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Review

Mesua ferrea L.: A review of the medical evidence for its phytochemistry and pharmacological actions

Manoj Kumar Chahar*, Sanjaya Kumar D. S., Geetha L., Lokesh T. and Manohara K. P.

Sree Siddaganga College of Pharmacy, B. H. Road, Tumkur- 572 102, Karnataka, India.

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The plant kingdom provides many plants with properties which are conducive to health and to secure the best results from the use of the plants as remedial agencies. *Mesua ferrea* Linn (Nagakesar) is a rare plant which is traditionally being used for its antiseptic, anti-inflammatory, blood purifier, anthelmintic, cardiotonic, diuretic, expectorant, antipyretic, purgative, antiasthmatic, antiallergic and several other effects. The scientific screening of the plant confirms its antioxidant, hepatoprotective, anti-inflammatory, central nervous system (CNS) depressant, analgesic, antimicrobial, antispasmodic, antineoplastic, antivenom and immunostimulant activity. The phytochemical screening confirms the presence of phenyl coumarins, xanthones, triterpenoids, fats and flavanoids as main constituents responsible for its biological activity. It is a substitute for petroleum gasoline. It is also used in cosmetics, as fire wood and the polymer obtained from seed oil is used in the preparation of resins. The present review summarizes the phyto-pharmacological role of this valuable medicinal plant.

Key words: *Mesua ferrea*, traditional medicinal uses, phytochemical screening, pharmacological activities.

INTRODUCTION

Ayurveda has related research efforts which have led to generation of enormous amount of scientific information concerning plants, crude plant extracts, and various substances from plants as medicinal agents during last 30 to 40 years. Although herbal medicine has existed since the dawn of time, our knowledge of how plants actually affect human physiology remains largely unexplored.

The research is going on with a view to provide the scientific evidence for the ethnomedical claim and for their clinical application. *Mesua* is a large genus consisting of about 48 species but the extensive research work has been carried out only on *M. ferrea* L. This review provides insight on the phytochemical and pharmacological profile with other useful information on the plant (Kirtikar, 1935). It is native to tropical Sri Lanka and a state tree of Tripura but it is disappearing from India. *M. ferrea* L. (Figure 1) is locally known as Cobra's saffron (English), Nagakeshara (Hindi), Nagasampige (Kannada), Nageshwar (Assam), Nagachampakam (Tamil). The tree is found throughout Southeast Asia in tropical evergreen forests up to 1,500 m elevation (Dassanayake, 1980).

*Corresponding author. E-mail: manojchahar7@gmail.com. Tel: 9964498676.

Distribution

It is widely distributed in tropical countries like India, Burma, Thailand, Indochina and New Guinea (Kritikar, 1981). In India, it is distributed in the mountains of Eastern Himalaya and East Bengal, Assam, Burma, Andaman, evergreen rain forests of North Canara and South Konkan, the Forests of Western Ghats from South Canara to Travancore (Anonymous, 2004).

Botany

Nagakesara is a medium to large sized tree that can attain a height between 18 and 30 m, with reddish-brown to grey colored bark that peels off in thin flakes, the wood is extremely hard. The leaves are simple, lanceolate, acute, and leathery, covered in a waxy bloom below, red when young, oppositely arranged, 7 to 13 cm long by 2 to 4 cm wide. The flowers are white with a floral fragrance,

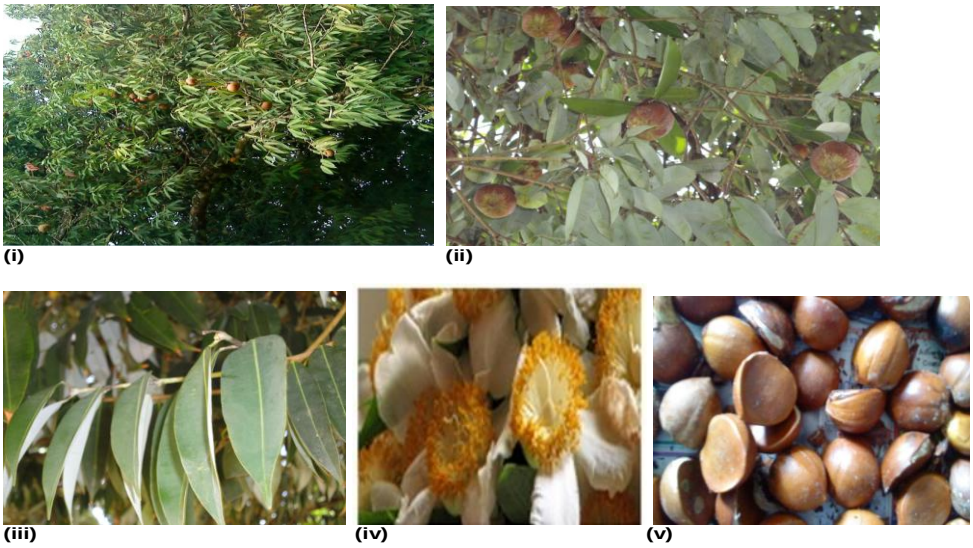


Figure 1. *Mesua ferrea* L. (i) Tree; (ii) Fruit; (iii) Leaves; (iv) Flower and; (v) Seeds

up to 7.5 cm in diameter, with numerous golden-colored stamens shorter than the length of the petals, the style is twice as long as the stamens, borne singly or in pairs, axillary or terminal. The fruits are ovoid with a conical point, 2.5 to 5 cm long; with a woody pericarp that contains one to four seeds (Dassanayake, 1980).

Uses

It is known for shade creation and radiation modification in improving human thermal comfort (Shahidana et al., 2010). The seed oil is substitute for petroleum gasoline, the fraction distilling between 200 and 300°C may be used as fuel for diesel engines (Konwer et al., 1984; Kallappa et al., 2003). The polymers obtained from seed oil are used in the preparation of resins (Dutta et al., 2004; Mahapatra et al., 2004, 2007; Dutta et al., 2005, 2006; Das et al., 2010).

Aqueous leaf extract was used to prepare silver nano particals (Konwarh et al., 2010). The seeds are brunt like candles, the wood is used for golf club heads, flowers and stamens are used to stuff pillows for the bridles bed (Sahni, 1998).

TRADITIONAL MEDICINAL USES

The plant is used in inflammation and septic conditions (Rai et al., 2000). The tribal's of Assam use this plant for its antiseptic, purgative, blood purifier, worm control, tonic properties (Parukutty et al., 1984). In Thai traditional medicine, it is used to treat fever, cold, asthma and as carminative, expectorant, cardiotonic, diuretic and antipyretic agent (Foundation of Resuscitate and Encourage Thai Traditional Medicine, 2005). The ashes of leaves are used for sore eyes. Kernels are used to poultice wounds and in skin eruptions (Burkill, 1966; Kumar et al., 2006). Leaf and flower are antidotes for snake bite and scorpion sting. The fixed oil is used for cutaneous infection, sores, scabies, wounds and rheumatism. The flower is stomachic, expectorant and astringent. The decoction or infusion or tincture of bark and roots is a bitter tonic and useful in gastritis, bronchitis (Sahni, 1998; Husain et al., 1992; Joy et al., 1992; Nadkarni, 1976) and to cure snake bite (Santamaría, 1978). The aerial parts are Chorionic villus sampling (CVS) active, spasmolytic, diuretic, (Husain et al., 1992; Joy et al., 1992), abortificient (Nath et al., 1992) and used in fever, dyspepsia, renal disorders and in cosmetics (Kumar et al., 2006). *M. ferrea* is an ingredient of various ayurvedic formulations like dasamoolarishta (Nishteshwar et al., 2008), mahakaleshwara rasa (Das et al., 2001) and in various churnas (Sharangadhara, 2000) used to cure many diseases (Roshy et al., 2010). Some important ayurvedic formulations containing *M. ferrea* are listed in Table 1. An Ayurvedic formulation containing *M. ferrea* exhibited haemostatic and astringent properties and is particularly useful in uterine bleeding (Husain et al., 1992; Joy et al., 1992). In Unani system, the drug is an ingredient of large number of recipes like, "Jawarish Shehryaran" a stomach and liver tonic, "Hab Pachaluna", an appetiser, "Halwa-i-supari pack" a general tonic (Joy et al., 1992; Thakur et al., 1989).

PHARMACOLOGICAL ACTIVITIES

Disinfection studies

Nahar (*M. ferrea*) seed kernel oil was investigated for its potential as natural disinfectant and disinfection kinetics. Heterotrophic plate count using CFU/ml, pour plate method

Table 1. Ayurvedic formulations containing *M. ferrea*.

Formulation	Use	Reference
Nagakeshara-adi-churna	In bacillary dysentery	Joy et al. (1998) and Thakur et al. (1989)
Nagakeshara yoga	In piles	Joy et al. (1998) and Thakur et al. (1989)
Vyaghrihareetaki avaleha	Shwasa, kasa, pinasa	Roshy et al. (2010)
Eladi churna	Carminative, in vomiting, indigestion anorexia	Tambekar et al. (2010)
Lavangadi churna	In cough, diarrohea, dysentery, mouth diseases, dental caries, anemia and fever	Tambekar et al. (2010)

method at 35°C/48 h, plate count agar were employed to evaluate the disinfection and its kinetics. Oil-water emulsion used as test and surface water samples were used for comparison of colonies produced using pour plate method. The crude oil emulsion showed total disinfection at a concentration of 2 mg/ml and above, while the data generated from the disinfection at 1 mg/ml fits first-order model. The study concluded that nahar seed kernel oil has a remarkable disinfection potential and the kinetics studies indicated that the oil fitted first-order model with a k value of -0.040 (Adewale et al., 2011).

Antioxidant and hepatoprotective activity

The methanolic extract of dried flowers of *M. ferrea* (100 and 200 mg/kg) was screened for *in vivo* antioxidant and hepatoprotective activity in experimental female Wistar mice. An artificial infection was induced by administration of *S. aureus* in drinking water for 24 h at the onset of experiment, sampling was done once a day and after one week. The biochemical parameters Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Creatinine phosphorkinase (CPK), Alkaline phosphatase (ALKP), Creatinine, Urea, Super oxide dismutase (SOD), Catalase (CAT), Glutathione peroxidise (GPX), Glutathione reductase (GR) were measured. There was significant increase in liver SOD and AST in treated groups. There was significant reduction in catalase (CAT), GPX, GR, and ALT activity. No significant difference was observed in CPK and creatinine activity (Garg et al., 2009).

The ethanolic extract of flowers showed potent inhibitory activity (96.03%) at 100 µg/ml against nitric oxide (NO) assay (Makchuchit et al., 2010). The water-ethanol (1:1) leaf extract showed potent inhibition on lipid peroxidation (Yadav, 2010). The ayurvedic formulations Brahma rasayana (Ramnath et al., 2009) and Maharishi AK-4 (Cullen et al., 1997) containing *M. ferrea* have reported to exhibit significant antioxidant activity in cold stressed chicken and isolated rat heart, respectively. The 2,2-diphenyl-1-picrylhydrazyl (DPPH) (56.67 mmol/100 g DW), 2,2'-azino-bis (ABTS) (35.22 mmol/100 g DW), ferric reducing/antioxidant power (FRAP) (8.99 µmol/g DW) assay and determination of total phenolic content (4.18 g/100 g DW) in *M. ferrea* seeds and pericarp showed antioxidant activity (Surveswaran et al., 2007). *Phomopsis* sp. GJJM07 (an endophyte) was isolated from *M. ferrea* and examined for the *in vitro* antioxidant activity by DPPH radical scavenging assay. It showed potent antioxidant activity with the half maximal inhibitory concentration (IC_{50}) value of 31.25 µg/ml compared to the IC_{50} value of standard ascorbic acid, 11.11 µg/ml (Jayanthi et al., 2011).

Analgesic activity

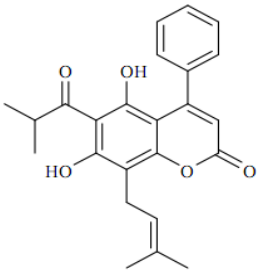
n-Hexane, ethyl acetate and methanol extracts of *M. ferrea* leaves (125 and 250 mg/kg) exhibited significant analgesic activity in acetic acid induced writhing response in mouse. The reduction in writhing response for lower dose of above extracts was 36.08, 16.33 and 10.21%, respectively and for higher dose it was 42.21, 19.63 and 17.06%, respectively (Hassan et al., 2006).

Antispasmodic activity

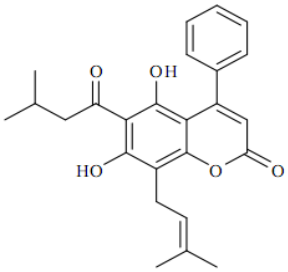
The petroleum extract of *M. ferrea* seed oil was evaluated for antispasmodic activity on isolated rat ileum *in vitro*. The contraction of rat ileum was measured on kymograph. Acetycholine and Carbachol caused contraction of 2.61 and 3.20 cm, respectively. The crude oil at concentration, which is 1:5 and 1:10, and the normal contraction of acetylcholine was reduced to 70 and 86%, respectively. Normal response of acetylcholine in presence of atropine was reduced to 55% (Prasad et al., 1999).

Anti-venom activity

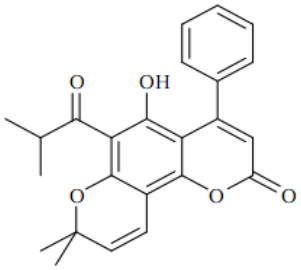
The aqueous extract of *M. ferrea* leaves was screened for its activity against fibroblast cell lysis after *Heterometrus laoticus* scorpion venom treatment. The extract was evaluated against viability of fibroblast cells after 30 min treatment with mock control or with 0.706 mg/ml plant extracts preincubated with *H. laoticus* venom. Viability of fibroblast cells after 30 min treatment with mock control or with 0.706 and 0.406 mg/ml showed efficiency in protecting against venom induced lysis (Uawonggul et al., 2006).



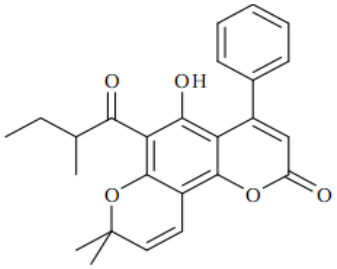
Mesuol



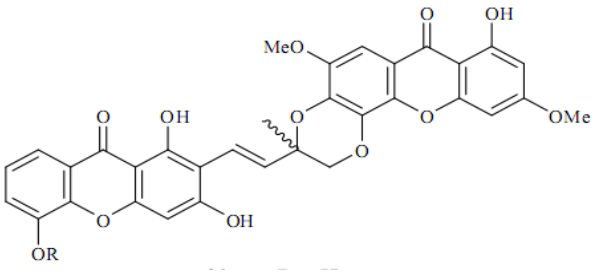
Mammeisin



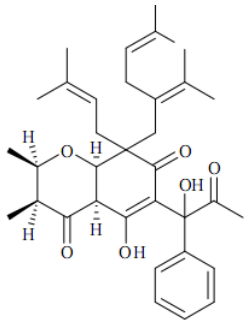
Mesuagin



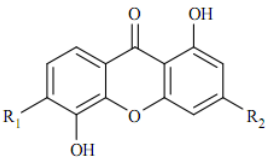
Mammeigin



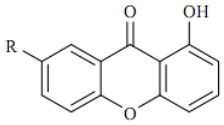
Mesuabixanthone A (R=H) and Mesuabixanthone B (R=Me)



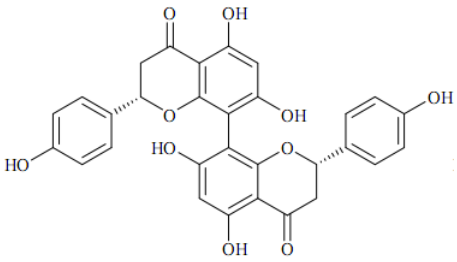
Mesuaferrol



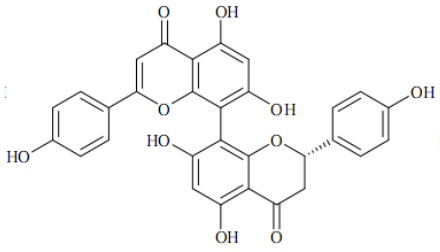
Mesuaxanthone A (R_1= H & R_2 = OMe)
Mesuaxanthone B (R_1 = OH & R_2 = H)



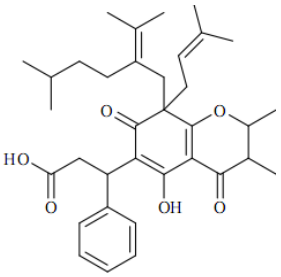
Euxanthone(R=OH)



Mesuaferrone A



Mesuaferrone B



Mesuanic acid

Figure 2. (I) Mesuol; (ii) Mammeisin; (iii) Mesuagin; (iv) Mammeigin; (v) Mesuabixanthone A (R=H) and Mesuabixanthone B (R=Me); (vi) Mesuaferrol; (vii) Mesuaxanthone A (R 1= H and R2 = OMe); Mesuaxanthone B (R1 = OH and R2 = H); (viii) Euxanthone(R=OH); (ix) Mesuaferrone A; (x) Mesuaferrone B; (xi) Mesuanic acid.

M. ferrea in the cancer chemotherapy

Maharisi amrit kalash-4 (MAK-4) containing *M. ferrea* was evaluated for its role in reduction of chemotherapy toxicity among women with breast cancer. 214 patients with breast carcinoma received cyclophosphamide, adriamycine,

and 5-flurocil (CAF) adjuvant or neo-adjuvant chemotherapy. All patients received same antiemetic therapy with ondensetrone and dexamethasone. The Anorexia, Karnofsky performance status, vomiting, weight stomatitis, leucopenia and other side effect such as diarrhea, alopecia, tumour response were checked. There was significant reduction in toxicities observed in MAK group throughout chemotherapy cycles: poor performance status was prevented by concomitant administration of MAK along with chemotherapy. {Prevented fraction (PF) = 6% (95% confi-dence interval, 22.1 to 80.1; p value = 0.005)}. Vomiting was prevented by MAK {PF = 40.3%, (95% confidence interval, 15.1 to 58.1; p value = 0.002)}. Similarly, anorexia was reduced with PF = 35.6% (95% confidence interval, 17.6 to 49.7; p value = 0.0001) in MAK group. No overgrowth of tumors occurred in the group treated with neoadjuvant chemotherapy receiving MAK (Saxena et al., 2008).

Immunomodulatory activity

A poly herbal formulation, ACII containing *M. ferrea* flower buds was evaluated for immunomodulation effect on radiation induced immunosuppresion. There was a significant increase in the amount of circulating antibody in animals treated with ACCII (250 mg and 1 g/kg). There was no significant change in body weight in treated as well as irradiated animals.

The lowered total white blood cells (WBC) count was significantly increased. There was no significant change in the hemoglobin content of irradiated animals when compared with drug treated or normal animals. ACII also did not produce any change on differential count especially in lymphocyte-neutrophil ratio. The bone marrow cellularity was improved significantly and α-esterase positive cells were found to be improved. The weight of thymus was found to increase in ACII treated animals compared to irradiated animals (Tharakan et al., 2006). Moreover, ACII was found to have an immunomodulatory effect in normal (Tharakan et al., 2004) as well as in cyclophosphamide treated animals (Tharakan et al., 2003).

Mesuol isolated from *M. ferrea* seed oil was evaluated for immunomodulatory activity in experimental animals by using specific and non-specific immune response models. In humoral immune response model, mesuol evoked a significant dose dependent increase in antibody titer values in cyclophosphamide (50 mg/kg, i.p, 9th and 16th day) induced immunosuppression which was sensitized with sheep red blood cells (SRBC) on the 7th and 14th day of experiment. In cellular immune response model, an increase in paw volume was recorded on the 23rd day in cyclophosphamide-induced immune-suppressed rats treated with SRBC (0.03 ml 2% v/v, s.c.) on the 21st day. Mesuol restored the hematological profile in cyclophosphamide induced myelosuppression model. Mesuol potentiated percentage of neutrophil adhesion in neutrophil adhesion test in rats and phagocytosis in carbon clearance assay. The study indicated immunomodulatory activity of mesuol (Chahar et al., 2012).

Anti-neoplastic activity

The crude ethanolic extract of *M. ferrea* was evaluated against human cholangio carcinoma (CL-6), human laryngeal (Hep-2), and human hepatocarcinoma (HepG2) cell lines *in vitro.* The extract showed promising activity against cholangio carcinoma (CL-6), with survival of less than 50% at the concentration of 50 µg/ml. There was potent cytotoxic activity against Hep-2 and HepG2 also (Mahavorasirikul et al., 2010). The methanolic extract was evaluated against Ehrlich Ascites carcinoma in mice. There was significant inhibition in tumour growth inhibition (Rana et al., 2004). Muthu Marunthu, a poly herbal formulation containing *M. ferrea* flowers (100 mg) was evaluated for antitumour effect on experimental fibrosarcoma in rats. Significant reduction in the levels of DNA and RNA were noticed after Muthu Marunthu treatment. A significant reduction in the levels of vitamins A, C and E were observed in fibrosarcoma rats. Muthu Marunthu treatment was able to enhance the levels of vitamins A, C and E. An elevated level of copper and decreased levels of zinc and selenium were noticed in fibrosarcoma rats.

Treatment with Muthu Marunthu for 20 days brought back the altered levels of these trace elements to near normal levels. When compared between normal and Muthu Marunthu treated control rats, there was no significant changes in the blood levels of glucose, urea, plasma protein and cholesterol, and activities of serum enzymes such as Lactate dehydrogenase (LDH), Glutamate oxaloacetate transaminase (GOT) and Glutamic-pyruvic transaminase (GPT), alkaline and acid phosphatase (Palani et al., 1999).

Anti-convulsant activity

The ethanolic extract of *M. ferrea* flowers was evaluated for anticonvulsant activity at 3 different dose levels (200, 400 and 600 mg/kg p.o.) by Maximum electroshock seizure (MES) test using albino mice. The extract reduced the duration of Hind limb tonic extension (HLTE) in a dose dependent manner against MES model. The ethanolic extract of *M. ferrea* inhibited MES-induced convulsions. The percentage inhibition achieved at the doses 200, 400, and 600 mg/kg were 100% ($p < 0.01$), 60% ($p < 0.01$) and 100% ($p < 0.001$), respectively. Data from this study showed that *M. ferrea* flowers significantly increased the onset time and decreased the duration of seizures by electroconvulsive shock (Tiwari et al., 2012).

Effect of xanthones isolated from *M. ferrea* on central nervous system

Gross behaviour

Xanthones from *M. ferrea* were screened for their effect on gross behaviour in mice in a dose of 10, 25, 50, 100, 200 and 500 mg/kg. Gross behavioural changes were recorded at 15, 30, 60 and 120 min. All the xanthones of the *M. ferrea* produced signs of CNS depression characterised by ptosis, sedation, decreased spontaneous motor activity and loss of muscle tone. The CNS depressant effect was predominant at the dose level of 200 mg/kg.

Anti-inflamatory activity

Mesuaxanthone A and mesuaxanthone B (MXA and MXB) from *M. ferrea* were evaluated using albino rats by carrageenan induced hind paw oedema, cotton pellet implantation and granuloma pouch tests. In all the methods, xanthones were administered at the dose level of 50 mg/kg. *M. ferrea* xanthones upon oral administration in carrageenan induced hind paw oedema test showed MXA (37%) and MXB (49%) reduction when compared to normal control group. The xanthones produced significant anti-inflammatory activity in normal, as well as in adrenalectomised rats, as the inflammation reduced significantly by MXA (38%) and MXB (22%) when compared to normal control group. In granuloma pouch tests, these xanthones showed MXA (46%) and MXB (49%) reduction in inflammation, and 47% reduction was observed in cotton pellets granuloma tests. The xanthones used in the present study have been found to produce significant anti-inflammatory activity (Gopalakrishnan et al., 1980).

Anti-ulcer activity

Xanthones from *M. ferrea* were screened for antiulcer activity by pyloric ligation method in albino rats. The ulcer scoring for the gum acacia treated rats was found to be 3.50 ± 0.27 which was significantly lesser than that of standards. The control animals showed extensive ulceration, haemorrhage and perforation, while the xanthones pre-treated animals exhibited only scattered areas of hyperemia and occasional haemorrhagic spots (Gopalakrishnan et al., 1980).

Anti-arthritic activity

M. ferrea seed extracts (petroleum ether, ethyl acetate and alcohol) were evaluated in the formaldehyde and Complete Freund's Adjuvant (CFA)-induced arthritis in rats. The results indicate that *M. ferrea* protects rats against formaldehyde and CFA induced arthritis. The body weight changes and the CFA-induced haematological perturbations, such as an increase in the WBC count, a decreased RBC count, a decreased haemoglobin (Hb) count and an increased erythrocyte sedimentation rate (ESR) which were significantly altered by *M. ferrea* treatment. The overall results indicated that *M. ferrea* extract has a potent protective effect against formaldehyde and adjuvant-induced arthritis in rats (Jalalpure et al., 2011).

Anti-microbial activity

In an *in vivo* experiment, the methanol extract of *M. ferrea* flowers protected mice challenged with *S. typhimurium* ATCC 6539.2 and 4 mg/mouse of the extract reduced the mice mortality. There was a significant reduction in the viable bacteria of blood, liver and spleen in the animals treated with the extract. In *in vitro* experiment, the extract inhibited 30 strains of *Staphylococcus aureus,* and all the tested strains of *Bacilllus* spp., *Salmonella* spp., *Pseudomonas* spp., *Streptococcus pneumonia*, *Sarcina lutea, Proteus mirabilis, Lactobacillus arabinosus* at 50 µg/ml concentration. One and two strains of *Staphylococcus* were inhibited by 100 and 200 µg/ml whereas 8 strains were resistant, strains of *Klebsiella, Vibrio cholera, Escherichia coli, Shigella* spp. were less sensitive (Mazumder et al., 2004).

Dichloromethane and methanol (1:1 v/v) extract of *M. ferrea* flowers showed complete inhibition against all tested bacteria at 500 and 1000 µg/ml. The screening was carried by agar dilution-streak method against *B. cereus varmycoides*, *B. pumilus*, *B. subtilis*, *Bordetella bronchiseptica*, *Micrococcus luteus*, *Sta. aureus*, *Sta. epidermidis*, *E. coli*, *K. pneumoniae, P. aeruginosa, Str. faecalis, Candida albicans, Aspergillus niger* and *Saccharomyces cerevisiae* (Prashanth et al., 2006).

The light petroleum ether, chloroform and ethanol extracts of *M. ferrea* seeds, leaves and stem bark were evaluated against antibacterial and antifungal study by disk diffusion method at 400 µg disk^{-1} against 14 pathogenic bacteria including 5 gram positive like *B. subtilis, B. megaterium, Str. β-haemolyticus, Str. aureus, Sarcina lutea* and 9 gram negative as *Shigella sonnei, E. coli, Klebsiella* species*, Shigella shiga, S. boydii, S. flexneriae, S. dysenteriae, Salmonella typhi* and *Pseudomonas aeruginosa* and 6 pathogenic fungi *Penicillum notatum, A. niger, Trichoderma viride, A. flavus, C. albican* and *Hensinela californica.* Chloroform extract of *M. ferrea* stem bark displayed strong activity against gram-positive *Str. aureus* (16 mm) and gram-negative *E. coli* (19 mm). The extracts of *M. ferrea* leaves were found to be mild to moderate active against most of the bacteria strains. Antifungal activities of *M. ferrea* extracts were not significant enough against most of the tested fungal strains (Ali et al., 2004).

Antibacterial activity of aqueous and alcoholic extracts of *M. ferrea* seeds were tested at 100 µl by the agar disc diffusion and agar well diffusion methods against *Enterobacter aerogenes* ATCC13048, *E. coli* ATCC25922, *K. pneumoniae* NCIM2719, *Proteus mirabilis* NCIM 2241, *P. vulgaris* NCTC8313, and *Salmonella typhimurium* ATCC23564. Maximum antibacterial activity was against *P. mirabilis* (23 mm) and *K. pneumoniae* (20 mm). The ethanol/methanol extracts were more active than aqueous extracts (Parekh et al., 2007).

The methanolic extract of *M. ferrea* seeds was evaluated for antifungal activity *in vitro*. The test fungal strains investigated include 7 yeasts; *C. albicans* (1) ATCC2091, *C. albicans* (2) ATCC18804, *C. glabrata* NCIM3448, *C. tropicalis* ATCC4563, *C. luteolus* ATCC32044, *C. neoformans* ATCC34664, *Trichosporon beigelli* NCIM3404, and 4 moulds; *A. candidus* NCIM883, *A. flavus* NCIM538, *A. niger* ATCC6275 and *Mucorheimalis* NCIM873. The methanolic extract was effective at the concentration of 125 µg/disc for *C. albicans* (1) ATCC2091, C. *albicans* (2) ATCC18804 and *Trichosporon beigelli* NCIM3404 (125, 250 and 500 µg/disc). The extract was effective against moulds as *A. candidus* NCIM883 (500 µg/disc), *A. flavus* NCIM538 (125 & 250 µg/disc), *A. niger* ATCC6275 (125 and 250) and *Mucorheimalis* NCIM873 (250 and 500 µg/disc) (Parekh et al., 2008).

A series of 4-Alkyl and 4-phenyl coumarins like 6-acyl-8-prenylderivatives (MF1 and MF2), 8-acyl-6-prenylderivatives (MF3 and MF4), 6-acyl-7, 8-dihydro furano derivatives (MF5 and MF7) and 6-acyl-7, 8-pyranoderivatives (MF8 and MF9) from *M. ferrea* blossoms were evaluated against gram negative bacteria, gram positive *Staphylococcus, Enterococcus* and a strain of *Str. durans*, fungi *P. falciparum.* All the samples tested, except MF5, MF8 and MF9, showed an activity of potential interest either against the *Enterococci* or against organisms of the genus *Staphylococcus*. The Mesua derivatives exhibited a higher minimum inhibitory concentration (MIC) 50% (2 to 4 µg/ml). When the concentrations inhibiting 90% of the strains (MIC 90%) were compared, some of the Mesua derivatives exhibited the best activity. There was a weak inhibitory activity against *P. falciparum* (Verotta et al., 2004).

M. ferrea leaves extracts were evaluated for the antibacterial activity (ethanol and methanol extract) by agar disc diffusion method and cytotoxicity activity (methanol extract). The micro broth dilution method was employed for the determination MIC and minimum bactericidal concentration (MBC), while Brine shrimp (*Artemia salina*) lethality bioassay was made use of for the cytotoxicity assay. The extract showed a remarkable antibacterial property against all the selected microbes (*E. coli, P. aeruginosa, B. subtilis and Sta. aureus*) with the inhibition zones ranging from 16.0 ± 0.5 to 18.0 ± 0.5 mm for all the tested bacteria. The MIC range of 2.5 to 0.625 mg/ml with MBC value of 5 mg/ml was obtained for the gram-negative bacteria while MIC range of 1.3 to 0.313 mg/ml with MBC value of 2.5 mg/ml was obtained for the gram-positive bacteria. The leaves extracts were found to be toxic to the Brine shrimps with LC_{50} of 500 ppm (µg/ml), suggesting that the extracts may contain bioactive compounds of potential therapeutic and prophylactic significance (Adewale et al., 2012).

Phomopsis sp. GJJM07 (an endophyte) was isolated from *M. ferrea*. The crude ethyl acetate extract of the fungus was evaluated for antimicrobial activity. The endophytic fungus were grown in different media and were tested against the test pathogens, gram positive bacteria; *B. subtilis*, *Micrococcus luteus*; gram negative bacteria; *E. coli*, *K. pneumoniae* and yeast, *C. albicans*. Among the different media, M1D medium showed good growth 1.57 g MDW/100 ml and broad spectrum of antimicrobial activity by exhibiting prominent zone of inhibition against the test pathogens such as *E. coli* (16 ± 0.14), *K. pneumoniae* (16 ± 0.19), *B. subtilis* (18 ± 0.13), *M. luteus* (12 ± 0.18) and *C. albicans* (12 ± 0.20) (Jayanthi et al., 2011).

Other therapeutic considerations

Ethanol and petroleum ether extract is used for sore throat, cough and asthma (Singhe et al., 1975; Bala et al., 1971; Sharma et al., 2002). The syrup of flower buds is used to cure dysentery. The leaves are used in the form of poultice which is applied to head in severe colds (Husain et al., 1992; Joy et al., 1998; Nadkarni, 1976). The LD_{50} of ether extract of whole plant in mice is 500 mg/kg IP, LD_{50} of acetone extract of stamens in mice was 400 mg/kg i.v. and non toxic up to 1600 mg/kg p.o. (Sharma et al., 2002).

PHYTOCONSTITUENTS

M. ferrea is the only species that has been chemically studied from the genus *Mesua* (Kirtikar, 1935; Rao et al., 1981). Phytochemical studies have revealed plants from this genus to be rich in many classes of secondary metabolites including phenylcoumarins, xanthones and triterpenoides (Chow et al., 1968; Bandaranayake et al., 1975; Raju et al., 1976). The kernels contain about 75% of yellowish oil, constituted by the glycerides of common fatty acids: linoleic, oleic, stearic, and arachidic acids. An oil called nahor is extracted from the seeds (Husain et al., 1992; Joy et al., 1998).4-Phenylcoumarins like mesuol, mesuagin, mammeisin, mammeigin and mesuone were isolated from the seed oil of *M. ferrea.* The trunk bark and the heartwood yielded 4-alkylcoumarins ferruols A and B, a lupeol-type triterpenoid guttiferol, mesuaxanthones A and B, ferraxanthone 1,7-dihydroxyxanthone, 1,5-dihydroxy-3-methoxyxanthone, 1,X6-trihydroxyxanthone, 1,5- dihydroxyxanthone, I-hydroxy-7-methoxyxanthone and β-sitosterol. Stamens give α and β-amyrin, β-sitosterol, biflavonoids- mesuaferrones A and B, mesuanic

acid, 1,5-dihydroxyxanthone, euxanthone 7-methyl ether and β-sitosterol. Other isolated constituents were mesuaferrol, leuco anthocyanidin, mesuone, euxanthone, etc. Presence of xanthone derivative and essential oil had also been reported from various parts of the plant (Sharma et al., 2002; Chow et al., 1968; Govindchari et al., 1967). Two new yellow pigments, meauxanthone A and memaxantbone B have been isolated from the heart-wood extracts of *M. ferrea* (Govindchari et al., 1967). The stamens which yield the drug Nagakeshara contain mesuferrone-A and B, mesuaferrol, mesuanic acid, α and β-amyrin (Handa et al., 1992).

CONCLUSION

M. ferrea is being used in India and several parts of world for its potential medicinal and several other properties. The plant is known for its antioxidant, analgesic, anti-inflammatory, antitumor, immunostimulant, antimicrobial, and several other activities. It is an ingredient of several ayurvedic and unani formulations. The phytochemical screening confirms the presence of phenyl coumarins, xanthones, triterpenoids, fats and flavanoids as main constituents of the plant. Apart from medicinal uses it is also being used commercially in polymer industry, painting, as a firewood and substitute for gasoline, preparation of nanoparticles. Therefore further studies may be carried out to prove the potential of this plant as well as the isolated products. Besides this, the systemic studies of pharmacological aspects of the plant are under way by our research team.

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