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Measua ferrea. medicinally and traditionally important plant

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INTRODUCTION:

Our daily lives depend heavily on medicinal herbs for everything from food, clothing, and shelter to medicines.Since ancient times, the herbs have been used for medical purposes. The general health of humans is improved by medicinal plants.According to sources, Hippocrates utilised about 400 distinct plant species for medical purposes at that time [1,2].Historically, these herbal plants were the main source of the therapeutic concoctions used [3].The Ayurvedic, Siddha, Unani, Egyptian, and Chinese medical systems have had a considerable influence on the use of herbal or plant-based remedies throughout history. [4].Asian populations have long used various types of mesua to cure a variety of diseases. [5,6].Lignans, alkaloids, flavonoids, tannins, phthalic acid, gallic acid, and terpenoids were some of the substances that were isolated from this plant during the chemical study.Mesuaferrone-A and B mesuaferrol, mesuanic acid, and the stamen components amyrin and sitosterol are the major constituents of Mesua ferrea Linn. [7].Additionally, coumarins, xanthones, and essential oils are rumoured to be present in its seeds [8,9,10].Bronchitis, gastroenteritis, and snakebites are all treated using a decoction made from M. ferrea seeds [11].The leaves of M. ferrea include an antiscorpion sting treatment. The plant's numerous extracts have proven to have anti-inflammatory, anti-venom, anti-cancer, antioxidant, and anti-ulcer qualities. [12].Dysentery is treated with the flower buds, and bleeding piles are said to benefit from the blossoms' astringent, stomachic, expectorant properties.In addition to treating Kapha and Pitta diseases, fever, itching, thirst, excessive sweating, nausea, vomiting, and bad odour, Nagakesara also aids in the digestion of undigested food. Visha [13].
Distribution: -The plant is widely prevalent in tropical countries like India, Burma, Thailand, Indochina, and New Guinea [14]. In addition to the evergreen rain forests of North Canara and South Konkan, as well as the Western Ghats from South Canara to Travancore, it also grows in the Eastern Himalaya and East Bengal mountains of India, Assam, Burma, and the Andaman Islands.[15]

TAXONOMICAL CLASSIFICATION: -
Kingdom – Plantae
Phylum - Tracheophyta
Class – Magnoliopsida
Order – Malpighiales
Family - Calophyllaceae / Guttiferae
Genus - Mesua Species - Mesua ferrea Linn [16].
Synonyms: -
Assam: Nagashwar
Bengali: Nagesvara, Nagesar
English: Cobra's saffron
Gujarati: Nagakesharaa, Sachunagakesharaa
Hindi: Nagakesharaa
Kannada: Nagasampige, Nagakesharai
Malayalam: Nangaa, Nauga, Peri, Veluthapala, Nagppu
Tamil: Naugu, Nagachampakam
Telugu: Nagachampakamu
Urudu: Narmushk, Nagakeshara[17].

BOTANICAL DESCRIPTION: -Mesua ferrea is a medium- to large-sized evergreen ornamental tree.
Bark: The rough-surfaced, flaky stem bark ranges in colour from reddish-brown to grey. The exterior of the bark is smooth.
Wood: With a lifespan of 10 to 15 years, wood is incredibly durable. In contrast to sapwood, which is creamy white or pinkish brown and relatively broad, heartwood is crimson or deep reddish brown, smooth, straight- to moderately interlocked-grained, medium- to coarse-textured, hard, strong, robust, and heavy.

Leaves: -Elliptical, lanceolate, coriaceous leaves with a waxy bloom occasionally on the underside. Mature leaves are 7 to 15 cm long and appear blue-gray to dark green, as opposed to young leaves, which are reddish-yellow in hue. The leaves are straightforward, have a full border, and are in opposition. Glaucous covers the lower surface, while glabrous covers the upper surface. The glossy

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leaves have numerous looping secondary veins that run parallel to the border, numerous reticulating tertiary veins, and a glossy texture. has modified interpetiolar leaves that resemble stipules and can be more or less permanent. either rounded or pointed shape of the base.

Fruits: -Ovoid almost spherical and essentially woody, the fruit matures to a length of 2.5-5.0 cm and has a consistently extended calyx. The pericarp was tough, warty, and two valved after dehiscence.
Seeds: -Smooth, angular, 1-4, 2.5 cm in diameter, dark brown, meaty, and greasy cotyledons [18].
Flowers: The ebracteate, pedicellate, pedicel short, axillary or terminal, single or in pairs (cluster), subglobose buds, and no bracts are present on the fragrant, large, sub-sessile, bisexual, cream-colored flowers. Once the flower portions are divided into their constituent parts, all four flower whorls are clearly visible. The four sepals have four characteristics: they are orbicular, cubbed, puberulous, depressed at the base, and slightly shorter on the outside than the inside. There are four petals visible, each of which is all-white, fragrant, spreading, obovatecuneate, and has an edge that is frequently ripped, crisped, and undulating. Stamens are many, golden yellow, and loosely linked at the base to form a fleshy ring. They are also shorter than the petals. Both the small, oblong anthers and filaments are present. Two times as long asThe ovary is superior, bicarpellary, and syncarpous, and both the stamens and stigmas capitate. In early fruit, style and stigma are enduring, but they disappear over time. [19]

Traditional uses: -The plant's market value is a result of the commercial production of seeds oil, also known as Kesar oil, which is used to treat wounds, rheumatism, sores, and scabies. The oil from the seeds is used in northern Canada to relieve itch and as an embrocation for rheumatism. [14] The plant is utilised for septic and inflammatory disorders. Abortifacient, diuretic, and antispasmodic [20,21,22,23]and used in snake bite, asthma, dyspepsia, renal diseases, fever, and cosmetics [24, 25].Bark and root decoction is beneficial for bronchitis and gastroenteritis. For its antibacterial, purgative, blood purifier, worm control, and tonic effects, Assamese tribal people use the plant.[26]It is employed as an antipyretic, expectorant, cardiotonic, diuretic, and carminative drug in Thai traditional medicine to treat fever, colds, and asthma. [27]Leaf ash is applied on irritated eyes. To treat skin outbreaks and to plaster wounds, use kernels.[28].

Phytochemical study: -

According to reports, Mesua ferrea Linn typically contains phytochemicals of the coumarin, xanthone, terpene, and sterol types. [29].

The components of oil vary depending on the plant part, for example, oil extracted from bark primarily contains (E)-bisabolene (31.3%) and selinene (12.2%), oils of tender and mature leaves contain copaene (19.3% and 9.9%) and caryophyllene (18.8% and 26.0%), and oil from buds and flowers primarily contains -copaene (28.7% and 20.2%) and germacrene D (19.0% and 16. Octadecatrienoic acid, octadecanoic acid (18:1), and hexadecanoic acid (26.8%) were present in the seed and kernel oil. [30].Additionally, mesuarin (I) coumarin was extracted from the M. ferrea seed oil [31].Betulinic acid, (-) epicatechin, 1, 6-dihydroxyxanthone, pyranojacareubin, and two new compounds, mesuabixanthone-A and mesuabixanthone-B, were also isolated from the stem bark of M. ferrea [32]. Additionally extracted from the stem bark were mesuferrol-A and -B, (-) epicatechin, 1, 7-dihydroxy-, and 5-hydroxy-1-methoxyxanthone [33]. One research team isolated several compounds from the root bark, including mesuaferrinA and -B, caloxanthone C, 1,8-dihydro-3-methoxy-6- methylanthraquinone, -sitosterol, friedelin, and betulinicacid [34].A range of natural antioxidants, including coumaric acid, ellagic acid, gallic acid, kaempferol, myricetin, rutin, quercetin, and vanillic acid, are shown by HPLC analysis of M. ferrea methanol and chloroform extracts. [35]The 4-alkylcoumarin ferruol A (C23H30O5), which was isolated from the trunk bark of M. ferrea L., comprises 1, 5-dihydroxyxanthone, euxanthone 7-Me ether, and -sitosterol in the heartwood of M. ferrea. The leaves of M. ferrea were used to isolate a flavone glycoside known as 5'-C-Me eriodictyol 3'-O--D-galactopyranosyl(14)--L-rhamnopyranose. The flavanone glycoside mesuien is the first to have a C-Me substituent in the B-ring. [36].

Pharmacological activities of Mesua ferrea Linn.

a) **Immunomodulatory activity:** -In experimental animals using sensitised + cyclophosphamide (50 mg/kg, i.p., 9th and 16th day) generated SRBC (sheep red blood cells) specific and non-specific immune response models, mesuol extracted from M. ferrea seed oil was assessed for

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immunomodulatory activity. In models of the humoral and cellular immune responses, respectively, the constituent significantly increased the antibody titer and paw volume. Rats' haematological profile, neutrophil adhesion, and phagocytosis in a test for carbon clearance all improved, indicating mesuol's immunomodulatory effect.[37].

b) **Analgesic activity: -**non-polar (n-hexane) fraction of M. ferrea leaf extract shown better antinociceptive efficacy in terms of percent reduction in writhing response as compared with polar fractions (methanol and ethyl acetate) in a mouse model of visceral pain caused by acetic acid. [38].

c) **Anti-inflamatory activity: -**Mesuaxanthones A and B (MXA and MXB) from M. ferrea were tested using albino rats, granuloma pouches, cotton pellets, and carrageenan-induced hind paw oedema. 50 mg/kg of xanthones were administered throughout each surgery. MXA (37%) and MXB (49%) decreased when M. ferrea xanthones were given orally in a carrageenan-induced hind paw oedema test in comparison to the healthy control group. MXA (38%) and MXB (22%), when compared to the normal control group, significantly reduced the inflammation, showing that the xanthones had a potent anti-inflammatory impact in both normal and adrenalectomized rats. These xanthones demonstrated a 47% reduction in inflammation in cotton pellet granuloma tests as well as an MXA (46%) and MXB (49%) reduction in inflammation in granuloma pouch testing. The xanthones used in this study were found to provide significant anti-inflammatory action. [39].

d) **Antispasmodic activity: -**An extract of nagkesar seed oil based on petroleum has been proven to have antispasmodic effects in the rat ileum in in vitro studies. Acetylcholine and carbachol cause contraction up to 2.61 cm and 3.2 cm, respectively. According to the crude oil content, which can range between 1:5 and 1:10, the contraction of acetylcholine is often reduced by up to 70% and 86%, respectively. Atropine typically reduces the cholinergic response by up to 55%. The rat ileum's activity was measured using a kymograph. [40].

e) **Antivenom activity: -**The anti-venom effect of the aqueous extract of Mesua ferrea leaves against fibroblast cell lysis following Heterometruslaoticus scorpion bite was examined by Uawonggul et alThe vitality of fibroblast cells was assessed after 30 minutes of treatment with either a phoney control or 0.706 mg/ml plant extracts pre-incubated with H. laoticus venom. After 30 minutes of treatment with fake control, 0.706, or 0.406 mg/ml, the viability of fibroblast cells demonstrated effectiveness in preventing venom-induced lysis.[41].

f) **Hepatoprotective activity:** In research, a methanolic extract of dried M. ferrea flowers (100 and 200 mg/kg) significantly increased liver SOD and AST and decreased catalase, GPX, GR, and ALT activity while having no impact on CPK or creatinine levels in mice that had been exposed to hepatotoxicity caused by S. aureus.[42].

g) **Anti-arthritis activity: -**The seed extract of Mesua ferrea displays potent anti-arthritis effect in two distinct in vivo models of arthritis in rats, including arthritis generated by formaldehyde and arthritis caused by Complete Freunds' Adjuvant (CFA). The findings showed that CFA injections into the paws of the rats used in the study decreased the swelling volume of the arthritis lesion. [43].

h) **Cardioprotectiveactivity:** -Anall-naturalmedicinecalledAshwagandharishta and its commercialised preparation that contains Mesua ferrea stamens have been found to prevent isoproterenol-induced myocardial infarction in the albino rat model.The serum levels of marker enzymes like alanine aminotransferase, aspartate aminotransferase, creatine kinase, and lactate dehydrogenase were significantly reduced during treatment with herbal formulation, and the serum lipid profile also improved.The rise in in vivo antioxidant level of GSH and suppression of lipid peroxidation of cardiac membranes in the treated rats were responsible for the herbal formulation's cardioprotective action. [44].

i) **Antidiabetic activity**:The methanol extract of Mesua ferrea leaves demonstrates promising antidiabetic effect in streptozotocin-induced diabetic rats. The extract was found to lower

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blood glucose levels and restore normal body weight in diabetic rats. [45].

j) **Diuretic activity:** -a commercialised preparation of Draksharishta-T and M, a polyherbal blend containing stamens from Mesua ferrea. The formulation was found to have considerable diuretic, kaliuretic, and natriuretic effects in albino rats over the duration of 5 hours in comparison to the control group [46].

k) **Wound healing activity:**In excision and incision models utilising albino rats, topical administration of ethanolic extract of dried flowers of Mesua ferrea (5% and 10% w/w) ointment of bark extract revealed considerable wound healing activity in contrast to the control group. [47].

l) **Protection against chronic obstructive pulmonary disease (COPD):**-The study showed that the herbal formulation (Bresol), which contained Mesua ferrea flowers, protected mice from developing COPD brought on by cigarette smoke. The rats were given doses of 250 and 500 mg/kg for five weeks. In terms of reduced tracheal inflammation, reduced TNF- and total protein levels in bronchoalveolar lavage fluid, and preservation of the trachea and lung's regular cellular architecture, the results demonstrated improvement. [48].

m) **Anti-ulcer activity:** In xanthones-pretreated animals, only albino rats with pyloric ligations demonstrated anti-ulcer efficacy. The rat arthritic model induced by Complete Freund's Adjuvant (CFA) and formaldehyde was significantly prevented by M. ferrea extracts in petroleum ether, ethyl acetate, and alcohol. Treatment enhanced the WBC, RBC, and haemoglobin counts in treated rats compared to control rats (an increase in WBC, a decrease in RBC, and an increase in haemoglobin). [39].

n) **Anti-convulsant activity:** The convulsions generated by an albino mouse's MES (maximum electroshock seizure) were significantly reduced by an ethanolic extract of M. ferrea flowers. Electroconvulsive shock convulsions lasted for fewer seconds and began more quickly. [49].

o) **Anti-histaminic activity:** A portion of Mesua ferrea seed oil that contains phenol was reported to have potentiated the relaxation of guinea-pig tracheal smooth muscle caused by isoprenaline both in vitro and in vivo. Additionally, in cases of chopped lung and passive peritoneal anaphylaxis, the phenolic fraction prevented histamine from being released [50].

p) **Anticancer activity:** -The preliminary in vitro anticancer screening assays have revealed promising anticancer properties for a number of crude extracts and purified compounds. With an IC50 value of 12.5 g/ml, a methanol extract of Mesua ferrea flowers rich in volatile oils demonstrated high cytotoxic activity against T-lymphocyte leukaemia cells [51]. In a different study, three human cancer cell lines—CL-6 (cholangiocarcinoma), Hep-2 (human laryngeal cancer), and Hep G2 (human hepatocarcinoma)—were tested against an ethanol extract of the Mesua ferrea flower.With an IC50 value of 19.22 g/ml, the results indicated that ethanol extract was specifically hazardous to the Hep-2 cell line [52]. KB (oral carcinoma), MCF-7 (breast adenocarcinoma), and NCIH1187 (metastatic lung carcinoma) are three cancer cell lines that were found to be sensitive to the essential oil of Mesua ferrea leaves. Normal kidney cell lines from green monkeys were not harmful.[53].

q) **Antioxidant activity:** In both in vitro and in vivo experiments, M. ferrea showed antioxidant activity, which was mediated by the inhibition of nitric oxide (NO) [54] and lipid peroxidation. In additional in vitro antioxidant studies, the stem bark of Mesua ferrea Linn. shown significant radical scavenging capacity against DPPH (89.70%), ABTS (77.64%), and nitric oxide (89.28% of the time). [55]

r) **Antimicrobial and antifungal activity:** - Various Mesua ferrea components' antibacterial activities have been highlighted in numerous scientific studies. Coumarins (4-alkyl and 4-phenyl 5,7-dihydroxycoumarins) isolated from Mesua ferrea flowers exhibit antibacterial activity against gram-positive bacteria strains, according to research by Verotta et al. [56]. In accordance with a different study, the bacteria Escherichia coli, Salmonella, Shigella, Staphylococcus aurens, and Lactobacillus arabinosus as well as the

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species of Basillus are all susceptible to the methanol extract of leaves. [57,58]. According to Ali et al., the stem bark of Mesua ferrea has a powerful antibacterial effect on both gram-positive Strptococcusaurens and gram-negative Escherichia coli bacterial strains. [59].Another investigation confirmed the antibacterial efficacy of Mesua ferrea floral extract against five distinct Salmonella spp. strains. The extract was found to be effective against all strains at a concentration of 50 g. Additionally, floral extract dramatically decreased the viable count of the S. Typhimurium NCTC 74 bacterial strain in the liver, spleen, and cardiac blood of S. Typhimurium NCTC 74 challenged mice when given at a dose of 2-4 mg/mouse. [60] Several fungi, including Candida albicans, Trichosporonbeigelii, Mucor hiemalis, and a few other species of Aspergillus, are resistant to the antifungal effects of the methanol extract from the seeds of Mesua ferrea, according to Linn et al. [61].Similar to this, a recent study found that the gram-positive Staphylococcus aurens and gram-negative Klebsiella pneumonia strains of bacteria were resistant to the antibacterial effects of epoxy resin made from Mesua ferrea seed oil. [62]. One of the six plants employed in a gel formulation that was the focus of research by Deshmukh et al. was Mesua ferrea. The mixture was found to be effective in preventing skin infections brought on by resistant Corynebacterium spp., Pseudomonas aeruginosa, and Staphylococcus aureus strains. [63]. The discovery by Phukan et al. that the bio-oil extract of Mesua ferrea possesses antibacterial activity against a number of bacterial and fungal strains gives a clue as to the possible medicinal use of bio-oils. [64].

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