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NANOTHERAPEUTIC APPROACHES, PHYTOCHEMISTRY AND PHARMACOLOGICAL PROSPECTS OF PLANT *MUSSAENDA FRONDOSA* LINN: A HOLISTIC INVESTIGATION

Aseem Setia [1], Sanjay Nagdev [2], Mrinal Sharma [3], Shashi Alok [4], Sandip Tiwari [1], Megha Verma [2], Pradeep Golani [2], Devendra Singh Lodhi [2] and Sankha Bhattacharya [*5]

Faculty of Pharmacy [1], Kalinga University, Naya Raipur - 492101, Chhattisgarh, India.
Department of Pharmacy [2], Gyan Ganga Institute of Technology & Sciences, Jabalpur - 482003, Madhya Pradesh, India.
Sachdeva College of Pharmacy [3], Gharuan - 140413, Punjab, India.
Institute of Pharmacy [4], Bundelkhand University, Jhansi - 284127, Uttar Pradesh, India.
School of Pharmacy & Technology Management Shirpur [5], SVKM'S NMIMS Deemed-to-be University, Shirpur - 425405, Maharashtra, India.

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Correspondence to Author:
Dr. Sankha Bhattacharya

Associate Professor,
School of Pharmacy & Technology Management Shirpur, SVKM'S NMIMS Deemed-to-be University, Shirpur - 425405, Maharashtra, India.

E-mail: sankhabhatt@gmail.com

ABSTRACT: Medicinal plants provide numerous benefits to human health. *Mussaenda frondosa* Linn belongs to the Rubiaceae family, which has 500 genera and 5300 medicinal plant species. Mussaenda is a flowering plant genus with many beautiful species. Ayurveda, an ancient Indian healing system, describes many herbs, oils, and minerals. People have known about plants' medicinal value since prehistoric times. Mussaenda contains many medicinal natural compounds such as steroids, triterpenes and flavonoids. The chief chemical constituent present in the whole plant is butanedioic acid, diethyl ester, caryophyllene, hexadecanoic acid, quinic acid, 4-((1E)-3-Hydroxy-1-propenyl)-2-methoxyphenol, Naphthalene, decahydro2-methoxy, 1, 2, 3-Benzenetriol, alkaloids, flavonoids, saponins and tannins. *Mussaenda frondosa* nanocomposite enhances bioavailability and therapeutic potential. The present review compiled data on the importance of plants and their treatment options. This paper will be very useful to those in the medical, therapeutic, pharmacognosy and pharmacology fields. This article examines the genus Mussaenda and its phytochemical and pharmacological properties.

INTRODUCTION: *Mussaenda frondosa* Linn. (Rubiaceae) is extensively spread in India and can alleviate a wide range of ailments. Other names for this plant in other languages include "Bedina" (Hindi), "Sriparnah" (Sanskriti) and the Telugu word for it, Nagavalli. As an astringent, expectorant, and antibacterial, the methanol extract of the whole plant has traditionally been used to treat a wide range of ailments, including fevers, jaundice, hyperacidity, coughs and ulcers [1]. The taxonomical classification of *Mussaenda frondosa* Linn is shown in **Fig. 1**.

There is additional evidence that the same extract of the plant can have a hypolipidemic effect and a hepatoprotective effect. Many chemical elements are found in the *Mussaenda frondosa* leaves and flowers, including beta-sitosterol glucoside, anthocyanins, rutin, hyperin, ferulic acid, quercetin, and sinapic acids [2]. The plant known as *M. frondosa* has been claimed to have a variety of therapeutic characteristics, including jaundice,

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asthma, hyperacidity, fever, ulcer, leprosy and a diuretic are just a few of the conditions historically treated with the plant. The leaf extract was found to have antimicrobial, diuretic, hepatoprotective, antipyretic, asthma, and cough properties. Mucilage, steroids, glycosides, saponins, resin, and flavonoids are all found in the leaves of *Mussaenda frondossa* Linn [3].

Throughout the ages, indigenous plants have been used to treat a variety of illnesses due to their medicinal properties. Natural and synthetic herbal remedies can be found in various plants. *Mussaenda frondosa* L. petals were extracted in methanol. The methanolic extract of the petals was analyzed using droplet counter-current chromatography to separate phytoconstituents such as rutin, quercetin, hyperin, sinapic acid, ferulic acid and stigluside [4]. Bacillus subtilis and Bacillus cereus were all killed by *Mussaenda frondosa* Linn's petals, which were found to exhibit antibacterial activity against various other bacteria, including saccharomyces cerevisiae and ustilago mayadis [5]. In rats fed a high-fat diet, a methanolic extract of *M. frondosa* showed hypolipidemic action. *Mussaenda frondosa* extracts, both aqueous and alcoholic, protected Wistar rats livers from paracetamol-induced liver damage in a model study. In the study of medicinal plants, the finding of bioactive chemicals from new perspective of medicine species is one way in which progress has been made. The genus Mussaenda has played a significant role in the discovery of numerous natural compounds useful to those in the field of pharmacology [6].

As a bonus, the plants in this family are easy to grow. They're resistant to disease and pests and can take a lot of thinning. Chemical and biological investigations have been conducted on only a few species. Medicine can be found in a wide variety of plants. As an excipient, an addition, or a medicinal ingredient, several of the plants demonstrated their importance. When it comes to treating eye problems, it has been used medicinally, as an expectorant and anti-inflammatory for leprosy and bronchitis. The herb is also said to have anti-infective properties, according to folklore. The unique surface features of nanoparticles are responsible for their distinctive properties. In addition to their properties, nanoparticles have an influence on the toxicity of the substances they are used for. Because nanocarriers mostly enter cells via the endocytic pathway, intracellular drug delivery is severely restricted. By altering the surface of nanoparticles, researchers have found a way to deliver medicine to diseased cells [7]. Numerous beneficial chemical components were found in the plant's phytochemical investigation. Throughout India, *Mussenda frondosa* Linn. can be used to treat a variety of ailments [8]. Mussaenda species and their chemical components and biological activities are the topics of this review. All the chemicals that are involved in *Mussaenda frondosa* Linn have been included in this guide for future studies.

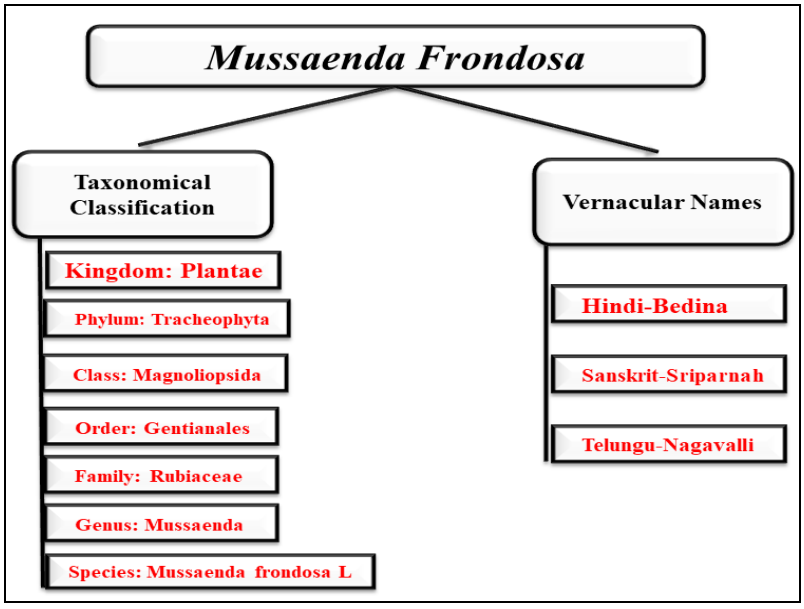

FIG. 1: TAXONOMICAL CLASSIFICATION AND VERNACULAR NAMES OF *MUSSAENDA FRONDOSA*

Information about Plant *Mussaenda frondosa:* Straying plants have pubescent branchlets. Pedicels to 1.5 cm long, broadly oval at base, caudate acuminate at tip; leaves up to 6-10 cm long, sparsely hairy both on the underside and the underside of the caudate acuminate leaf 9. Stipules to 3-4 mm long, oblong, bifurcated at apex. 5-merous blooms in the terminal, loose and tomentose cymes linear, 1 to 1.5 centimeters long, and covered with hairs, bracteoles are linear bracts. When one of the five calyx-lobes was transformed into an 8-12 x 4.5 cm leaf-like structure that was covered in white hairs, it was quite stunning. Lobes 6 -7 mm long, ovate-lanceolate, are attached to the corolla, which is 2.5-3 cm long, funnel-shaped and dilated above the center, orange or yellow, tomentose outside and villous at the mouth. The berry is globose and about 1 cm in diameter [10].

A Detailed Description of Various Species of *Mussaenda:* More than 200 Mussaenda species could be found worldwide, from West Africa to the Indian subcontinent, Asia, and as far south as New Guinea and the western Pacific Oceans. The detailed outlook is shown in **Fig. 2**. Far North Queensland and the Torres Islands are home to one species. A total of five species can be found flourishing in the sunnier climes of Australia. One well-known species can also be found in the allied genus Pseudomussaenda, which was originally part of Mussaenda [11].

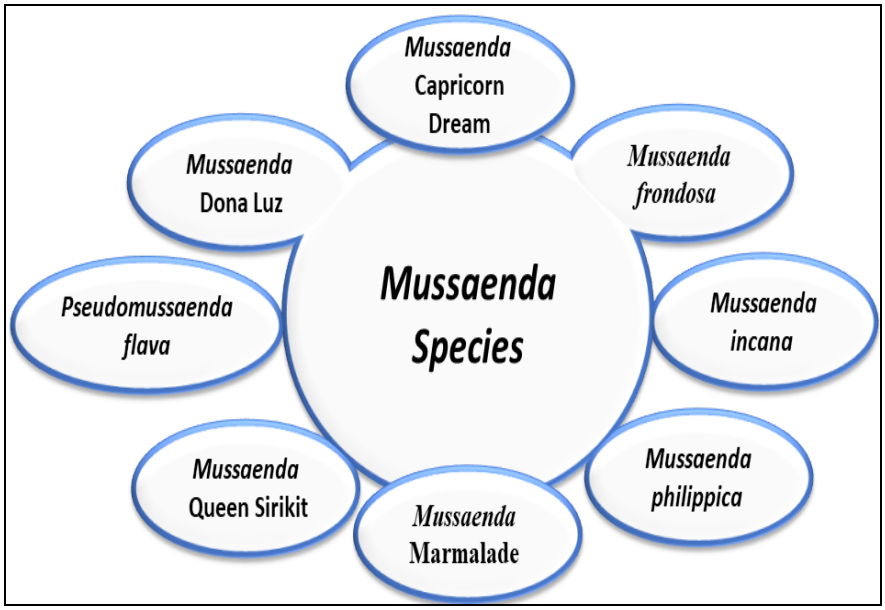

FIG. 2: VARIOUS SPECIES OF *MUSSAENDA FRONDOSA* LINN

Mussaenda erythrophylla: Angola, Burundi, Cabinda, Cameroon, Ivory Coast, Gabon, Ghana, Guinea, Kenya, Liberia, Nigeria, the Central African Republic, Sierra Leone, Sudan, Tanganyka, Togo, Uganda and Zaire are all home to *Mussaenda erythrophylla* (Ashanti Blood, Red Flag), also known as the "Red Flag". White flowers with red centres and scarlet sepals make up this spreading shrub. Often in the wild, it can clamber up nearby trees. It can be grown as a sprawling shrub, ranging in height from 1 to 1.5 metres (3 to 4.5 feet) and in width from 2 to 3 metres (6 to 9 feet) [12].

***Mussaenda frondosa*:** Several species of Mussaenda frondosa (Dhobi Tree) can be found throughout the Indian subcontinent. Reddish-orange blossoms adorn its white sepals. A smaller shrub that grows to a height of 1.5 to 2 metres and spreads to a width of 1.5 to 2 metres. The leaves are a more delicate shade of green than those of many other plants [13].

Mussaenda incana: In India and Malaysia, the Dwarf Mussaenda (*Mussaenda incana*) is found. Flower and sepal colouration are both yellow and creamy on this plant. This is a low-growing shrub with a height of between 1 and 2.5 feet and a width of between 1 and 2 meters (3 to 6 feet wide). It looks fantastic when used as a ground cover and should be more widely distributed [14].

Mussaenda philippica: Tropical Dogwood, *Mussaenda philippica*, is a native of the Philippines, Indonesia and New Guinea. White sepals and orangy-yellow blooms make up the flowers. Wild specimens can reach heights of 3 to 5 metres (9 to 15 feet), although in cultivation, it is more usually seen as a shrub 1.8 to 2.5 metres (6 to 7 feet) high and 1.2 to 1.8 metres (4 to 6 feet) broad. *Mussaenda philippica* 'Dona Aurora' is a more well-known cultivar of this plant. On Mt. Makiling in 1915, Calixto Mabesa stumbled onto a random sport that he brought back to the University of the Philippines Los Banos' College of Forestry grounds in 1930 with Hugh Curran and Mamerto Sulit. Instead of one sepal per flower, this variety has several more. In 1930, Mrs Aurora Quezon, the first lady of the Philippines, was given this as a gift. Almost all hybrids may be traced back to this one plant [15].

***Mussaenda marmalade*:** *Mulberry 'marmalade,'* also known as Mussaenda 'Marmalade,' is a patented shrub that was grown from seed in an Alipore, India, nursery in 1995. The hardiness and vigour of this shrub can be attributed to the use of *P. flava* in its breeding.

It can reach heights of 1.8 to 2 metres. The sepals of the shrub range from salmon and yellow to orange and yellow. These plants are among the most eye-catching hybrids despite their diminutive size [16].

Osram Nursery in Rockhampton, Queensland, has also developed a variety of Mussaenda hybrids. The first two releases have been well-received both domestically and abroad, proving that they can stand the test of time. Following the international patenting of plants, other plants will be released in the future.

***Mussaenda glabrata* (Hook. F.):** Glucoside and sinapic acid are found in the leaves, as well as resins and sugars, mucilage and mucilage-like substances. The leaves of this species are used in the treatment of hepatitis and/or jaundice. As a source of antioxidants and anti-inflammatory properties, roots can be found in many foods [17].

***Mussaenda arcuata* Poir:** Extracts from the leaves include rutin, astragalin, isoquercitrin, kaempferol 3-O-D-rutinoside, melilotoside, dihydro-melilotoside and kaempferol-3-O-β-D-rutinoside, as well as melilotoside. In ancient times, it was used as a febrifuge and purgative, as well as an asthmatic, a purgative, an albuminuric and a dermatosis treatment for infants; the whole plant was also used for the treatment of gastroenteritis, conjunctivitis, and skin rashes [18].

***Mussaenda dona-aurora* (*Mussaenda Philippica* A. Rich. var. *aurora* Sulit):** Three iridoid glycosides and four flavonoids were extracted from the sepals as phytoconstituents. Glycoside-derived Sanshiside D inhibits the growth of Vero cells and the growth of HeLa and SMMC-7721 cells in the presence of Vero (African green monkey) and heptoma cell lines. *Mussaen-da-dona* aurora extracts and compounds identified by Vidya-Lakshmi *et al*. have been shown to have antioxidant and hepatoprotective action [19].

***Mussaenda erythrophylla* Schumach. & Thonn:** Phytoconstituents isolated are 5 hydroxy-7, 4'-dimethoxy flavones, β-sitosterol, 4 -hydroxy-3-methoxy cinnamic acid and 3- isocumaryloxy–cyclopropane-1-oic acid. The leaf is used for paracetamol-induced hepatotoxicity; alcohol-induced hepatotoxicity. The stem is found to be hepatoprotective against carbon tetrachloride-induced hepatotoxicity and used for antioxidant and free radical scavenging activity. Roots are found to be anthelmintic diuretic, used for the treatment of cough jaundice, and acts as an appetizer**.** The whole plant is used as an *antiarthritis* and anthelmintic [20].

***Mussaenda erosa* Champ. ex Benth:** For burns, ulcers, and numbness of the limbs, the stems and leaves of the M. erosa plant were employed [21].

***Mussaenda esquirolli* Levl:** The leaves contain linolenic acid, phytol, squalene and β-sitosterol acetate, are all phytoconstituents of the species [22].

***Mussaenda flava* (Verdc.) Bakh. F:** Bacillus subtilis is inhibited by Mussaenda flava flower extracts [23].

Phytochemistry and Chemical Constituent of the Plant *Mussaenda frondosa* Linn: The different parts of the plant consist of different beneficial chemical constituents **Fig. 3**. Some of the chemical constituents of the plant are mentioned in **Table 1.**

TABLE 1: CHEMICAL CONSTITUENTS OF DIFFERENT PARTS OF PLANT *MUSSAENDA FRONDOSA* LINN

S. no.	Plant Part	Chemical Constituents	References
1.	Leaves	Flavonoids, steroids, glycosides, Carbohydrates, Phenol, tannins, Saponins, Quercetin	[24]
2.	Flower	Quercetin, hypenin, ferulic acid, sinapic acid, β-sitosterol, β-sitosterol glucoside.	[25]
3.	Whole plant	Butanedioic acid, diethyl ester, Caryophyllene, Hexadecanoic acid, Quinic acid, 4-((1E)-3-Hydroxy-1-propenyl)-2-methoxyphenol, Naphthalene, decahydro2-methoxy, 1, 2, 3-Benzenetriol, alkaloids, flavonoids, saponins, and tannins	[26]

***Mussaenda frondosa* L:** A total of 20 phytoconstituents were found in the whole plant and identified. Quercetin is found in the leaves as well as other flavonoids and phenolic compounds. β -sitosterol, β-sitosterol-glucoside are all found in flowers, as are quercetin, hypenin, ferulic acid, sinapic acid. Jaundice, asthma, hyperacidity, and ulcers can be treated with the leaves. They can also be used as a diuretic. Leaf extracts have been shown to have anthelmintic, wound-healing, antibacterial, and antimicrobial properties, amongst other things, when used in conjunction with ethanol. Antioxidant and diuretic properties can be found in the plant as a whole. Using the root for blemishes on the tongue and the sepals for diuretic purposes is common practice. A variety of uses for root include wound healing, wound scavenging, stress reduction, and antistress. *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli* are all susceptible to the antibacterial effects of the root [2].

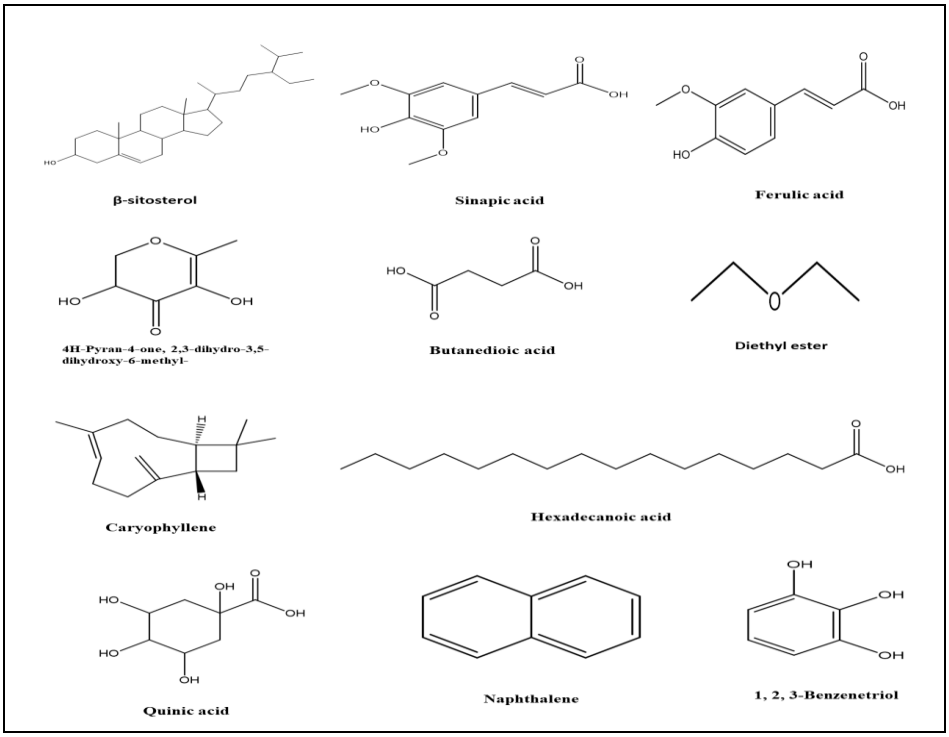

FIG. 3: CHEMICAL CONSTITUENTS OF *MUSSAENDA FRONDOSA* LINN

Phytochemical and Pharmacognostical Evaluation of *Mussaenda Frondosa:* S. Shanthi *et al.*, 2020 investigated Pharmacognostical studies on leaves of *Mussaenda frondosa* Linn. The essential qualitative properties of the drug were determined using a variety of examinations, including pharmacognostical assays, preliminary phyto-chemical screening, and High-Performance Thin Layer Chromatography (HPTLC). Idioblast, collenchyma and unbranched unicellular covering trichomes were discovered during a microscopic examination of the leaf. Flavonoids, steroids, glycosides, mucilage, and proteins were shown to be present in preliminary phytochemical tests. Ten phytoconstituents with Rf values ranging from 0.11 to 0.88 were detected in the ethanol extract of *M. frondosa* L. using HPTLC. There are four major Rf peaks: 0.11, 0.16, 0.23, and 0.81. The *Mussaenda frondosa* leaves, even in powder form, may be identified and standardised using these results.

To distinguish between Mussaenda species that are almost identical, this information is critical. Pharmacognostic and phytochemical profiles for *Mussaenda frondosa* may significantly define the plant's monograph, which may be critical in determining the plant's precise identity and classification [27].

***Mussaenda frondosa* Loaded Nanoparticles Based Approaches:**

Cellular Mechanism of Zinc Oxide Nanoparticles: The unique qualities of nanoparticles can be attributed to their unique surface characteristics [28]. Nanoparticles are not only useful in medicine because of their features, but they also have an impact on their toxicity. This process is known as "opsoninization " It is the process by which the MPS removes bare nanoparticles from the body when they come into contact with human fluids [29]. The blood-brain barrier, for example, cannot be crossed by nanoparticles that have a short circulation half-life [30]. Nanoparticles may be modified by affixing different coupling agents to their surfaces, allowing them to bind diverse molecules. This reduces the opsonization process, which in turn increases the half-life of nanoparticles in circulation. Opsonization and consequently absorption by mononuclear phagocytes have been delayed by hydrophilic polymer coating of chitosan, PEG, and polycaprolactone [31].

As a result, the vehicles that have been created to be stealthy have a longer travel time. Improved water stability and less aggregate formation can be achieved by applying polymers to the surface. Due of its solubility in both aqueous and organic solvents, PEG has seen considerable usage [32]. All macrophage phenotypes showed a decreased propensity to phagocytose PEG-coated nanoparticles [33]. Drug delivery to intracellular destinations is severely constrained due to the fact that nanocarriers enter cells largely via an endocytic route [34]. There are two stages in the endocytosis process: early and late endosomes. The pH changes from 6 to 5 during the latter stage of the endosomal maturation process. Enzymes in lysozymes, such as proteases, glycosidase, nucleases and lipases, can break down the drug contained during the late phase of the endosomal-lysosomal process [35].

The surface charge of nanoparticles considerably affects the absorption of nanoparticles by intestinal epithelial cells. Particles with a positive charge are more likely to bind to a cell membrane with a negative charge, leading to cargo release into the cytoplasm [36]. This has led to substantial research into nanoparticle surface modifications to improve absorption and drug delivery. A cationic surfactant, for example, didodecyldimethyl ammonium bromide, boosted the nanoparticle surface's positive charge, which resulted in a longer cell-surface retention period. Particle absorption was boosted, which increased medication bioavailability. Targeted medication delivery to malignant cells has been studied using surface charge modification [37]. Due to the overabundance of negatively charged phospholipids on cancerous cells, they are more prone to interact with positively charged nanoparticles than normal cells. Positively charged zinc oxide nanoparticles, as opposed to negatively charged polyacrylic acid-coated zinc oxide nanoparticles, showed more specific cytotoxic capability against cancer cells **Fig. 4**. Because of their higher rate of aggregation and disintegration in the presence of water, cationic nanoparticles have less bioavailability and hence less anticancer potential.

On the other hand, negatively charged nanoparticles had a lower dissolution and better dispersion capabilities than positively charged nanoparticles but were less selective against cancer cells [38]. As a vital mineral in our bodies, zinc may be found in the brain, muscle, bone, etc. Enzymes involved in protein and nucleic acid synthesis are activated as a result. Helps digest protein and blood coagulation as well as bone metabolism as an antioxidant. When it is lacking, the liver releases vitamin A. Toxic effects of zinc are strongly reliant on the concentration of Zn^{2+} ions, which are absent in normal circumstances (pH=7.4). For normal mammalian cells, ZnONPs are biocompatible because of their low dissolution rate [39]. In addition, ZnONPs have a wide range of medicinal applications, including tissue engineering, drug delivery systems, bioimaging and antibacterial, antioxidant, and antidiabetic properties [40]. Precursors for ZnONPs may be easily synthesized from a variety of low-cost sources.

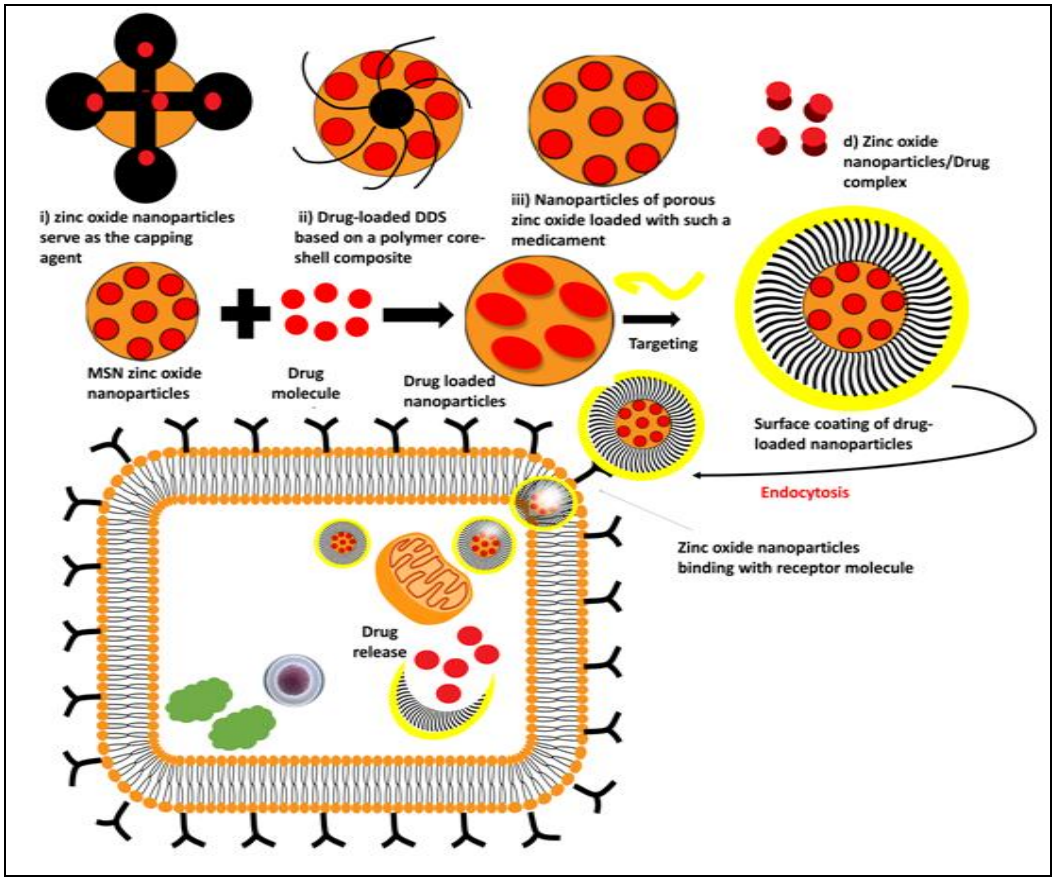

FIG. 4: CELLULAR MECHANISM OF DRUG-LOADED ZINC OXIDE NANOPARTICLES

Synthesis of ZnONPs: It is common to use either a top-down or bottom-up approach when creating nanoparticles (NPs). The cutting of bigger materials into smaller nano-sized particles is referred to as the top-down technique [41]. On the other hand, NPs are synthesized from the ground up, starting with atoms and molecules. Specifically, we're interested in colloidal ZnO nanopowder production methods. Preparation of ZnONPs via burning, thermal decomposition, the sol-gel technique, and hydrothermal methods have all been used in the past. However, ultrasonication, co-precipitation, microwave-assisted combustion, and green synthesis are the most recent approaches employed to create ZnONPs [42].

Manasa *et al.*, 2021 developed copper oxide nanoparticles using *Mussaenda Frondosa*. The outcomes of the study revealed that the CuO-NPs were found to have a pure monoclinical crystalline structure with an average grain size ranging from 2–10 nm in the XRD spectrum. Surface Plasmon Resonance (SPR) between 300 and 400 nm clearly demonstrates the presence of an exceptionally strong SPR. The process of making CuO-NPs spherical structures was discovered by SEM and TEM research. Copper's existence was demonstrated through the use of EDS spectra. Nanomaterials include both carbons. A molecule's potential bioactivity was shown via FTIR spectra. It is responsible for reducing copper ions. The stability was confirmed by DLS and Zeta potential readings. An A549 human lung cancer cell line demonstrating the powerful anti-cancer properties of CuO-NPs. UV-light results in 97.36 percent destruction of methylene blue dye, according to photocatalytic activity results. The light has been on for 140 min [43].

Babitha *et al.*, 2019 developed zinc oxide nanoparticles (ZnONPs) and nano-sheets (ZnO-NRs) by microwave heating (MHM) and modified sol-gel (SGM) method, respectively, using *Mussaenda frondosa*. UV-Visible diffuse reflectance (DRS) and photoluminescence spectroscopy (PL) spectroscopic techniques were used to analyze optical properties and calculate band gaps. The bandgap of ZnO-NPs and ZnO-NRs was measured using the Kubelka-Munk method, and it was found to be 3.37 eV and 3.32 eV,

respectively. *Bacillus subtilis, Staphylococcus aureus, Proteus mirabilis* and *Salmonella typhi* were all examined for their antibacterial properties by the modified disc diffusion method and ZnO-NPs and ZnO-NRs showed significant antibacterial activity against *P. mirabilis* and *S. typhi*. In experiments with solar lighting, the degradation of methylene blue (MB) dye by ZnO nanocatalyst (ZnO-NPs and ZnO-NRs) was explored, and the results showed that samples of ZnO-NPs with smaller particle size significantly degraded MB more than ZnO-NRs [44]. Jayappa *et al.,* 2020 prepared zinc oxide nanoparticles of *Mussaenda frondosa*. The outcomes of the study show that ZnO-NPs from leaf (L-ZnO-NP), stem (S-ZnO-NP), and callus (C-ZnO-NP) aqueous extracts revealed a high absorption peak at 370, 376 and 373 nm, respectively, which corresponds to the bandgap energy of 3.33, 3.27 and 3.30 eV. Wurtzite formations with grain sizes ranging from 5 to 20 nm in diameter were validated by XRD investigation. Nanoparticle reduction and stabilization are aided by stretching vibrations in the –O–H, C–H, C–N, and C = O groups, as evidenced by FTIR spectra. It is evident from SEM pictures that the nanoparticles are spongy (spherical, porous, and agglomerated). The stability of ZnO-NPs was confirmed by DLS and zeta potential measurements. ZnO-NPs have photocatalytic activity and biological uses (antioxidant, anti-inflammatory, antidiabetic, antibacterial, anticancerous) examined in this study. An effective, simple, and environmentally friendly ZnO-NP synthesis technique is being described and evaluated for its potential in a variety of industrial and medicinal applications in the current study [45].

Phytochemical Screening and *In-vitro* Callogenesis of *Mussaenda frondosa:* Manasa *et al.,* 2017 investigated qualitative and quantitative phytochemical analysis of leaf, stem and callus cultures. Plant leaves were inoculated into Murashige and Skoog media with various concentrations of growth regulators, such as 2, 4-D and NAA and benzylaminopurine, Kn to induce callus formation. Leaf, stem and callus total phenol, flavonoid and alkaloid content was analysed qualitatively and quantitatively using conventional procedures. Reducing power and 1, 1-diphenyl-2-picryl hydrazyl radical-scavenging methods were used to evaluate antioxidant activity. Membrane stabilising activity was used as a measure of anti-inflammatory efficacy. NAA (2 mg/l)+Kn (4 mg/l) resulted in a robust, friable and rapidly developing callus that was pale green in colour. Analysis of total phenols, flavonoids, and alkaloid concentrations revealed that the methanolic extract of in vitro grown callus had the highest concentration of total phenolics (101.1 mg of GA/g of extract), flavonoids in methanolic stem extract and alkaloids in methanolic extract of the leaf (118.3 ± 1.5 mg/10 g of extract). The free radical scavenging activity of methanolic leaf extract was found to be the highest, with an inhibitory concentration half (IC50) of 40.6±10.06 µg/ml. It was found that chloroform from the leaf has the greatest ability to stabilize membranes (66.02 percent). The callus cultures of *M. frondosa* used in this early phytochemical and pharmacological research could be the basis for future medication development [46].

Pharmaceutical / Pharmacological Activities: *Mussaenda frondosa*, also known as "Vellai ilai" in Tamil, is a medicinally significant member of the Rubiaceae family. Jaundice, asthma, hyperacidity, ulcers, leprosy, diuretic, wound, swelling, antibiotic, diuretic action, hypolipidemic impact, hepatoprotective activity, fever, and cough are all traditionally treated with plant parts **Fig. 5**. The next paragraphs provide an in-depth analysis of numerous published studies:

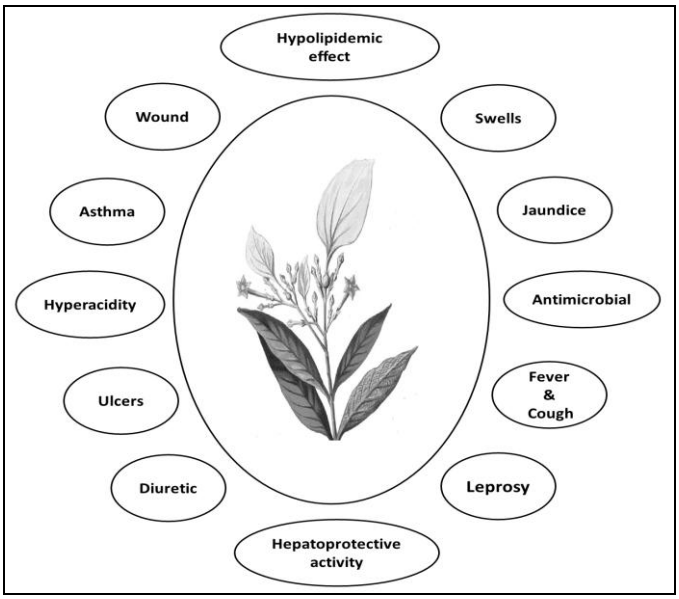

FIG. 5: PHARMACOLOGICAL ACTIVITIES OF THE WHOLE PLANT

Wound Healing Activity: Patil S.A. *et al.,* 2010 studied alcoholic leave extract of the leaves of *Mussaenda frondosa* Linn. for wound healing and antibacterial activity. In an animal model with an incision wound, extract increased wound breaking strength and hydroxyproline content. The antibacterial activity of leaves extract was also demonstrated by various species of bacteria that were utilized to test the extract [47]. Whereas, Suhas A.P. *et al.,* 2011 investigated the activity of *Mussaenda frondosa* Linn by using different types of wound healing models such as excision, incision, and dead space wound. The results were achieved in terms of wound contraction, epithelialization time, and tensile strength. The wound healing activity of alcoholic extract-treated mice was found to be significantly different from that of control groups in all parameters. Preliminary phytochemical research, TLC, HPTLC, IR, and mass spectroscopy approaches confirmed the presence of flavonoids, steroids, saponin, and resin in diverse extracts [48].

Antimicrobial Activity: Shanthi S. *et al.,* 2020 investigated the n-hexane, chloroform, ethyl acetate and methanol extracts of the leaves of *Mussaenda frondosa* Linn. F or its antimicrobial activity against nine bacteria and four fungi. The plant's methanol extract demonstrated superior antibacterial and antifungal efficacy to other leaf extracts. Additional research was done on the phytochemical profiles of the various extracts from *Mussaenda frondosa* Linn leaves [49].

Antibacterial Activity: Rifqi Efendi M. *et al.,* 2019 studied different fractions of *Mussaenda frondosa* Linn. petals for the antibacterial activity. An agar diffusion method was employed to test the bactericidal activity of three fractions: n-hexane, n-butanol, and ethyl actetate. Pathogenic bacteria were shown to be inhibited by various fractions of *Mussenda frondosa* Linn. petals, suggesting the plant's good antibacterial potential [50].

Anti-Inflammatory, Antipyretic and Analgesic Activity: Bose *et al*., 2020 studied methanolic extract of plant Mussaenda frondosa Linn leaves. The anti-inflammatory activity was determined by the production and participation of various inflammatory components. The analgesic activity was evaluated using Eddy's hot plate method, the tail-flick method and the acetic acid-induced writhing method. Pyrexia was induced using Brewer's yeast to test the antipyretic efficacy. The methanolic extract of *Mussaenda frondosa* Linn. leaves has good anti-inflammatory, analgesic, and antipyretic properties, according to the results of this study [51].

Hepatoprotective Activity: Sambrekar S.N. *et al*., ***2010*** investigated the hepatoprotective activity of petroleum ether, chloroform, alcohol, and aqueous extract of leaves of *Mussaenda frondosa* Linn. in a paracetamol-induced liver damage model. In terms of the hepatoprotective effects, both the aqueous and the alcoholic extracts performed well, according to the findings [52].

Cytotoxic Activity: Pappachen L.K. *et al.,* 2017 studied methanol extract of leaves of *Mussaenda frondosa* Linn. and isolated flavonoid and phenolic fraction for *in-vitro* anticancer activity on HepG2 cell line. The methanolic extract and isolated flavanoid and phenolic fraction of *Mussaenda frondosa* leaves were subjected to *in-vitro* cytotoxic studies on HepG2 cell line by MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) assay method and isolated flavonoid fraction showed better activity against HepG2 cell line. The methanolic extract shows a CTC_{50} value 125µg/ml. The isolated flavonoid fraction showed a CTC_{50} value 375µg/ml, and the isolated phenolic compound showed a CTC_{50} value 550 µg/ml, which indicates a good anticancer activity [53].

Antioxidant Activity: Siju E.N. *et al.,* 2010 investigated the in vitro antioxidant effects of the ethyl alcohol and aqueous extracts of the whole plant of *Mussaenda frondosa*. For the DPPH radical scavenger, *Mussaenda frondosa*'s ethyl alcohol extract shows a positive response. *Mussaenda frondosa's* ethyl alcohol and aqueous extracts also showed positive results at higher concentrations. Positive control and standard antioxidant, BHA, was used in this study. Raised DPPH radical scavenging activity was observed as the concentration of the extract was increased, and ascorbic acid was used as a standard reducing agent to test the extract's reducing power. Ethyl alcohol and aqueous extract of *Mussaenda frondosa* exhibited good reducing power. The reducing power of both extracts of *Mussaenda frondosa*

along with that of ascorbic acid at concentration between 500mg/l was high due to high absorbance *i.e* 0.45±0.07 for alcoholic extract & 0.58±0.07 for aqueous extract. The reducing power of ethyl alcohol and aqueous extracts of *Mussaenda frondosa* increases with increase in the concentration. All the analysis was made with the use of a UV-Visible spectrophotometer (Shimadzu 1700, INDIA) at 700nm. The *Mussaenda frondosa* could be used in pharmaceuticals for its antioxidant capabilities, according to the study [54].

Diuretic Activity: Sreelakshmi *et al.,* 2015 evaluated the diuretic activity of the plant *Mussaenda frondosa* Linn, using the Lipschitz method. The albino Wistar rat was divided into four groups of six rats each. As a conventional diuretic, Furosemide (20 mg/Kg p.o) was utilized.

The experiment employed two dosages of plant extract. At the completion of 24 h the volume and concentration of electrolytes in urine were measured. Higher urinary output and higher concentrations of sodium, potassium and chloride ions were found after single-dose administration of alcoholic extract of *M. frondosa*, 200 and 400 mg/kg, and conventional furosemide (20 mg/kg). The excessive diuretic activity was found in the alcoholic extract of M. frondosa, which was similar to the standard furosemide (20 mg/kg) [55].

Hypolipidemic Activity: Wesley J. *et al.,* 2009 investigated the hypolipidemic activity of *M. frondosa* using methanol extract. High fat diet fed rats showed significant increased levels of plasma and total cholesterol, triglycerides, free fatty acids, phospholipids plasma LDL cholesterol and decreased level of plasma HDL cholesterol. After administering the methanolic extract of *M. frondosa* to rats on a high-fat diet, lipid levels in plasma and tissues were found to be near normal.

When used with the commonly prescribed statin medicine atorvastatin (1.2mg/kg), larger doses of the extract (400-450 mg/kg body weight) demonstrated notable effects. An anti-lipidemic action may be attributable to the prevention of cholesterogenesis by methanolic extract of *Mussaenda frondosa,* according to this study's findings. Methanolic extract of *M. frondosa* has hypolipidemic action in rats fed high-fat diets [56].

Anthelmintic Activity: Siju E.N. *et al.,* 2010 evaluated ethyl alcohol and aqueous extract of *Mussaenda frondosa* for their anthelmintic activity against *Pheretima posthuma, Raillietina spiralis, Ascaridia galli*. Each extract was tested at three concentrations (10, 25 and 50 mg/ml) in order to determine the time of paralysis and death of the worm. As a reference standard, piperazine citrate (10 mg/ml) was employed and pure water was used as a control. Ethyl alcohol extract of *Musaenda frondosa* showed the paralysis as well as death of worm in a less time as compared to piperazine citrate especially at higher concentration (50 mg/ml). While water extract also showed significant activities. Results reveal that the aqueous extract and ethyl alcohol have anthelmintic properties [13].

Anti-stress Activity: Koul S. *et al.,* 2011 investigated the in vitro free radical scavenging effect and stress-induced changes in brain neurotransmitters as well as monoamine oxidase levels in albino rats in different models. To counter the effects of cold immobilization stress-induced alterations in norepinephrine (NE), dopamine (DA), 5-hydroxy tryptamine (5-HT) and 5-hydroxy indole acetic acid (5-HIAA), an ethanolic extract of *Mussaenda frondosa* roots was found to have normalizing activity.

The results show that the extract examined has antistress action on a biological level. Researchers discovered inhibitory concentrations (IC_{50}) of DPPH, Superoxide scavenging activity and hydroxide scavenging activity to be 51.3, 24.6, and 52.7 g/ml, respectively. According to the results of this study, the ethanolic root extract of Mussaenda frondosa may be able to alleviate oxidative stress. Thus, the study demonstrates the extract's ability to scavenge free radicals and alleviate stress [57].

Anti-seizure Activity: Guggilla S. *et al.,* 2017 investigated the anti-seizure activity of *Mussaenda frondosa* in male Wistar albino rats by using Cobalt induced Epilepsy. MEMF (Methanolic extract of *Mussaenda frondos*a) was given three times at 12-hour intervals at doses of 200 and 400 mg/kg p.o., along with the usual medication Silymarin (100 mg/kg p.o.) and Cobalt (1ml/kg) to all groups except the normal control group.

After 36 h of Cobalt treatment, several biochemical measures and histological examinations were used to determine the anti-seizure effect. The biochemical and histological effects of cobalt-induced brain damage in Wistar albino rats were reduced by MEMF at 200 and 400mg/kg doses. The methanolic extract of aerial parts of *Mussaenda frondosa* afforded significant protection against Cobalt-induced epileptogenic cortical injury [58].

Other Properties:

Mucilage as Tablet Excipient: Dilip C. *et al.*, 2010 investigated the efficacy of the mucilage obtained from the leaves of *Mussaenda frondosa* Linn as tablet excipient. Using standard characteristics such as diameter, thickness, weight fluctuation, hardness, friability, disintegration, and an in-vitro dissolution investigation, the extracted mucilage-based tablets were compared to those created with starch paste as the standard binder. When used as an excipient in tablet formulation, mucilage has good physicochemical qualities. Tablets manufactured with 5-10% mucilage have a continuous release rate, while tablets created with 1 percent mucilage release more than 90% of the medication within four hours, making this the optimal concentration for tablet manufacturing. It is possible to employ mucilage from *Mussaendia frondosa* at low concentrations as a good binding agent. The manufactured tablets form a sticky hydration film on the surface, which decreases the release rate of the medicine and may therefore be assessed for its efficacy in sustaining the release of the drug [59].

Green Synthesis of Zinc Oxide Nanoparticles for Photocatalytic and Biological Activities: Dogganal Jayappa M. *et al.*, 2020 biosynthesised the zinc nanoparticles from the leaf, stem and callcus of plant *Mussaenda frondosa* Linn. by utilizing and capping potential of them. UV–visible spectra of ZnO–NPs showed a strong absorption peak at 370 nm corresponding to the bandgap energy of 3.33 eV for ZnO–NPs obtained from leaf (L-ZnO-NP), stem (S-ZnO-NP) and callus (C-ZnO-NP) aqueous extracts. According to the results of XRD investigation, there were hexagonal wurtzite formations with average grains between 5 and 20 nm in diameter. Stretching vibrations of –O–H, C–H, C–N and C=O groups have been detected in FTIR spectra, indicating their involvement in the reduction and stability of nanoparticles. Nanoparticles in the form of spongy, spherical, porous agglomerations can be seen using SEM imaging. DLS and zeta potential measurements confirmed the stability of ZnO-NPs. This study explores biological uses of ZnO-NPs (antioxidants, anti-inflammatory agents, anti-diabetics, anti-microbes, and anti-cancer agents) are explored in this study [60].

CONCLUSION: There are many key phytoconstituents in Mussaenda, including triterpenes, steroids, and flavonoids, all of which have medicinal uses. Antibacterial, anti-inflammatory, antioxidants, antipyretic, antiviral, cytotoxic, and diuretic qualities are attributed to this genus. Several natural compounds of interest to pharmacologists have been provided by the genus Mussaenda. As an added bonus, the plants in this family are easy to grow. They're resistant to disease and pests and can take a lot of thinning. Chemical and biological investigations have been conducted on only a few species. Phytochemical, pharmacognostic, pharmacological aspects and nanotherapeutic potential of the Mussaenda genus are emphasized in detail in this article. This article will help all the researchers who are conducting their studies and research on the genus Mussaenda.

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