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PHYTO-PHARMACOLOGICAL REVIEW OF *MESUA FERREA* LINN

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ABSTRACT

India has a rich culture of medicinal herbs and spices, which includes Ayurvedic, Unani, Siddha and other traditional medicines but only very few have been studied chemically and pharmacologically for their potential medicinal value. According to the World Health Organization, most populations still rely on traditional medicines for their psychological and physical health requirements. People living in rural areas from their personal experience know that these traditional remedies are valuable source of natural products to maintain human health, but they may not understand the science behind these medicines, but knew that some medicinal plants are highly effective only when used at therapeutic doses. Herbal medicines are in great demand in both developed and developing countries as a source of primary health care owing to their attributes having wide biological and medicinal activities, high safety margins and lesser costs. *Mesua ferrea* Linn. belonging to the family Clusiaceae (Guttiferea) is known in Hindi as 'Nagkeshar' and in English as Ceylon Ironwood. It is a medium to large evergreen tree with short trunk, often buttressed at the base, found in the Himalayas from Nepal eastward, in north-eastern India, Deccan Peninsula and the Andaman Islands, ascending to an altitude of 1.500m. The different parts of the plant contain glycosides, coumarins, flavanoids, xanthones, triglycerides and resins. Specifically it contains α -copaene and germacrene D , ve β-amyrin, β-sitosterol, and a new cyclohexadione compound named as mesuaferrol (I), mesuanic acid(13), triterpenoids and resins, reducing sugars, and tannins , saponins, Mesuaferrone B, mesuol etc. The plant has shown various pharmacological activities including antibacterial, immunomodulatory etc.

Key words: Indian medicinal plants, *Mesua ferrea*, Nagkeshar, Mesuferrol, Mesuol (I), Kesar oil.

INTRODUCTION

According to WHO's (WORLD HEALTH ORGANISATION) report around 65-85% of world population relies on traditional medicines of plant origin for their primary health care needs. India, one among 12 Bio-diverse countries of the world, is abode of 45000 floral species, out of which 15000 are those of Medicinal Plants. Approx. 85% to 90% of these come from the wild. Department of ISM&H, Ministry of Health & Family Welfare, Govt. of India, has identified 1500 medicinal plants of which 500 are commonly used in the preparation of herbal drugs. There are about 45,000 medicinal plant species in India, with concentrated spots in the region of Eastern Himalayas, Western Ghats and Andaman & Nicobar Island. The officially documented plants with medicinal potential are 3000 but traditional practitioners use more than 6000. It is estimated that about 80,000 species of plants are utilized in some form or other by the different systems of Indian medicine. The knowledge about plants and plant products is detailed, sophisticated, and has evolved into a separate shastra itself, called Dravya Guna Shastra. Plants have been studied on the basis of clearly defined biological parameters like rasa (taste), vipaka (metabolicproperty),guna (quality), prabhava (biological effect) and virya (potency). The codified traditions have about 25,000 plant drug formulations that have emerged from such studies. In addition to this, over 50,000 formulations are believed to be existing in the folk and tribal traditions. All these point to the deep passion for an exhaustive knowledge about medicinal plants that have existed in this land from time immemorial. Many herbs and spices are used in Indian cooking, such as onion, garlic, ginger, turmeric, clove, cardamom, cinnamon, cumin, coriander, fenugreek,

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fennel, ajowan (ajwain), anise, amchur, bay leaf, hing (asafoetida) etc. Ayurvedic medicine uses all of these either in diet or as an medicine. Some of these medicinal plants have been featured on Indian postage stamps (Lai PK *et al*., 2004 & Sandhu DS *et al*., 2005). The first set of stamps showing medicinal plants came out in 1997. The set had four stamps showing four different medicinal plants - Tulsi (*Ocimum sanctum*), Haridra (*Curcuma longa*), Sarpagandha (*Rauwolfia serpentina*), and Ghritkumari (*Aloe barbadensis*). Now large global pharmaceutical corporations and "inventors" out for a quick buck have got into the act. Medicinal plants are not only a major resource base for the traditional medicine & herbal industry but also provide livelihood and health security to a large segment of Indian population. The domestic trade of the AYUSH industry is of the order of Rs. 80 to 90 billion (1US$ = Rs.50) (Tapsell LC *et al*., 2006) The Indian medicinal plants and their products also account of exports in the range of Rs. 10 billion. There is global resurgence in traditional and alternative health care systems resulting in world herbal trade which stands at US$ 120 billion and is expected to reach US$ 7 trillion by 2050. Indian share in the world trade, at present, however, is quite low. *Mesua ferrea* is one of the well known medicinal plant having high therapeutic potential.

PHARMACOGNOSTICAL REVIEW

About the plant

Mesua ferrea Linn. belonging to the family Clusiaceae (Guttiferea) is known in Hindi as 'Nagkeshar' and in English as Ceylon Ironwood. It is a medium to large evergreen tree with short trunk, often buttressed at the base, found in the Himalayas from Nepal eastward, in north-eastern India, Deccan Peninsula and the Andaman Islands, ascending to an altitude of 1.500 m. The tree is cultivated in the gardens and avenues for its flowers and foliage which are attractive, particularly when young (Wealth of India, 1962). *Mesua ferrea* Linn. is found in moist or semi-evergreen forest, either scattered or in more or less pure patches or belt. It requires well drained, deep fertile soil with a neutral pH; stiff clay and low lying situations are unsuitable. It is a strong shade bearer, particularly when young and this makes it a valuable component of the middle storey in forest (Wealth of India, 1962). It is susceptible to frost and drought, but these conditions are practically unknown in its natural habitat (Kadambi K, 1954). The tree is affected by brown cubical rot and white sap and heart rot. It is also attacked by beetles like *Xyleborus discolor* Blandford, *Xyleborus interjectus* Blandford and a few others as well as by a buprestid borer, *Chryosochroa* species (Mathur RN, 1958).

The plant exists popular to the market for its oil production which is known as *Kesar oil* which is extracted directly from the seeds. Seeds kernel, forming 53-73 percent of the weight of seeds (150-200 seeds weigh per pound). Its flowers and leaves are used as an antidote to snake bite, and a paste of the flowers with butter and sugar is used in bleeding piles and burning of the feet. In north Canada the oil of the seeds is used as an embrocation in Rheumatism and found useful in the treatment of itch (Kirtikar KR *et al*., 1935).

Vernacular names

Sanskrit- *Nagakesar*; English- *Ceylon ironwood*; Hindi and Bengali- *Nagkeshar*, Gujarati and Marathi- *Nagchampa*; Malayam- *Nanga, veluthapala*; Assam- *Nahor*.

Morphology (Wealth of India, 1962)

Bark: Bark surface is smooth to adherent scaly, greyish or reddish brown in colour, exfoliating in large thin flakes.

Leaf: Elliptical shape, Lanceolate, coriaceous, generally covered with a wazy bloom underneath, red when young, opposite and simple with an entire margin. Upper surface is glabrous where as Lower surface glaucous. Leaves texture are shiny with numerous secondary veins, looping, running parallel nearly to the margin, frequently with equally prominent reticulating tertiary veins. Sometimes with more or less persistent stipule-like interpetiolar modified leaves. The base is somewhat rounded or acute in shape.

Wood: The wood is very durable; graveyard test indicate a life of 10-15 years. Sapwood is creamy white or pinkish brown, rather broad; whereas the heartwood is red or deep reddish brown, smooth, straight- or somewhat interlocked grained, medium, to coarse-textured, hard, strong, tough and heavy.

Fruit: Ovoid almost round nearly woody with a prominent beak when matured, 2.5-5.0 cm long with persistence enlarged calyx. Pericarp hard, warty, two valved after dehiscence.

Seed: Angular in shape, smooth, 1-4 in number, dark brown, up to 2.5cm diameter, cotyledons are fleshy and oily.

Flowers: The flowers are fragrant, cream coloured, ebracteate, pedicellate, pedicel short, axillary or terminal, solitary or in pairs (cluster) and 2.5-7.5 cm in diameter, bisexual**,** large, sub-sessile and buds are sub-globose, bracts nil. After the flower parts are dissected it was found that all the four whorl of the flower parts are seen to be clearly visible. Sepals are seen to be 4 in number, 2 outer slightly shorter than the inner ones and depressed at the based, orbicular, cubbed and puberulous. Petals are 4 in number, pure white fragrant, spreading, obovate-

cuneate, with crisped and undulate margin often torn. Stamens are very numerous golden yellow united much shorter than the petals and are slightly united at the based into a fleshy ring. Filaments are small and anthers oblong. Ovary is seen to be superior, bicarpellary, syncarpous, style is found to be twice as long as the stamens, stigmas capitate, style and stigma persistent in young fruit but are shaded away later on(Sahu Alakh N *et al.*, 2013).

Microscopical characters

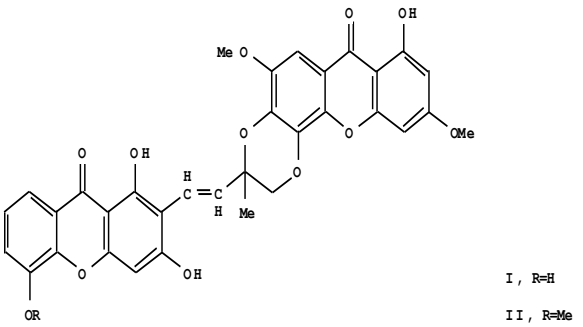
The transverse section has showed that the section composes of a two layered epidermis upper and lower one. Numerous trichomes are found to be present on the upper layer of the epidermis. Trichomes having the characteristics which are multicellular multiseriate type. The epidermis constitutes of a thick cuticle and is formed by few layers of cells. Below the epidermis is the ground tissue (cortex region) made of several layers of rounded collenchymatous cells. The cortex also constitutes of sclerenchymatous celled layers that is made up of sclerenchymatous fibres. In addtition several numerous oil glands are also seen scattered in the cortical region. The ground tissue layer is followed by the lower epidermis which is also made up of few layers of round collenchymarous cells. The transverse section through the ovary shows the clear visbility of the ovary with its two ovules arranged in axile placentation manner (Shome U *et al.*, 1982 & Sahu Alakh N *et al.*, 2013).

PHYTOCHEMICAL REVIEW

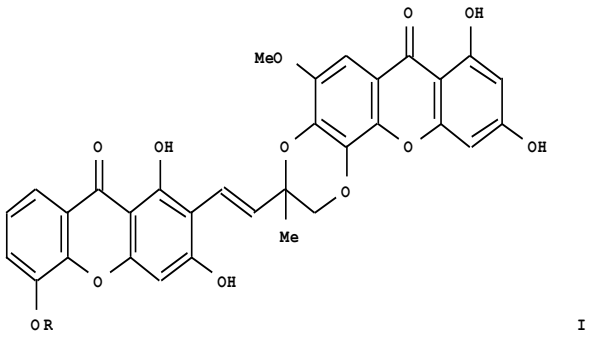
Flower parts of the plant have shown the presence of various constituents such as glycosides, coumarins, flavanoids, xanthones, triglycerides and resins. But in spite of these a lot more investigation has been found out which leads to the discovery of certain new compounds that has different activities on the human body. A few numbers of phytochemical studies that have been carried out so far are outlined below chronologically:

- The essential oils from the bark, leaves, buds, and flowers (full bloom) of *Mesua ferrea* Linn., Guttiferae, were analyzed by high resolution GC and HRGC/MS. The bark oil was rich in (E)-**α**-bisabolene (31.3%) and **α** -selinene (12.2%). The predominant components in the oils of tender and mature leaves were **α** -copaene (19.3% and 9.9%) and β-caryophyllene (18.8% and 26.0%). The bud and flower oils also contained **α** -copaene (28.7% and 20.2%), and in additionn germacrene D (19.0% and 16.1%) **(**Choudhury S, 1998**).**

- From the stem bark of *Mesua ferrea* betulinic acid, (-)-epicatechin, 1,6-dihydroxyxanthone, pyranojacareubin and two novel bis-xanthones have been isolated. The bis-xanthones were characterized, on the basis of 2D homo- and heteronuclear correlation NMR spectroscopy as (E)-2ξ-methyl-2ξ-{2-(2,7,9-trihydroxyxanthon-8-yl)ethen}-dioxan-({5,6c:2,3e-}-7-hydroxy-4,9-dimethoxyxanthone)(I, mesuabixanthone-A) and its monomethyl ether (E)-2ξ-methyl-2ξ-{2-(7,9-dihydroxy-2-methoxyxanthon-8-yl)ethen}-dioxan-({5,6c:2,3e}-7-hydroxy-4,9-dimethoxyxanthone) (II, mesuabixanthone-B) (Singh S *et al*., 1993).



- Two new dimeric xanthones mesuferrol A (I;R=H) and B (I;R=Me) were isolated from the bark of *M. ferrea*, in addition to two known xanthones {(1,7-dihydroxy- and 5-hydroxy-1-methoxyxanthone) and a flavonoid (-)-epicatechin}. The structures of these compounds were established by spectroscopy, including 2D NMR (Iinuma, M *et al.*, 1996).

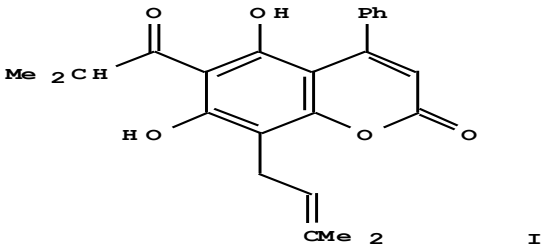


I

(Mesuferrol A)

- A report on the fatty acid composition of *Mesua ferrea* L. seed oils was investigated. The purified and refined oil did not show the presence of epoxy or cyclopropenoid moieties. Octadecatrienoic acid was identified the seed oil. The kernel oil was rich in octadecanoic (18:1) acid. The other major acid was the hexadecanoic (16:0) acid (26.8%) (Chowdhury A *et al.*, 1992).

- A single crystal x-ray structure analalysis confirmed the structure of mesuol (I) from the plant *M.ferrea*. This mesuol was optically inactive and was reported to have bitter antibiotic property (De, Amitabha *et al*., 1991).

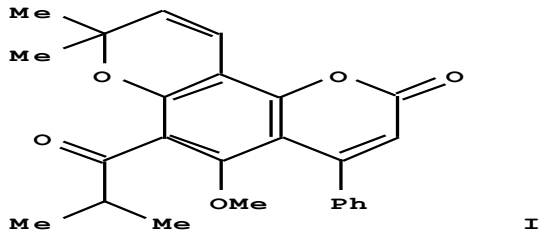


I

(Mesuol)

➢ Petrol extracts of the stamens of *M. ferrea* gave **β**-amyrin, **β**-sitosterol, and a new cyclohexadione compound and named as mesuaferrol (I) (Dennis TJ *et al*., 1988).

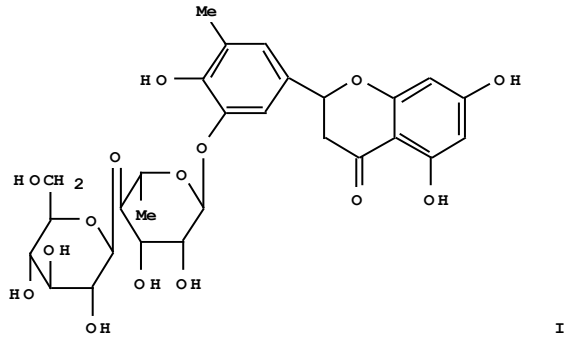
➢ A new coumarin named mesuarin (I) was isolated from the seed oil of *M. ferrea* and its structure was detected. In a test for antibacterial activity against gram-positive and gram negative bacteria, Mesuarin (I) was active only against *Bacillus firmis* (Bhattacharyya P *et al*., 1988).



I

(Mesuarin)

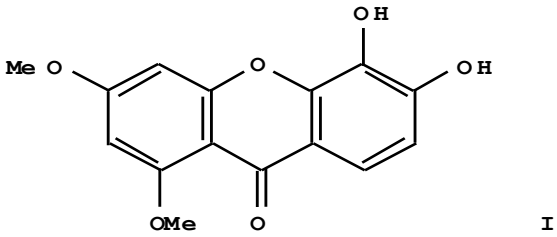
➢ Spectral and chemical methods indicated that mesuein (I) a novel flavones glycoside was isolated from the leaves of *M. ferrea* and was identified as 5'-C-Me eriodictyol 3'-O-**β**-D-galactopyranosyl(1→4)-**α**-L-rhamnopyranose. Mesuien is the first flavanone glycoside having a C-Me substituent in the B-ring (Alam *et al*., 1987).



I

(Mesuein)

➢ Ferrxanthone, a 1,3,5,6-tetraoxygenated xanthone was isolated from *Mesua ferrea* and its structure was detected by chemical and spectral data (Walia, S., *et.al*, *1984*).

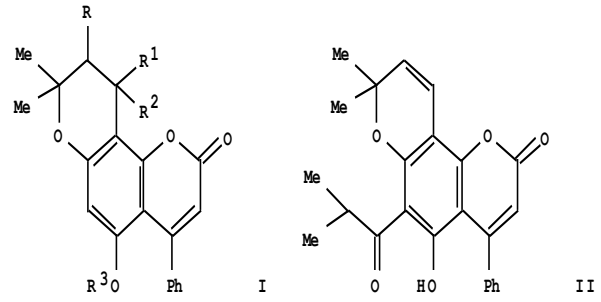


I

(Ferrxanthone)

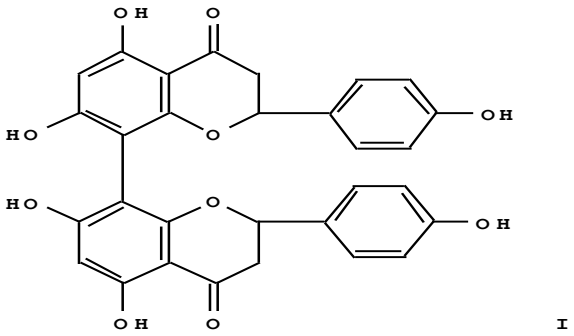
➢ Pharmacognostic and phytochemical features of the flowers of the crude drug *Mesua ferrea* (Nagkeshar) were investigated. The flowers and stamens were extracted seperately with various solvents such as hexane, benzene, CHCl3, alcohol and H2O, the percentage of each extract calculated and the extracts screened for triterpenoids, flavonoids, alkaloids, and tannins by means of color tests with various reagents. TLC of these extracts indicated the presence of a mixture of compounds. The hexane and benzene extracts showed the presence of triterpenoids and resins, while the alcoholic and H2O extracts were rich in reducing sugars, and tannins and saponins, respectively (Shome U *et al*., 1982).

➢ Condensation reaction of 5, 7-dihydroxy-4-phenylcoumarin with $Me_2C{:}CHCO_2H$ gave the compound (I) with nomenclature (R = R3 = H, R1R2 = O) which on reduction with $NaBH_4$ gave (I) with nomenclature (R = R1 = R3 = H, R2 = OH). Dehydration of this with p-$MeC_6H_4SO_3H$ gave (I) with nomenclature (R2 = R3 = H, RR1 = bond) which on treatment with $Me_2CHCOCl$ gave with nomenclature (I) (RR1 = bond, R2 = H, R3 = Me2CHCO). Treatment of the last with AlCl3 in $PhNO_2$ gave mesuagin (II) (Bhattacharyya P *et al.*, 1979).



I II

➢ Raju MS *et al*., (1976) pictured the structure of Mesuaferrone B by means of spectral and chemical analysis. The optical activity of is largely due to atropisomerism. In 1978 he and his co-workers again reported the structure of mesuaferrone A from the stamens of the same plant and the structure was established as 8,8'-binaringenin as shown below:



I

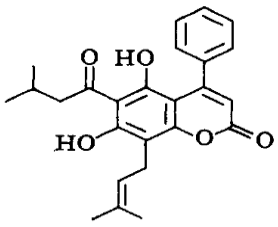
(Mesuaferrone B)

➢ Various forms of xanthones component were isolated from the timber of *Mesua ferrea* L. and were reported to be 2-Hydroxy-, 2-methoxy-, 4-hydroxy-, 1,5-dihydroxy-, 1,7-dihydroxy-, 1-hydroxy-5-methoxy-, 1-hydroxy-7-methoxy-, 3-hydroxy-4-methoxy- and 1,5,6-trihydroxyxanthone and the new xanthones (I) (R = H, Me). The structures of (I) were detected from the chemical and spectral data **(**Gunasekera SP *et al*., 1975**).**

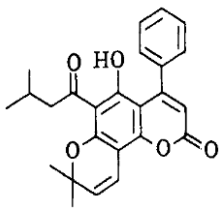
➢ From the acetone ext. of *Mesua ferrea* stamens, a new carboxylic acid (I) designated as mesuanic acid was isolated. Mesuanic acid possesses cyclohexadienone ring system, commonly encountered in the acids occurring in Calophyllum species such as calophynic acid and pseudobrasiliensic acid **(**Raju MS *et al*., 1974**).**

➢ The biosynthesis of isobutyryl group in mesuol (4-phenylcoumarin) was done by incorporating L-valine-U-14C into the isovaleryl side chain of mammeisin and into the isobutyryl side chain of mesuol (Kunesch G *et al*., 1971).

➢ In 1971 Bala, K. R. reported two main phenolic components from the seed oil of *M. ferrea* of which one compound was identified as mammeigin (I) and the other as mesuol (II). The synthesis of mammeisin and mammeigin (I) was carried out and also the conversion of mesuol (II) into mesuagin (III) also take place.

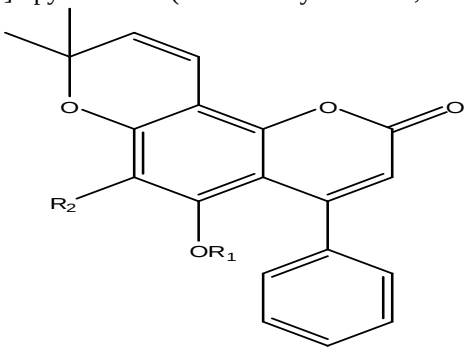


Mammeisin



Mammeigin

➢ The structure of Mesuagin a new 4-phenylcoumarin was isolated from the seed oil of *Mesua ferrea* and its structural formula was pictured as 5-hydroxy-6-isobutyryl-8,8-dimethyl-4-phenyl-2H,8H-benzo[1,2-b:3,4-b']dipyran-2-one (Chakraborty DP *et al*., 1969).



II, R_1=H; R_2= $CO.CH(CH_3)_2$

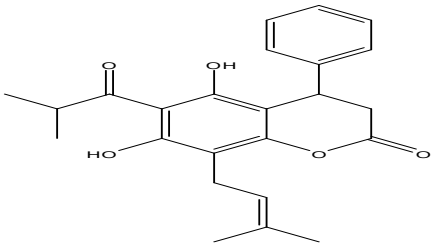
(Mesuagin)

➢ Chloroform extract of Mammeisine (4-phenylcoumarin) isolated from the young seedling of *M.ferrea* was chromatographed on silicic acid with C_6H_6-EtOAc (9:1) as the solvent system. Mammeisine was transformed to its methyl di-ether derivative and repeatedly crystallize from hexane. Then it was further treated with 70% H2SO4 for 72 hours in which coumarin (II) got precipitated. The supernatant liquid was then extracted with ether and finally after evaporation the residue was mixed with p-bromophenacyl bromide, yielding the p-bromophenacylate of isovaleric acid (III) (Kunesch, G., et al., 1969). According to Raju, M., *et.al* (1969) the seeds of *M. ferrea* gives a crystallized compound which was isolated and identified as mammeisin on the basis of chemical and spectral studies of its acetate and of the product obtained by acid hydrolysis of the acetate, the latter is the cyclized product which was identified as dihydromammeigin.

➢ The heartwood of *M. ferrea* contained 1, 5-dihydroxyxanthone, euxanthone 7-Me ether and **β**-sitosterol, in addition to the two xanthones previously isolated. The I.R. and N.M.R. spectra of xanthones were discussed **(**Chow YL *et al*., 1968**).**

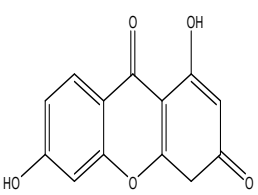
➢ Ferruol A ($C_{23}H_{30}O_{5)}$ which is a new 4-alkylcoumarin was isolated from the trunk bark of *M. ferrea* L. (Govindachari TR *et al.*, 1967).

➢ N.M.R. and degradation studies suggest the structure of Mesuol which after isomerization leads to the formation of the new derivatives with a m.p of 171° on treatment with 5% methanolic or 10% aqueous NaOH. When mesuol was treated with 40% aq. KOH it gave Me_2CO, PhCOMe, isovaleric acid, and a 4-phenylcoumarin having a m.p of 268ºC. The dimethylmesuol is stable toward 40% aqueous KOH (Chakraborty DP *et al.*, 1966).

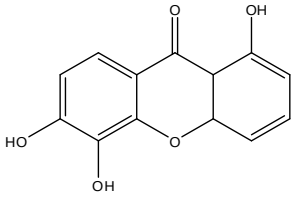


(Mesuol)

➢ Two new yellow pigments, mesuaxanthone A and mesuaxanthone B, and the known euxanthone were isolated from the heartwood extracts of *Mesua ferrea* L. Evidence is presented to show that mesuaxanthine A is 1,5-dihydroxy-3-methoxyxanthone and mesuaxanthone B is 1,5,6-trihydroxyxanthone. Mesuaxanthone A has been synthesized (Govindachari TR *et al.*, 1967).



Mesuaxanthone A



Mesuaxanthone B

➢ Paper chromatography of the oil of *Mesua ferrea* L. fruit was analysed and it was found to contain 23% of the total protein content. The amino acids reported are cystine, arginine, serine, citrulline, hydroxyproline, proline, alanine, methionine, phenylalanine, isoleucine, leucine, and 3 unidentified spots (Chaudhuri SB *et al.*, 1964).

➢ According to Gupta, A.C., *et.al* (1951) the seed of *Mesua ferrea* yields yellow, malodorous oil with saponification number of 196 and Iodine number of 90.0. Its fatty acid contents are palmitic 8.2%, stearic 15.8%, arachidic 1.0%, oleic 55.4%, and linoleic 19.6%.

➢ A yellow crystal compound (m.p 152ºC) which has the bitter principle was obtained from the oil of *M.ferrea* L. This was identified as Mesuol which gave green color with $FeCl_3$ to form a dimethyl derivative containing a lactone ring (m.p 132ºC) (Dutt P *et al.*, 1940).

➢ Several types of fatty acids were found out from the plant *Mesua ferrea* L. and their percentage compositions occur to be different from one location to another. The fatty acid that was obtained from *Mesua ferrea* L (malabar) had the percentage composition of myristic acid (1.8%), palmitic acid (6.3), stearic acid (10.7), oleic acid (49.2), linoleic acid (7.3) and unsaponifiable (24.7%). The fatty acids of Mesua ferrea (Bengal) in percentage composition were: myristic (1.4%), palmitic (7.5%), stearic (9.2%), arachidic (1.7%), oleic (58.7%), linoleic (9.9%) and unsaponifiable (11.6%). (Dhingra DR *et al.*, 1931). The fatty acids obtained from the *Mesua ferrea* (Western Ghats) were extracted with petroleum ether giving a 60% yield of the oil. The fatty acids were separated into a solid form (stearic 10.45% and palmitic acids 7.95%) and a liquid fraction (linolic 21.05% and oleic acids 60.55%). (Phadnis KD *et al*., 1949). *M.ferrea* collected from Assam forest, Eastern Himalayas and Burma was reported to contain the total fatty acids which are palmitic 8.2, stearic 15.8, arachidic 1.0, oleic 55.4 and linoleic 19.6 (Chatterji NG *et al*., 1937).

PHARMACOLOGICAL REVIEW

The pharmacological review about the plant is outlined below chronologically:

➢ Seven coumarins from *Mesua ferrea* were tested for modulator activity using ethidium bromide (EtBr) as a substrate. Compounds 1, 4-7 modulated the MIC of EtBr by ≥2 fold against wild type clinical strains of S. aureus 1199 and S. aureus 1199B, whereas compounds 4-7 modulated the MIC of EtBr by ≥16 fold against MRSA 831. Compounds 1, 4-7 also reduced the MIC of norfloxacin by ≥8 fold against S. aureus 1199B, and 4-6 reduced the MIC of norfloxacin by ≥8 fold against MRSA 831 at half of their MICs. Inhibition of EtBr efflux by NorA-overproducing S. aureus 1199B and MRSA 831 confirmed the role of compounds 4-6 as NorA efflux pump inhibitors (EPI) (Roy SK *et al*., 2013

➢ The cytotoxic structure-activity relationships among a series of xanthone derivatives from *Mesua beccariana, Mesua ferrea and Mesua congestiflor a* were studied. Eleven xanthone derivatives identified as mesuarianone (1), mesuasinone (2), mesuaferrin A (3), mesuaferrin B (4), mesuaferrin C (5), 6-deoxyjacareubin (6), caloxanthone C (7), macluraxanthone (8), 1,5-dihydroxyxanthone (9), tovopyrifolin C (10) and α-mangostin (11) were isolated from the three Mesua species. The human cancer cell lines tested were Raji, SNU-1, K562, LS-174T, SK-MEL-28, IMR-32, HeLa, Hep G2 and NCI-H23. Mesuaferrin A (3), macluraxanthone (8) and α-mangostin (11) showed strong cytotoxicities as they possess significant inhibitory effects against all the cell lines. The structure-activity relationship (SAR) study revealed that the diprenyl, dipyrano and prenylated pyrano substituent groups of the xanthone derivatives contributed towards the cytotoxicities (Teh SS *et al*., 2013).

➢ The antibacterial efficacy of leaf and fruit extracts of *Mesua ferrea* on the growth and morphology of *Staphylococcus aureus* was evaluated. Both extracts displayed good antibacterial activity against *S. aureus* with a minimum inhibition concentration of 0.048 mg/mL. Both extracts were bacteriostatic at a minimum bacteriostatic concentration of 0.39 mg/mL. Scanning

electron microscopy study indicated potential detrimental effect of the extracts of leaf and fruits of *M. ferrea* on the morphology of *S. aureus.* The treatment with the extracts caused extensive lysis of the cells, leakage of intracellular constituents, and aggregation of cytoplasmic contents forming an open meshwork of the matrix (Aruldass CA *et al*., 2013)

- In humoral immune response model, mesuol from *Mesua ferrea* 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 immunosuppressed 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 neutrophil adhesion in neutrophil adhesion test in rats and phagocytosis in carbon clearance assay. The study indicated immunomodulatory activity of mesuol (Chahar MK *et al*., 2012)

- *Mesua ferrea* protected rats against formaldehyde and CFA induced arthritis. The body weight changed and haematological perturbations induced by CFA were maintained. The overall results indicated that *Mesua ferrea* exerts a potent protective effect against formaldehyde and adjuvant-induced arthritis in rats (Jalalpure SS *et al*., 2011)

- The whole flower extract of *Mesua ferrea* Linn. was recently reported to be effective as antibacterial activity and was tested for its *in vitro* antimicrobial efficacy against five different strains of Salmonella species. All the strains were found to be highly sensitive to the extract, MIC of the extract against each organism being 50 microg/ml. The extract was tested in vitro for its mode of antibacterial activity against *S. Typhimurium* NCTC 74 and it was found to be bactericidal in action. In vivo studies of this extract offered significant protection to Swiss albino mice at doses approximately 2 and 4 mg/mouse when challenged with 50 median lethal dose of *S. Typhimurium* NCTC 74. Further, the extract caused statistically significant reduction in viable count of the strain in liver, spleen and heart blood of challenged mice (Mazumder R *et al*., 2005).

- The two coumarins compounds namely 4-alkyl- and 4-phenyl 5,7-dihydroxycoumarins that were obtained by supercritical CO_2 extraction from the blossom of *M.ferrea* were shown to be a promising multidrug resistant antibacterials. These compound were shown to have a weak antiprotozoal activity and a potent antibacterials on some gram positive bacteria (Verotta L *et al*., 2004).

- Methanolic extract of the whole flower parts of *M.ferrea* Linn was proved to have activity on various strains of Gram positive and Gram negative bacteria at concentration range of 100 to 50 microgram/ml or even as lower, in addition not only bacteria it is also active against vibrios and *Escherichia coli*. Moreover a test has been performed in which different dose of the extracts was given to Swiss strain of albino mice and the effective dose was found to be 200 microgram/gm of the body weight that reduces the viable count of the strain *Salmonella tuphimurium* ATCC 6539 in liver, spleen and heart blood of mice (Mazumder R *et al*., 2004).

- The crude extract of *M.ferrea* L. showed a strong cytotoxic activity toward T-lymphocyte leukemia cells and weak antimicrobial activities against bacteria, namely *Staphylococcus aureus, Bacillus subtilis, and Pseudomonas aeruginosa* (Nordin K *et al*., 2004).

- Various medicinal plants including *M.ferrea* was shown to have a significant inhibitory effect on the activity of the pancreatic lipase enzymes (Gowadia N *et al*., 2000).

- A formulation containing drug mixtures of *Foeniculum vulgare* seeds, *Curcuma zedoaria* tubers, *Mesua ferrea* flowers, *Nigelia sativa* seeds, *Terminalia chebula* seeds and *T. arzuna* stem bark when administered orally (500ml/kg) to rats showed to have increase the percentage of fetal loss and inhibited implantation by 60% (Sheshadri C *et al*., 1981).

- The xanthones obtained both from *M.ferrea* and its adulterant *C.innophylum* namely dehydrocycloguanandin [17623-63-1], calophyllin-B [17623-60-8], jacareubin (JR) [3811-29-8], and 6-deoxyjacareubin (DJR) [16265-56-8], mesuaxanthone-A [3561-81-7], mesuaxanthone-B [5042-03-5], and euxanthone [529-61-3] were shown to have CNS depression characterized by ptosis, sedation, decreased spontaneous motor activity, loss of muscle tone, potentiation of pentobarbitone sleeping time, and ether anesthesia in mice and rats. When administered by i.p and oral routes they were found to have anti-inflammatory activity and anti-ulcers activity was found to be effective with phytoconstituents like jacareubin and 6-deoxyjacareubin (Gopalkrishnan C *et al*., 1980).

- A phenol containing fraction of *Mesua ferrea* seed oil was reported to lacked bronchodilatory activity but potentiated isoprenaline [7683-59-2]-induced relaxation

of guinea-pig tracheal smooth muscle both in vitro and in vivo. The phenolic fraction also inhibited the release of histamine [51-45-6] in passive peritoneal anaphylaxis and chopped lung anaphylaxis (Bhide MB *et al*., 1976).

➢ The essential oils of various plants were studied for their antibacterial activity. Five plants viz. *Apium graveolens (celery), Mesua ferrea, Miliusa tomentosa*, *Vateria indica,* and *Ferula narthex* and the essential oil was detd. by the filter-paper disk method. The oils and their combinations were screened against 15 pathogenic and nonpathogenic microbes. *V. indica and M. tomentosa* exhibited the greatest antibacterial activity against Salmonella typhi and Streptococcus faecalis; A. graveolens and *M. ferrea* were effective against *Pseudomonas solanacearum; and F. narthex* was effective against *Corynebacterium diphtheriae, Streptococcus faecalis, Streptococcus pyogenes, and P. solanacearum (*Kar A *et al*., 1971).

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