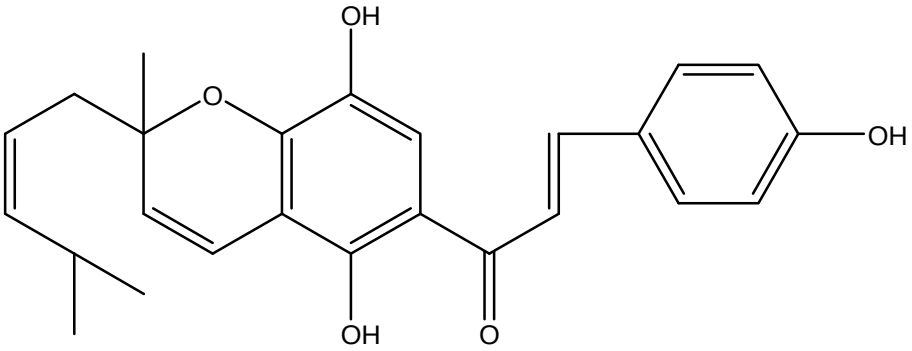
Desoxy-homoflemingin
R=H
Homoflemingin
R=OH



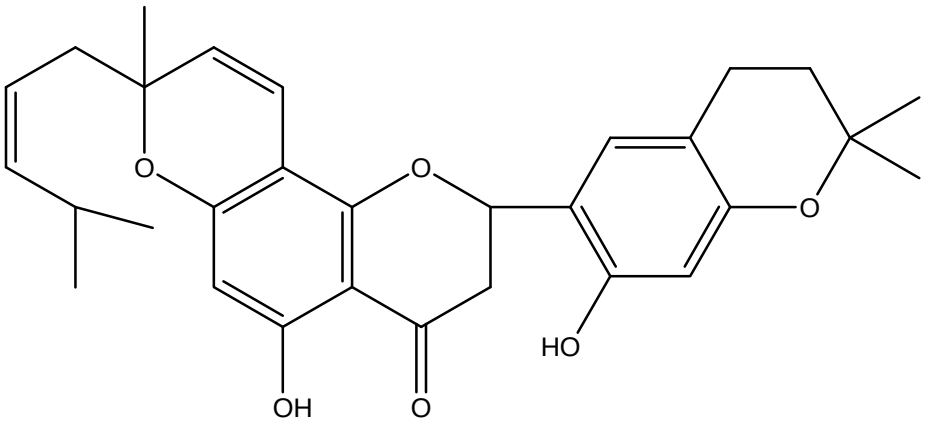
FleminginA
R,R'=H
FleminginB
R=OH,R'=H
FleminginC
R=H,R'=OH



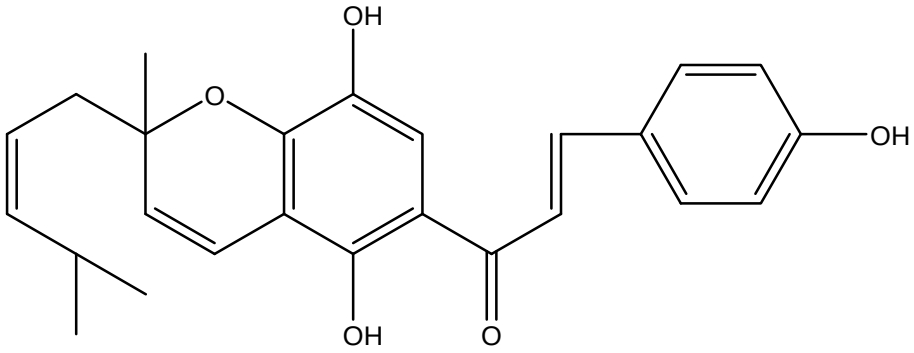
FleminginA
R,R'=H
FleminginB
R=OH,R'=H
FleminginC
R=H,R'=OH



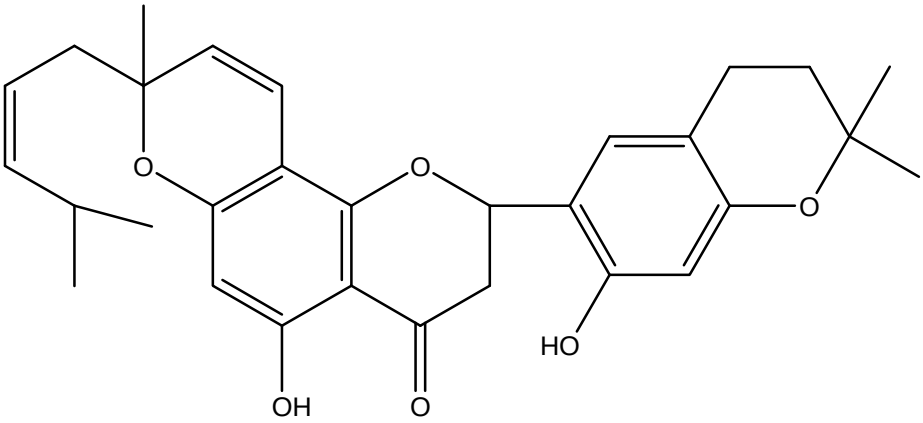
FleminginD



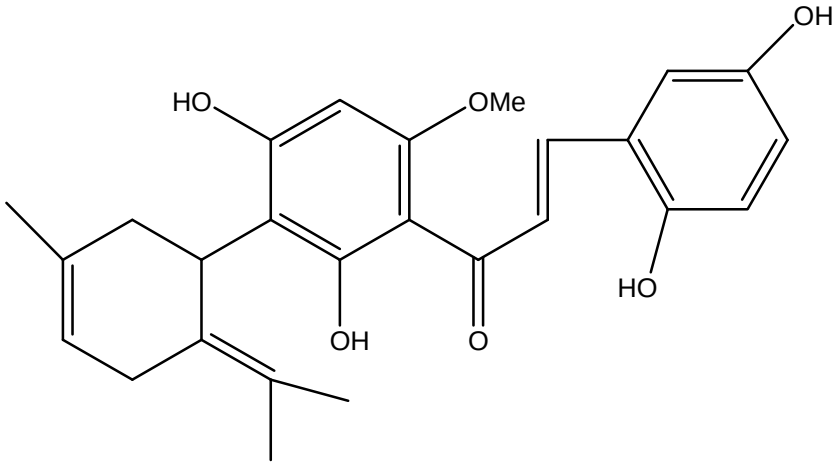
FleminchinA



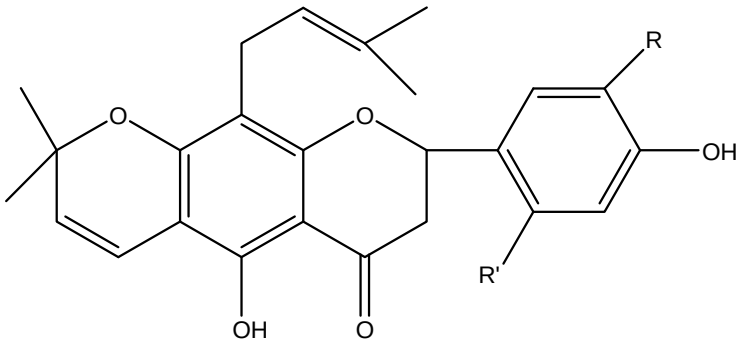
FleminginD



FleminchinA

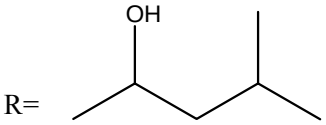


Flemiwallichin C

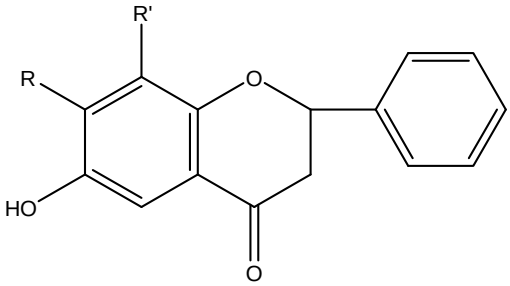


FleminchinB,R,R'=H

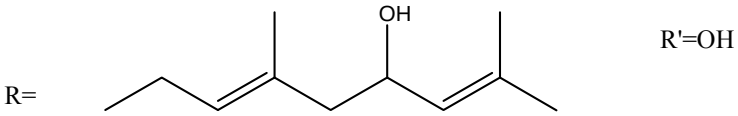
FleminchinC



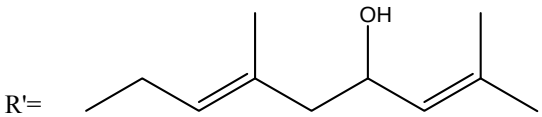
FleminchinD
R=H, R'=OH

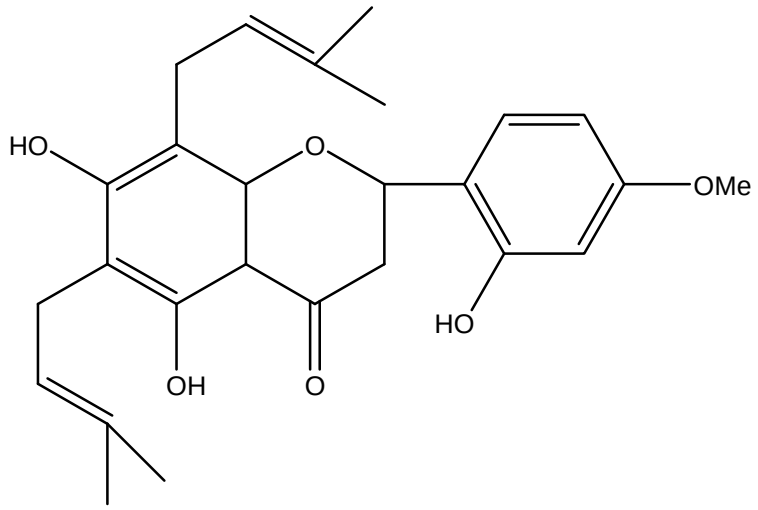


FlemiflavanoneB



FlemiflavanoneC, R=OH





Flemiflavanone A

significantly (P<0.001) as compared to control group. Whereas there is significant (P<0.05, P<0.001) reduction in gastric mucosal Malonaldehyde levels when compared to control [33]. An *in vitro* study showed that a 75% ethanolic extract of *F. macrophylla* (FME) inhibited osteoclast differentiation of cultured rat bone marrow cells, and the active component, lespedezaflavanone A (LDF-A), was responsible for that [34]. Aqueous extract of *Flemingia macrophylla* (AFM) has protective effect against hepatic injury induced by CCl_4. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were detected as biomarkers in the blood to indicate hepatic injury. Oral administration of AFM, 0.5 g/kg and 1.0 g/kg doses significantly decreased ALT and AST, attenuated the histopathology of hepatic injury, ameliorated oxidative stress in hepatic tissue [35]. Shiao et al. reported the neuroprotective action from flavonoids of *F. macrophylla* [36]. Tubers of *Flemingia vestita* have been reported as anthelmintic The root-tuber peel of *F. vestita* and its active component, genistein, were tested in respect of glucose metabolism in the cestode, Raillietina echinobothrida. Live R. echinobothrida, collected from the intestine of freshly slaughtered domestic fowl, were incubated at 39+/-1 degrees C in defined concentrations of the root-peel crude extract (5 mg/ml), genistein (0.2 mg/ml) and praziquantel (1 microg/ml) in phosphate buffered saline with 1% of dimethyl sulphoxide with simultaneous maintenance of controls. In the treated worms, there was a significant decrease in the glycogen concentration accompanied with the decrease of glucose by 14-32% [37].The alcoholic crude root-peel extract of *Flemingia vestita* and its major isoflavone, genistein, have been shown to have a vermifugal/vermicidal effect by causing a flaccid paralysis accompanied by alterations in the structural architecture of the tegumental interface and metabolic activity in *Raillietina echinobothrida*, the cestode of domestic fowl [38]. The crude root-peel extract and pure genistein were tested in vitro with respect to Ca^{2+} homeostasis and the occurrence of some metal ions was detected in the parasite. The changes in Ca^{2+} homeostasis may be related to the rapid muscular contraction and consequent paralysis in the parasite due to the anthelmintic stress caused by the phytochemicals of *F. vestita* [39].

Conclusion

About 105 species of the genus *Flemingia* have been reported in various floras. An exhaustive survey of literature revealed that sporadic information is available only on 15 species. Among these 15 species, most of ethnopharmacological reports are available on 5 species of *Flemingia*. Further, only 6 species of *Flemingia* (Table 1) have been partially investigated for their phytoconstituents.

A close scrutiny of literature on *Flemingia* reveals that 5 species have been investigated pharmacologically. Among these, *F.chappar* and *F. strobilifera* have been exhaustively explored for their antimicrobial and antioxidant activity. Pharmacological studies infer that *F.vestita* has anthelmintic activity due to presence of isoflavones. *F.macrophylla* has been reported to possess anxiolytic and hepatoprotective effect due to flavonoids.

Despite a long tradition of use of *Flemingia* species for treatment of various ailments, no pharmacological work has ever been carried out to prove its traditional claims for epilepsy. Additionally, the plant has been included in number of herbal formulations, which are in clinical use for the treatment of various ailments. Keeping in view the traditional, alternative and complimentary medicinal uses, sporadic phytochemical and pharmacological reports, low toxicity, *Flemingia* species seems to hold great potential for in depth investigation for various biological activities, especially its effect in the epilepsy and central nervous system. The authors are involved in bioactivity-directed-fractionation of this plant with a view to isolate bioactive fraction / constituent(s).

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