MESUA FERREA LINN. (NAGKESAR): A POTENT ANTIMICROBIAL PLANT SPECIES

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ABSTRACT

Many plants have not been investigated thoroughly, which are used traditionally as a medicine to cure various diseases. Herbal plants play a vital role in the development of new drugs which can be used for various therapeutic indications. Mesua ferrea linn, commonly known as ‘Nagchampa’ or ‘Nagkesar’, is one such herbal plant having many potential therapeutic activities. It is used in diseases like rheumatism, asthma, inflammation, fever, dyspepsia, renal diseases, dysentery, bleeding piles, a bacterial and fungal infection. This plant possesses many bioactive chemical constituents like coumarins, xanthones, pyranoxanthones, flavonoids, terpenoids and steroids which can be easily isolated. It can act as precursors on many ailments. These bioactive constituents have many pharmacological activities such as anti-cancer, antimicrobial, antifungal, anti-inflammatory, anti-arthritis, analgesic, diuretic, anti-hemorrhoid, antiallergic and many more. Almost every part of the plant is reported to have beneficial medicinal properties. But further studies are still needed to explore the pharmacological activities of Mesua ferrea linn plant so as to gain benefit for the treatment of various diseases. This review highlights the general description, phytochemical profiling, traditional uses and proven pharmacological attributes of Mesua ferrea linn. plant.

Keywords: Mesua ferrea, Antimicrobial activity, Nagkesar, Cobra saffron, Ayurveda

INTRODUCTION

Medicinal herbs play a major role in our day-to-day life from providing food, shelter, clothes to medicines. The plants are being in use for medicinal purposes since ancient times. Medicinal plants have beneficial effects on the overall health of humans. As per the reports, Hippocrates used almost 400 different plant species at that times for medical purpose [1, 2]. In the past times, medicinal preparations were primarily derived from these herbal plants [3]. The plants play a vital role in the traditional medicinal system like Ayurveda, Siddha, Unani, Chinese and Egyptian system [4]. Some plants are greatly promoted due to the associated ethnobotanical belief of different cultures [5]. Many modern drugs in the present era have developed from plant sources because these contains phytochemicals which exhibit various medicinal properties [6, 7]. Almost half of the modern drugs have the presence of plant contents in them [8, 9]. WHO is continually promoting the use of herbal drugs as these drugs are considered superior than synthetic drugs because these are easily available, less expensive, compatible action mechanisms inside the living system, multi-target actions and produces negligible side effects [10-14]. One of the most ancient medicinal plant with significant value in many cultures is Mesua ferrea, locally known as Nageswar or Nagkesar. The plant belongs to the Guttiferae family. It is comprised of 47 genera with more than 100 species. The well-known genera of this family are Gratiosaum, Hypericum, Garcinia, Mesua and Vomia [15, 16]. Traditionally various species of Mesua are utilized by the inhabitants of Asian countries for the treatment of a variety of ailments [17, 18]. Mesua ferrea linn. is a medium-sized to a large evergreen tree with a short trunk buttresses at the base. The leaves of the plant are lanceolate, curvaceous, generally with a waxy bloom underneath. The leaves are red in color when mature. Flowers are large, white and fragrant and seeds are dark brown. The leaves and seeds were used as a remedy for cold, fever, sore, scabies by ayurvedic, unani doctors and local kabiraj [19, 20]. The volatile oil isolated from the flower possesses antifungal and anticanter activities [21-23]. The chemical examination of this plant has been carried out and several constituents were isolated such as lignan, alkaloids, flavonoids, tannins, phthalic acid, gallic acid and terpenoids. The principal constituents of Mesua ferrea linn. include mesuferrene-A and B mesuferreol, mesufernic acid, α- and β-amin and β-sitosterol present in stamen [24] while it is also reported that seeds contain essential oils, xanthones and coumarins [25-27]. The plant is widely used in folk remedies for numerous human ailments. Each part of the plant is utilized in various folk remedies of numerous diseases like rheumatism, piles, asthma, ulcers, hemuihthiasis, dysentery, hemorrhage and many other issues. In Ayurveda, the plant holds a significant place in the treatment of many diseases. Mesua ferrea is also used in herbal formulation to treat piles [28] and cancer [29]. It is also known for shade creation and radiation modification in improving human thermal comfort [30]. Konwer et al, reported that seed oil is a substitute for petroleum gasoline, the fraction distilling between 200 and 300°C may be used as fuel for diesel engines [31]. In recent years, plenty of research has been conducted to explore the pharmacological activities of the Mesua ferrea plant. Reported studies showed that the plant exhibits important biological properties like antimicrobial, anticancer, anti-inflammatory and immunomodulatory etc. Vernacular names and taxonomical classification of the Mesua ferrea linn. are given in table 1 and 2 respectively.

Table 1: Vernacular names of Mesua ferrea linn

| Language | Vernacular name |
|----------|----------------|
| Sanskrit | Kesara, Nagapuspa, Naga, Hema, Gajakesara |
| Hindi    | Nagkesara, Pila Nagkesara |
| English  | Cobras Saffron |
| Assam    | Naboor, Nabhor |
| Farsi    | Naremshah |
| Thai     | Bunnak, Bhra ba kaw |
| Phillipine | Kuliwas |
| Malaysia | Penaga |
| Italian  | Croco di cobra |
| Arabic   | Narae-kaisar |
| Russian  | Mezuza zheleznaia |
| Chinese  | Tie li mu |
| Bihar    | Nagkesur |
| Bengali  | Ngesvagesara, Nagesar |
| Gujarati | Nagchampa, Nagkesara, Sachanagkeshera, Pihngkesar, Tamranagkesar |
| Marathi  | Nagkesara |
| Telugu   | Nagachampakamu, Kesaramu |
| Tamil    | Nangu, Naugaliral, Nagachampakam |
| Kannad   | Nagakesari, Nagsampige |
| Assam    | Nagakesari, Nahar |
| Andamanas | Gangane |
| Malayalam | Nangaa, Nauga, Peri, Nagppu, Nagappovu, Veluthapala |
| Orissa   | Nageswar |
| Punjabi  | Negeswar |
| Urdu     | Narmushik, Nagkesar |
Table 2: Taxonomical classification of Mesua ferrea linn

| Taxonomical classification | Taxon                  |
|---------------------------|------------------------|
| Kingdom                   | Plantae                |
| Division                  | Tracheophyta           |
| Class                     | Magnoliopsida          |
| Order                     | Malphighiales          |
| Genus                     | Mesua L.               |
| Family                    | Guttiferae/Calophylacea |
| Species                   | Mesua ferrea           |
| Common Name               | Nagkesar               |

Botanical description of Mesua ferrea linn

Mesua ferrea linn. is an evergreen medium to large-sized ornamental plant. It is a medium-sized plant long up to 13 mm, often buttressed at the base with the trunk up to 90 cm in diameter. Leaves are about 3 to 5 inches long, simple, narrow, ovate and egg-shaped. Leaves are dark green with a whitish underside, the newly growing leaves are red then slowly turn into yellow. Flowers (fig. 1) are about 4 to 7.5 cm in diameter with four white petals and a center of numerous yellow stamens. Fruits are oblong in shape they are about 2.5 to 5.0 cm long with persistent calyx. Seeds are dark brown in color and cotyledon is fleshy and oily. The flower, fruit, seeds and leaves of this plant are edible [32].

Geographical distribution of Mesua ferrea linn

Mesua ferrea linn. is a known native plant in most of the Asian countries including Burma, Cambodia, Indochina, Malaysia, Myanmar, Nepal, Philippines, Sri Lanka, and Thailand. In India, it is distributed in the mountains of Eastern Himalaya and East Bengal, Assam, Burma, Andaman, evergreen rain forests of Western Ghats from South Canara to Travancore [33, 34].

Phytochemical constituents of Mesua ferrea linn

Kritikar and Rao, reported that the Mesua ferrea is the only species that has been chemically studied from the genus Mesua [35, 36]. Phytochemical studies have revealed plants from this genus to be rich in many classes of secondary metabolites including phenylcoumarins, xanthones and triterpenoids [37-39]. The kernels contain about 75% of yellowish oil, constituted by the glycerides of common fatty acids like linoleic, oleic, stearic, and arachidic acids. An oil called nahr is extracted from these seeds [40]. 4-Phenylcoumarins like mesuol, mesuagain, mammesin, mammnig and mesunone were isolated from seed oil of Mesua ferrea. The trunk bark and heartwood yielded 4-alkylcoumarins ferruols A and B, a lupeol-type triterpenoid guttiferol, mesuaxanthone, 1,5-dihydroxy-3-methoxyxanthone, 1-hydroxy-7-methoxyxanthone and β-sitosterol. Stamens give α and β-amyrin, β-sitosterol, bioflavanoids-mesuaferrones A and B, mesuanic acid, 1,5-dihydroxyxanthone, euxanthone 7-methyl ether and β-sitosterol. Other isolated constituents were mesuaferrrol, leuco anthocyanidin, mesuone, euxanthone, etc. Presence of xanthone derivative and essential oil had also been reported from various parts of the plant [41]. Two new yellow pigments, meauxanthone A and memaxantbone B have been isolated from the heart-wood extract of M. ferrea. The stamens which yield the drug Nagakeshara contain mesuaferrone-A and B, mesuaferrrol, mesuanic acid, α and β-amyrin [42].

Traditional and modern view

a. Folk view

There are many social and cultural beliefs associated with some plants representing their rich ethnobotany. Mesua ferrea linn. is one of the rich ethnobotanical plant found in many countries. Rai et al., reported that the plant Mesua ferrea linn. is used in inflammation and septic conditions [43]. This plant was used for its antiseptic, purgative, blood purifier, worm control and tonic properties by the tribes of Assam [44]. In Thai traditional medicine, it is used to treat fever, cold, asthma and as a carminative, expectorant, cardiotonic, diuretic and antipyretic [45, 46]. The ashes of leaves are utilized for sore eyes. Seeds were used to poultice wounds [47, 48]. Leaf and flower are antidotes for snakebite 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 [49, 50]. The aerial parts are choricronine containing active, spasmylocytic, diuretic, abortifacient and used in fever, dyspepsia, renal disorders and in cosmetic [51-53]. The local communities of Bangladesh used powder of dried fruits and leaves of Mesua ferrea mixed with ghee to get relief from burning sensation in hands and feet, joint pain and cold [54].

b. Ayurvedic view

As per Sushruta Samhita (Surgical compendium of Ayurveda), health is a balanced state of Doshas (three biological humors i.e. Kapha (Water and Earth), Pitta (Fire) and Vata (Space and Air), dhatus (seven body tissues), digestion, peace of soul, mind and senses [55-57]. Life is not merely to be alive, but to be well and to live a healthy life Ayurveda has mentioned immense herbs, one such amazing herb is Nagkesar. It is also known as Cobra Saffron, Ceylon Ironwood, Indian rose chestnut and Sirunagappu in Ayurveda. It balances the three Doshas of the body. It is considered mainly in bleeding disorders that occur due to the Pitta (heat) imbalance. Nagkesar is mostly indicated in bleeding disorders like piles, menorrhagia, metrorrhagia and epistaxis because it pacifies the Pitta that maintains the heat imbalance. This plant cures excessive bleeding. It also acts as an aphrodisiac and hemostatic. Its major action is on the blood capillaries due to its Kashaya rasa (astringent) and sheet Virya (Cool nature). It also helps to improve the conditions in blood capillaries due to its Kashaya rasa (astringent) and sheet Virya (Cool nature). It also helps to improve the conditions in blood capillaries due to its Kashaya rasa (astringent) and sheet Virya (Cool nature).

Table 3: Rasa panchak of Mesua ferrea linn. (Nagakeshara)

| Sanskrit/English       | Sanskrit/English       |
|------------------------|------------------------|
| Virya/Potency          | Ushana/Hot Potency     |
| Vipaka/Metabolic property | Katu/Pungent       |
| Guna/Physical Property | Laghu, Ruksa/little, Dry |
| Rasa/Taste             | Kashya, Tik/TAstringent, Bitter |

Ayurvedic formulations of masua ferrea linn. (Nagakeshara)

Mesua ferrea linn. is present in many Ayurvedic formulations like dasamoolarishta, mahakaleshwara rasa, kanakasava and various churnas which are used for the treatment of many ailments [65, 66].
c. Modern view

Herbal medicines are primarily known for their negligible adverse impacts, and high toxicity is a major challenge for medicines around the world [67]. But over the past few years, some deliberate practices have been noticed which are majorly responsible for the gradual fall in the quality of herbal products for example adulteration, contamination etc. As per the quality control guidelines of WHO, the definition of adulteration is "herbal material, an herbal constituent or related substance that is either deliberately or non-intentionally (through cross-contamination or contamination) added to an herbal material, herbal preparation, or finished herbal product" [68]. The authenticity and quality of these drugs must be checked carefully as adulterated herbal products have so many health risks associated with them. More checkpoints need to be placed during the whole process from the processing of the raw material to the formation of the end product so that authenticity and quality can be ensured [69, 70]. Some reported studies showed that Mesua ferrea plant is also utilized in modern medicine. Ethanol and petroleum ether extract of Mesua ferrea is used for sore, throat, cough and asthma [71]. The syrup of flower buds is utilized to cure dysentery. The leaves are used in the form of poultice which is applied to the head in severe colds [72, 73].

Based on the scientific studies, Mesua ferrea has the potential to be developed as a polyherbal pharmaceutical product in the form of topical antibacterial gel/cream or as a standardized extract for internal bleeding disorders. Apart from the pharmacological properties, numerous studies have highlighted the industrial applications of Mesua ferrea seed oils as an alternative biofuel in diesel and compression ignition engines. Seed oil is also used in the paint industry, as a multi-purpose industrial coating preparation and as biomaterials. Stemms of the plant are used as fragrant stuffing for cushions and pillows. Wood is considered suitable for all types of heavy construction including railways sleepers, transmission posts, heavy furniture, posts and tool handles [74, 75].

Reported therapeutic studies of Mesua ferrea

Various studies have been conducted on this plant to know its pharmaceutical and therapeutic uses. Large-scale clinical studies are still needed to prove the clinical efficacy of Mesua ferrea against a variety of human ailments. Reported therapeutic and pharmacological uses of Mesua ferrea L. Plant are shown in table 4.

Antioxidant activity

The anti-oxidant potential of Mesua ferrea L. was evaluated by Prashad et al., in an in vitro study. The ethanol extract of Mesua ferrea leaves was tested for its antioxidant activity by using a test like 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging. The findings revealed that 70% of ethanol extract of Mesua ferrea leaves possess significant antioxidant activity [76]. Another study conducted by Sahu Aalakh and colleagues showed modest antioxidant activity of methanol extract of flowers in DPPH free radical, superoxide and hydrogen peroxide scavenging assays [77]. Teh et al., reported that the polar extract (methanol) of Mesua ferrea roots was more active as compared with less polar and non-polar extracts [78]. Makuchuch et al., reported the promising antioxidant activities of water and hot water extracts of Mesua ferrea flowers in the DPPH scavenging assay. The finding revealed that water extracts of Mesua ferrea flowers possess stronger antioxidant activity than standard agent i.e., butylated hydroxyltoluene (BHT) with an EC50 values of 7.49 and 6.95 µg/ml respectively [79]. Rajesh et al., reported that the chloroform and methanol extracts of Mesua ferrea stem bark have good antioxidant activity in the in vitro models. It was found that the extracts protect erythrocytes, hemoglobin and DNA against oxidative stress-induced damage. The finding revealed that methanol extract possesses strong activity as compared with chloroform extract [80]. In another recent study, n-hexane extract of Mesua ferrea stem barks has been reported to possess good free radical scavenging activity with an IC50 value of 66.3 µg/ml [81]. Garg et al., investigated that both hexanolic and chloroformic extract of Mesua ferrea has antioxidant and hepatoprotective activity in female Wistar mice. An artificial infection was induced by the administration of S. aureus in drinking water for 24 h at the onset of the experiment. The result showed a significant reduction in catalase (CAT), Glutathione (GPK), Glutathione reductase (GR) and Alanine aminotransferase (ALT) activity. No change was observed in Creatinine phosphokinase (CPK), and creatinine in mice [82].

Antalgesic activity

Hasan et al., investigated that the non-polar (n-hexane) fraction of Mesua ferrea leaf have better antinociceptive activity against an acetic acid-induced visceral pain in mouse. The finding revealed that the non-polar fraction possesses better analgesic activity as compared to the polar fraction [83].

Anti-inflammatory activity

Gopalakrishnan et al., reported that the xanthones i.e., mesuaxanthone-A, mesuaxanthone-B, calophyllin-B, dehydrocylogoumanin, eukanthone, jaicareubin and 6-deoxy jaicareubin have promising anti-inflammatory activities in carrageenam-induced paw oedema rat models [84]. In addition, an Ayurvedic formulation (Shirshavaleha) containing Mesua ferrea in combination with other herbs has been shown to inhibit oedema development in the carrageenan-induced paw oedema model [85]. Similarly, another recent study reported that 80% ethanol extract of stem bark of Mesua ferrea have promising anti-inflammatory activity in a variety of in vitro bioassays. Results revealed that ethanol extract at the concentration of 100, 200 and 500 µg/ml has stronger anti-inflammatory activity in all in vitro bioassays as compared to the standard drug i.e. Indomethacin [86].

Anti-arthritis activity

Jalalpure et al., investigated that the seed extract of Mesua ferrea possesses potent anti-arthritis activity in two different in vivo models i.e., Formaldehyde-induced and Complete Freund's Adjuvant (CFA) induced arthritis in rats. The result showed a reduction in the arthritis lesion by swelling volume in CFA injected paw in rat models [87].

Antispasmodic activity

An in vitro study was conducted by Prashad et al., for the evaluation of the antispasmodic activity of petroleum extract of Mesua ferrea in the rat ileum. The contraction of the rat ileum was measured on a kymograph. The normal contraction of acetylcholine was reduced up to 70 and 86% whereas the normal response of acetylcholine in presence of atropine was reduced to 55% [88].

Antivenom activity

Uawonggul et al., investigated that the aqueous extract of Mesua ferrea leaves possesses anti-venom activity against fibroblast cell lysis after Heterometrus laoticus scorpion bite. The extract was evaluated against the viability of fibroblast cells after 30 min treatment with mock control or with 0.706 mg/ml plant extracts pre-incubated 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 [89].

Antimicrobial and antifungal activity

Antimicrobial activities of different parts of Mesua ferrea have been highlighted by various scientific studies. Verotta et al., investigated that the coumarins (4-alkyl and 4-phenyl 5,7-dihydroxycoumarins) isolated from flower of Mesua ferrea have antimicrobial activity against the strains of gram-positive bacteria [90]. Another study evaluated that the methanol extract of leaves also possesses antimicrobial activities against Basillus species, Escherichia coli, Staphylococcus aureus, Shigella, Salmonella and Lactobacillus arabinosus bacterial strains in the mice [91, 92]. Ali et al., reported that the polar extract of stem bark of Mesua ferrea have strong antibacterial activity against gram-positive Strptococcus aureus as well as gram-negative Escherichia coli/bacterial strains [93]. Likewise, another study revealed the antibacterial efficacy of flower extract of Mesua ferrea against the different strains of Salmonella spp. The extract was found to be active towards all the strains at the concentration of 50 µg. In addition, flower extract also showed promising in vivo antibacterial activity in S. Typhimurium NCTC 747 challenged mice and caused a statically significant reduction in the viable count of bacterial strain in liver, spleen and heart blood at the dose of 2-4 mg/mouse [94]. Lim et
al, reported that the methanol extract of Mesua ferrea seeds has antifungal activities against different strains of fungi including Candida albicans, Trichosporon beigelii, Macor hiemalis and some other species of Aspergilus [95]. Similarly, a recent study reported that the antibacterial activity of Mesua ferrea seed oil epoxy resin against Klebsiella pneumoniae (gram-negative) and Staphylococcus aureus (gram-positive) strains of bacteria [96]. Deshmukh et al., investigated a gel formulation containing six different herbs, including Mesua ferrea. The formulation was found to be beneficial in preventing skin infection associated with resistant strains of Staphylococcus aureus, Pseudomonas aeruginosa and Corynebacterium spp. [97]. Phukan et al., reported that the bio-oils extract of Mesua ferrea has antimicrobial activity against a variety of bacterial and fungal strains, which gives a hint about the possible pharmaceutical application of bio-oils [98].

Water disinfectant activity
Adewale et al., examined that the seed kernel oil of Mesua ferrea have potent water disinfectant properties and is also used as a natural disinfectant alternative to chlorine. The study showed that kernel oil has remarkable disinfection potential and the kinetic studies suggested that NSKO fitted a first-order model with a k value of 0.040 [99].

Diuretic activity
Tiwari et al., reported a polyherbal combination (Draksharista-T and-M) and its marketed formulation comprising of stamens of Mesua ferrea. The formulation was found to induce significant diuretic, kaliuretic and natriuretic effects in the albino rats over 5 h compared to the control group [100].

Anti-hemorrhoid activity
Parajpe et al., evaluated a polyherbal formulation containing Mesua ferrea for its efficacy to treat bleeding piles in a preliminary clinical study using 22 human subjects. The finding revealed that out of 22 subjects, 16 patients showed improvement in terms of bleeding with no noticeable adverse effects [101]. Another recent study also highlighted the efficacy of standardized herbal preparations (Daflon and Roidosanal) containing Mesua ferrea in terms of improvement of ano-rectal conditions in Grade I and II patients [102].

Wound healing activity
Chaudhary et al., reported that the tannins isolated from the ethanol extract of aerial parts of Mesua ferrea have promising wound healing activity in excision and incision wound rat models. The extract was applied in the form of an ointment. Increased epithelialization and wound contraction were found in the animal models [103].

Central nervous system depressant and anticonvulsant activity
From a reported study, Xanthones (mesuaxanthone-A, mesuaxanthone-B, calophyllin-B, dehydrocycloguanandin, euxanthone, jacearubin and 6-deoxy jacearubin) were found to have CNS depressant effects in both mouse and rat models. Typical CNS depressant effects i.e., ptosis, sedation, loss of muscle tone and reduced spontaneous motor activity were observed in the xanthones treated animals. Chakma et al., reported that the flower extract of Mesua ferrea has significant anticonvulsant activity in the pentobarbital-induced mouse model [104].

Immunomodulatory and hormone balancing activities
Chahar et al., studied the effect of mesuel isolated from the seed oil of Mesua ferrea for immunomodulatory activities using both humoral and cellular immune assay. In humoral immune response assay, mesuel was significantly increased the antibody titer values in the rats. In addition, flower extract of Mesua ferrea has also been shown to possess estrogen and progesterone-like effect which were helpful in the correction of hormonal imbalance during menstrual disorders [105].

Antidiabetic activity
Balekar et al., reported that the methanol extract of Mesua ferrea leaves have promising antidiabetic activity in streptozotocin-induced diabetic rats. It was found that the extract reduced the blood glucose levels and normalized the body weight in diabetic rats [106].

Hepatoprotective activity
Garg et al., evaluated the hepatoprotective effects of methanol extract of Mesua ferrea flowers in Staphylococcus aureus inoculated male Wistar rats. One weak treatment with 50,100 and 200 mg/kg of methanol extract showed significant improvement in the levels of liver enzymes like CAT, SOD, GPx and GR with a concomitant decrease in the level of AAT and AST enzymes [107]. In another study, hepatoprotective effects of different extracts of stamens were evaluated using in vivo carbon tetrachloride-induced oxidative stress liver slice culture model. The finding revealed n-hexane and ethanol extracts of stamens protect cultured liver slice cells against carbon tetrachloride-induced oxidative stress [108].

Cardioprotective activity
A polyherbal drug (Ashwagandharishta) and its marketed preparation containing stamens of Mesua ferrea which have been shown to protect against isoproterenol-induced myocardial infarction in the albino rat model. Treatment with herbal formulation also significantly prevented the isoproterenol-induced adverse changes in the levels of serum marker enzymes such as alanine aminotransferase, aspartate aminotransferase, creatine kinase and lactate dehydrogenase with concomitant improvement in the serum lipid profile. The cardioprotective activity of herbal formulation was due to an increase in in vivo antioxidant level of GSH and inhibition of lipid peroxidation of cardiac membranes in the treated rats [109].

Protection against chronic obstructive pulmonary disease (COPD)
Rafiq et al., conducted a study in rats. The study showed herbal formulation (Bresol) comprising of Mesua ferrea flowers has protective effects against cigarette smoke-induced COPD in rats. The rats were treated with 250 and 500 mg/kg for five weeks. The finding revealed improvement in terms of reduction in tracheal inflammation, decrease in TNF-α and total protein levels in the bronchoalveolar lavage fluid and maintained the normal cellular architecture of the trachea and lungs [110].

Anticholinesterase and α-amylase inhibitory activity
Teh and colleagues in their recent study highlighted that the secondary metabolites isolated from different species of Mesua including Mesua ferrea have acetylcholinesterase inhibitory activities and have the potential to be used in Alzheimer’s disease [78]. Charabarti et al., revealed that Mesua ferrea extract have moderate α-amylase inhibitory activity with an IC50 value of 146.8 µg/ml while standard drug, acarbose showed strong α-amylase inhibitory activity with IC50 value of 14.24 µg/ml [111].

Anticancer activity
Various crude extracts and pure compounds have shown promising anticancer activities in the preliminary in vitro anticancer screening assays. Volatile oils-rich methanol extract of Mesua ferrea flowers showed strong cytotoxic activities against T-lymphocyte leukemia cells with an IC50 value of 12.5 µg/ml [112]. In another study, ethanol extract of Mesua ferrea flower was tested against three human cancer cell lines viz., CL-6 (cholangiocarcinoma), Hep-2 (Human laryngeal cancer) and Hep G2 (human hepatocarcinoma) cell lines. The result showed that ethanol extract was selectively toxic towards Hep-2 cell line with an IC50 value of 19.22 µg/ml [113]. Another study revealed that essential oil of Mesua ferrea leaves possesses cytotoxic activities against three cancer cell lines viz., KB (oral carcinoma), MCF-7 (breast adenocarcinoma) and NCI-H1187 (metastatic lung carcinoma). No toxic effects were found against green monkey normal kidney cell lines [114].

Toxicology
Acute toxicity studies on different extracts of Mesua ferrea were conducted using albino mouse and rat models. In rat model, 5g/kg doses of three different seed extracts i.e. petroleum ether, ethyl acetate and alcoholic extract did not show any signs of toxicity during the first 24 h and mortality in any of the test groups was observed [115]. Likewise, acute toxicity studies of methanol extract
Table 4: Reported therapeutic and pharmacological uses of *Mesua ferrea* L. plant

| S. No. | Extract | Method In vivo/In vitro | Pharmacological activity | Reference |
|--------|---------|-------------------------|--------------------------|-----------|
| 1.     | Ethanol Extract | In vitro | Antioxidant | [76] |
| 2.     | Methanol Extract | In vitro | Antioxidant | [77] |
| 3.     | Chloroform and Methanol Extract | Female Wister Rats | Antioxidant | [81] |
| 4.     | Methanolic Extract | Mouse model | Analgesic | [82] |
| 5.     | N-hexane | Rat model | Anti-inflammatory | [83] |
| 6.     | Xanthones | Rat model | Anti-arthritis | [84] |
| 7.     | Ethanol Extract | Rat model | Anti-inflammatory | [85] |
| 8.     | Seed Extract | In vitro | Antispasmodic | [86] |
| 9.     | Petroleum Extract | Mice Model | Anti-venom | [87] |
| 10.    | Aqueous Extract | Gram+Ve strains | Antimicrobial | [88] |
| 11.    | Coumarins | Male Wister Rat | Antimicrobial | [90] |
| 12.    | Methanolic Extract | Streptococcus aureus and *E. coli*. | Antibacterial | [91] |
| 13.    | Polar Extract | Ethanol Extract | Antibacterial | [92] |
| 14.    | Methanol Extract | *Candida albicans*, *Trichosporon beigelli*, | Anti-fungal | [93] |
| 15.    | Polyhedral Formulation containing mesus of *Mesua ferrea* | Albino rats | Diuretic | [100] |
| 16.    | Polyhedral Formulation containing flowers of *Mesua ferrea* | Clinical study | Anti-hemorrhoid | [101, 102] |
| 17.    | Ethanol Extract | Rat Model | Wound Healing | [103] |
| 18.    | Flower Extract | Rat models | Anticonvulsant | [104] |
| 19.    | Seed oil | Rat models | Immunomodulatory | [105] |
| 20.    | Methanol Extract | Diabetic Rats | Antidiabetic | [106] |
| 21.    | Methanol Extract | Male Wister Rat | Hepatoprotective | [107] |
| 22.    | Stamens Extract | In vitro | Anti-inflammatory | [108] |
| 23.    | Polyhedral Formulation containing leaves of *Mesua ferrea* | Albino rat model | Cardioprotective | [109] |
| 24.    | Polyhedral Formulation containing *Mesua ferrea* plant | Rat model | Protection against COPD | [110] |
| 25.    | Crude Extract | In vitro | Anticancer | [112] |
| 26.    | Ethanol Extract | Human cell line | | [113] |

CONCLUSION

The present study is an attempt to provide the detailed information about the medicinal plant, *Mesua ferrea* L. The reported pharmacological studies indicated that this plant has extraordinary biological potential. It is strongly believed that the present review on the phytomedicinal value of *Mesua ferrea*, might draw the attention of researchers to use this plant in modern medicines. Apart from medicinal uses it is also being used commercially in polymer industry, painting as firewood and substitute for gasoline. Recent scientific studies have highlighted that *Mesua ferrea* is a rich source of secondary metabolites which are having multiple health-promoting benefits including antioxidant, anti-inflammatory, antimicrobial, anticancer and many others. Therefore, there is a need to carry out further studies to prove the potential of the plant.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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