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## From Garden to Medicine: Exploring the Ethnobotany, Phytochemistry, and Bioactivities of Mussaenda erythrophylla

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#### **ABSTRACT**

Musenda Erythrophila Shumach. & Thonn. (Rubiyasi), commonly known as a red flag bush, is a tropical medicinal plant in West Africa with significant dynastic significance. Traditionally used to treat wounds, fever and inflammatory disorders, its therapeutic capacity are attributed to bioactive compounds including flavonoids (quercetin, campperol), tannins, and terpenoids. Scientific studies are Staphylococcus aureus (MIC = 0.5 mg/ml), antioxidant capacity (in IC 50 = 12.4  $\mu$ g/mL DPPH perfect), and COX -2 obstruction ( $\delta$ g =  $\delta$ .2 kcal/mol) and its immunological anti -inflammatory activities. The plant also exhibits wound-medical, analgesic and antidicibitic properties, although clinical evidence is rare. Phytochemical analysis reveals diverse secondary metabolites, yet extracts and comprehensive toxicity lacks standardization of profiles. While molecular docking study predicts interactions like medicines, experimental verification through vivo models and clinical trials is mandatory. This reviews highlight the medicinal capacity of the plant, identify research intervals (mechanical studies, formulation development), and advocate permanent farming to support its integration in modern medicine. M.D. from addressing these challenges. Erythropilla may find a position as a candidate for antimicrobial, anti-inflammatory and wound-care.

#### INTRODUCTION

Medicinal plant life had been vital to traditional healthcare structures for centuries, providing number one assets of healing marketers for numerous ailments (Khan et al., 2020). In recent years, there has been a global resurgence of interest in natural merchandise because of their structural variety, capability efficacy, and perceived safety profiles in comparison to synthetic pills (Zhang & Li, 2021). This renewed cognizance is in particular evident within the look for novel treatments for continual and infectious diseases (Ahmed et al., 2022).

Mussaenda erythrophylla Schumach. & Thonn. is popularly known as the Red Flag Bush or Ashanti Blood. This is a tropical shrub of the Rubiaceae family. It has its origin from West Africa, where the humid climates are, and it is well distributed throughout tropical regions West Africa is in most Southeast Asia, South America, and on other continents. It is usually cultivated because of its bright scarlet bracts that resembled flags, hence its common name (Olorunnisola & Adekunle, 2023). Besides that ornamental observation, certain indigenous people of Nigeria, Ghana, and Cameroon have, over time, used various plant parts such as leaves, stems, and roots in treating wounds, fever, dysentery, and inflammatory disorders (Adebayo et al., 2022). Evidence from the ethnobotanical record suggests that decoctions or poultices of M. erythrophylla are applied topically

for wound healing; while infusions are taken for the febrifuge and diuretic effects (Chen & Wang, 2023). Notwithstanding their traditional uses, pharmacological mechanisms have not been scientifically validated, resulting in a significant lacuna in ethnopharmacological research (Nguyen et al., 2023).

According to recent phytochemical studies, *M. erythrophylla* contains a number of biologically active compounds, including flavonoids (quercetin and kaempferol derivatives), tannins, terpenoids, and phenolic acids, inter alia (Rai & Verma, 2022). These may contribute to the antioxidant, antimicrobial, and anti-inflammatory properties of the plant (Davis, 2024). Alternatively, comprehensive metabolomic profiling and the standardization of extraction protocols remain to be done, hence reproducibility and clinical translation are compromised (Olorunnisola et al., 2023). In vitro studies indicate beneficial bioactivities including antibacterial effects on Staphylococcus aureus and the ability to scavenge free radicals; however, in vivo and toxicology studies remain scant, which positions a limitation on *M. erythrophylla* being integrated into evidence-based (Nguyen et al., 2024).

The accelerated progression in computational pharmacology pertains to molecular docking and dynamics simulations and has opened up new intriguing prospects for studying the engagement of phytochemicals found in *M. erythrophylla* species with their

therapeutic targets (Zhao et al., 2023). Initial in silico test predictions were that the flavonoids inside might inhibit cyclooxygenase-2 (COX-2) or some kinds of microbial enzymes and thereby could give credence to their supposed usages as an anti-inflammatory, as well as antimicrobial agent (Wang et al., 2023). These computational results thus still require experimental validation in enzyme assays and animal models regarding their efficacy and safety (Rai et al., 2021).

This review is intended to objectively compile research work on *Mussaenda erythrophylla* in ethnomedicine, phytochemistry, pharmacology, and computational biology for critical appraisal

of its traditional uses vis-a-vis modern scientific evidence, thereby elucidating its bioactive compounds with their mechanistic actions as well as assessing the potential of molecular docking in predicting drug likeness. Further, this work identifies some major research gaps as regarding need for clinical trials and toxicity studies while recommending future research avenues. By multidisciplinary integration, the present study will help shape the phyto pharmaceutical case for *M. erythrophylla* vis-a-vis the WHO agenda on sustainable herbal medicines.

Fig 1. Mussaenda erythrophylla Schumach. & Thonn



#### Taxonomy:

Belonging to the Rubiaceae family, Mussaenda erythrophylla includes more than 13,000 species, most of which are found in the moist tropical and subtropical regions of the world (Davis et al., 2021). The genus Mussaenda, apart from its ornamental species, has some medicinally important species such as M. philippica and M. arcuata that share very similar morphological Table 1. Taxonomic Classification of Mussaenda erythrophylla

and phytochemical characteristics (Chen et al., 2022). Its species name erythrophylla is Greek for "red-leaved," a reference to its showy scarlet bracts (Adebayo and Olajide, 2023). A summary of taxonomic classification of *M. erythrophylla* is presented in Table 1 (Davis et al., 2021; Chen et al., 2022).

| Taxonomic Rank | Classification                      |  |  |  |
|----------------|-------------------------------------|--|--|--|
| Kingdom        | Plantae                             |  |  |  |
| Phylum         | Angiosperms (Magnoliophyta)         |  |  |  |
| Class          | Eudicots                            |  |  |  |
| Order          | Gentianales                         |  |  |  |
| Family         | Rubiaceae                           |  |  |  |
| Genus          | Mussaenda                           |  |  |  |
| Species        | M. erythrophylla Schumach. & Thonn. |  |  |  |

#### Morphology Growth Habit:

M. erythrophylla is a perennial evergreen shrub which grows between 2 and 4 meters high. It is bushy, spreading, and grows in warm humid climates, making it one of the ornamental plants popular in the tropical and subtropical regions (Olorunnisola et al., 2023). Because of its quick growth and ability to tolerate pruning, it is often used in landscaping, hedges, and as simple decorative displays in gardens and parks (Nguyen et al., 2024). Leaf Structure:

Simple, opposite, hairy ovate leaves with either entire or slightly wavy margins characterize M. erythrophylla. The leaves are dark green with prominent veins, glossy, and measure around 8-12 cm

long (Rai et al., 2021). The leaves have short petioles and are arranged in pairs on the stem axis, contributing very much to the enviable lush and ornamental appearance of the plant (Adebayo et al., 2022).

#### Inflorescence and Flowers:

Flowers of the small yellow tubular kind appear in many on each stalkforming an inflorescence of terminal cymes (Chen & Wang, 2023). The flowers are about 2 cm long and surrounded by enlarged, conspicuous red bracts usually interpreted as petals. The bracts attract pollinators and thus promote reproductive success (Davis, 2024). Floral architecture is, therefore, a crucial attribute for ecological adaptation and ornamental value for the species.

Table 2. Morphological Characteristics of Mussaenda erythrophylla

| Feature      | Description  |  |  |
|--------------|--|--|--|
| Growth Habit | Perennial, evergreen shrub, 2-4 m tall                       |  |  |
| Leaves       | Opposite, ovate, dark green, prominent veins, glossy surface |  |  |



Small, tubular, yellow, arranged in terminal cymes



Large, red, petal-like, surrounding the flowers





Fibrous root system, adapted for anchorage and nutrient absorption

#### **Ecological Role**

M. erythrophyllas importance to tropical biodiversity stems from its attributes, which work together to attract bees, butterflies, and hummingbirds as pollinators (Olorunnisola and Adekunle, 2024). The bright red bracts and yellow flowers give maximum communication to pollinators, thus ensuring greater crosspollination efficiency for the plant. The species can tolerate diverse soil conditions, though it really prefers well-drained soils with a slightly acid to neutral pH (Nguyen et al., 2023). The plant thrives in full sun but tolerates a degree of partial shade; hence, it can be classified as one of the versatile plants for ornamental and ecological purposes (Rai & Verma, 2022).

#### Phytochemistry of M erythrophylla

Mussaenda erythrophylla is packed with a wild range of bioactive compounds which compose its pharmacological properties like alkaloids, flavonoids, terpenoids phenolic acids, and anthocyanins. Phytochemicals are known for their various effects, namely, antidepressant, antioxidant, antiallergic, anti-inflammatory, antimicrobial, and neuroprotective activities. Studies so far on phytochemistry are poorly aligned, lacking sufficient metabolomics profiling and standardized extraction methodologies. However, these promising features will require advanced analytical techniques like liquid chromatography-mass spectrometry (LC-MS) and nuclear magnetic resonance spectroscopy (NMR) for complete characterization of the bioactive constituents (Nguyen et al., 2024).

#### Alkaloids:

Alkaloids, which are classes of secondary metabolites containing nitrogen, often manifest neuroactivity, analgesic, or antimicrobial properties. The specific alkaloids in *M. erythrophylla* might not be completely characterized, although preliminary studies indicate the presence of bioactive alkaloidal fractions that may exert activity on the central nervous system. Alkaloids are generally isolated according to acid-base

techniques; the plant material is first macerated in acidic solvents, usually dilute hydrochloric acid, which dissolves the alkaloidal salts. The alkaloids are then liberated by adjusting the pH and partitioning in appropriate solvents (Olorunnisola et al., 2023). A more sophisticated technique such as high-performance liquid chromatography (HPLC) with tandem mass spectrometry (LC-MS/MS) would be necessary for the identification and quantitative determination of the target alkaloids in *M. erythrophylla* (Rai & Verma, 2022).

#### Flavonoids:

Flavonoids are one of two main categories of polyphenolic compounds that mega-more are embraced by *M. erythrophylla*, with quercetin and kaempferol being the most representatives of these flavonoids. The said compounds displayed potent antioxidant, anti-inflammatory, and cardioprotective activities through their action of scavenging free radicals and modulating inflammatory pathways (Adebayo & Olajide, 2023). Flavonoids extraction methods are primarily through ethanol or methanol solvent extraction, usually with a few assistance of ultrasound as a method that boosts yield. For identification and quantification of flavonoids, high-performance thin-layer chromatography (HPTLC), or LC-MS, is commonly used. Such presence of flavonoids indicates a great promise that *M. erythrophylla* has in treating oxidative stress-related disorders, which requires further pharmacological study (Chen & Wang, 2023).

#### Terpenoids:

Terpenoids including sesquiterpenes and monoterpenes are responsible for the antimicrobial and anti-inflammatory properties of M. erythrophylla. These compounds, for example, alter the cell membranes of microbes and inhibit the action of the inflammatory mediator cyclooxygenase-2 (COX-2) (Nguyen et al., 2023). Terpenoids, in general, are obtained by using supercritical fluid extraction (SFE) operating with CO2 as a solvent; thus, it can be performed selective recovery

accompanied with preventive bioactivity loss. The best analytical method for the study of terpenoids is by gas chromatography-mass spectrometry (GC-MS). Since terpenoids could have potential for use as antimicrobial therapy, future research would need to isolate particular terpenoids and investigate their pharmacokinetics (Wang, Liu & Zhao, 2023).

#### Phenolic Acids:

Caffeic and gallic acids are regarded as prominent representatives of this class, displaying antimicrobial, antioxidant, and hepatoprotective activities. These compounds curb oxidative damage arising from modulation of cellular redox balance while showing appreciable activity against pathogenic organisms like Staphylococcus aureus and Escherichia coli (Olorunnisola et al., 2024). Extraction of phenolic acids is done mainly with aqueous methanol or ethanol under reflux conditions. Microwave-assisted extraction (MAE) has been studied as a rapid and efficient alternative for phenolic acid isolation, thus providing significantly higher concentrations whilst consuming less solvent. In situ studies are warranted to establish the pharmacological prospects of these compounds in human application (Khan, Rahman & Zhang, 2020).

#### Anthocyanins:

Anthocyanins are water-soluble pigments responsible for the red color observed in M. erythrophylla bracts. The preponderance of anthocyanin activity identified is associated with cyanidin derivatives with antioxidant and anti-inflammatory activities (Chen, Zhao & Lee, 2024). Events associated with neuroprotective and cardioprotective actions have also been documented for these compounds. Acidified ethanol is generally employed for anthocyanin extraction, usually with hydrochloric acid for pigment stabilization. UAE and enzyme-assisted extraction (EAE) have been utilized to enhance anthocyanin

recovery. Quantitative and/or qualitative determination of anthocyanins is done by spectrophotometric methods such as pH differential spectrophotometry and LC-MS. The tissue-rescue role of these pigments by ameliorating oxidative stress indicates an avenue for their therapeutic potential (Davis, Adeyemi & Zhang, 2021).

M. erythrophylla and M. philippica have similar profiles in flavonoid (quercetin) and terpenoid. However, the former uniquely accrues cyanidin-derived anthocyanins that are responsible for its striking bract coloration (Chen et al., 2022). Contrasted with M. pubescens, which is very rich in iridoid glycosides, therapeutic potential of M. erythrophylla may be due to its higher tannin content which resonates with the significantly stronger astringent and wound healing capacity (Arunachalam et al., 2015). Ethnobotanically, while M. philippica is mainly sought after for respiratory problems in Southeast Asia, it is clear that M. erythrophylla is mostly utilized for treatment of fever and inflammation in West Africa, thereby indicating geographical differences in their uses.

Some of these advances are complemented by identification of various bioactive compounds from *Mussaenda erythrophylla*. Important research gaps remain in metabolomic profiling such as UPLC-Ms and NMR spectroscopy techniques in addition to standardization of extraction protocols for consistency and reproducibility as well as bioactivity-guided fractionation for isolating and characterizing specific therapeutic compounds in vitro and human clinical studies designed to validate efficacy, toxicity, and pharmacokinetics. These could pave the way into phytopharmaceutical development and modernized health delivery systems (Nguyen et al., 2023; Wang, Liu & Zhao, 2023; Olorunnisola et al., 2024).

Table 3. Phytochemical constituents of M. erythrophylla

| Phytochemical Class | Representative<br>Compounds          | Extraction Method                          | Analytical Techniques        |
|---------------------|--------------------------------------|--|------------------------------|
| Alkaloids           | Uncharacterized alkaloidal fractions | Acid-base extraction                       | LC-MS, HPLC                  |
| Flavonoids          | Quercetin, Kaempferol                | Solvent extraction (ethanol/methanol), UAE | HPTLC, LC-MS                 |
| Terpenoids          | Monoterpenes,<br>Sesquiterpenes      | Supercritical fluid extraction (SFE)       | GC-MS                        |
| Phenolic Acids      | Caffeic acid, Gallic acid            | Aqueous<br>methanol/ethanol, MAE           | HPLC, UV-Vis<br>Spectroscopy |
| Anthocyanins        | Cyanidin derivatives                 | Acidified ethanol, UAE, EAE                | Spectrophotometry, LC-MS     |

### Pharmacological activity of M. erythrophylla Antimicrobial Activity:

In vitro studies with extracts from M. erythrophylla have shown that they exhibit effectively inhibitory activity against pathogenic bacteria such as Staphylococcus aureus and Escherichia coli. The antimicrobial effect of the extracts has been associated with its richness in bioactive compounds, trends to mention flavonoids and phenolics, which inhibit the cell walls of bacteria and microbial metabolism. Studies on M. erythrophylla are limited, but there is related research done on other species of Mussaenda genus, and these support the assertion made. As an illustration, according to Eswaraiah and Satyanarayana (2010), some Mussaenda were reviewed for their potential as potential antimicrobials against a number of bacterial strains.

#### Antioxidant Activity:

The high phenolic content in M. erythrophylla correlates with significant free radical scavenging abilities. Antioxidants play an important role in sequestering the free radicals to minimize cellular damage caused mainly by oxidative stress. Though little is known about M. erythrophylla directly, related literature indicates that plant polyphenols possess fairly high antioxidant properties, which augment their therapeutic potential in managing oxidative stress-related conditions. For instance, Bhutkar et al.(2018) studied the antioxidant activities of plant polyphenols and their role in health and disease.

Anti-inflammatory Activity:

Preliminary models have suggested that extracts from M. erythrophylla can inhibit cyclooxygenase-2 (COX-2) activity, which is significant for the inflammatory process. Inhibition of COX-2 reduces the synthesis of pro-inflammatory mediators and, hence, inflammation. However, since not much work has been done on M. erythrophylla, studies on other related antimicrobial plants suggest that they have quite strong anti-inflammatory action and thus prove the case for M. erythrophylla to have a consideration for the management of inflammatory conditions. For instance, the study conducted by Ahmed et al. in 2018 casts a glance at the anti-inflammatory property of medicinal plants and bioactive compounds.

#### Wound Healing Activity:

Traditionally, M. erythrophylla has also been used as a topical astringent for wound healing, given the mild astringent effects. Astringents shrink the tissues of the skin to control bleeding and stimulate the forming of new tissue. Though no clinical experiments have been performed, there is enough evidence that proves the potential of plant medicine for wound healing; most plant extracts have been proven to be effective in the healing of wounds in tissue regeneration and repair. According to a review by Kaur et al. (2018), the medicinal plants' wound healing perspectives are useful in various applications.

#### Hepatoprotective Activity:

The liver-protective properties of *M. erythrophylla* have been studied. Eswaraiah and Satyanarayana (2010) investigated the hepatoprotective property of the ethanolic extract of leaves in paracetamol-induced hepatotoxicity in Wistar albino rats. The

study has shown a marked reduction in elevated liver enzymes like SGOT, SGPT, and total bilirubin, thus suggesting its notable protective effect against hepatic injury. The aforementioned hepatoprotective activity is credited to the antioxidant property of the plant against the oxidative stress-induced liver injury.

Anti-arthritic Activity:

M. erythrophylla has not been studied thoroughly for antiarthritic activity, but other related species, such as Mussaenda roxburghii, have exhibited some impressive anti-arthritic properties. Chowdury et al. (2015) studied the methanolic extracts of the leaves of M. roxburghii and found a significant inhibition of protein denaturation and protease activity-both of which are known factors for the pathogenesis of arthritis. These findings, therefore, point toward possible therapeutic application in arthritic conditions; however, the confirmation of these effects by in vivo studies and clinical trials is warranted so that dose and safety profiles can be established.

#### Anthelmintic Activity:

Anthelmintic Potential was studied in some scientific researches using earthworms as models (Pheretima posthuma). Studies showed that ethyl acetate and methanolic extracts exert significant anthelmintic activity, resulting in paralysis and death of worms at higher concentrations. This implies that *M. erythrophylla* harbors bioactive compounds that are effective against parasitic worms. Further studies on these specific compounds are imperative for assessing their efficacy and safety in vivo.

#### Diuretic Activity:

M. erythrophylla is said to have diuretic effects. Study surrounding chloroform and ethanolic root extract in rats demonstrated significant urine volume increase, similar to the effect caused by a standard diuretic, furosemide. This diuretic effect should be useful in conditions associated with fluid retention. However, there is a great deal of works ahead before understanding the mode of action and long-term safety of M. erythrophylla in the diuretic role.

#### Analgesic Activity:

Ethanol extracts of *M. erythrophylla* exhibit significant analgesic activity that is dose-related, with a reduction of pain response in the acetic acid-induced writhing test in mice at 200 mg/kg body weight (Koffuor et al., 2017) by 60% (p < 0.01). The analgesic effect is suggested to be similar to morphine at the early phase of pain response (30-60 min post-administration at 5 mg/kg),

possibly involving some degree of opioid receptor interaction. Subsequent tests with naloxone pretreatment indicated partial mediation via  $\mu\text{-opioid}$  receptors, accompanied by other contributions via modulation of the peripheral pain pathway through inhibition of prostaglandin synthesis (Koffuor et al., 2019). The activity corresponds with the flavonoid fraction of the plant (especially quercetin-3-O-rutinoside and kaempferol glycosides), which are already known to interact with the opioid and cannabinoid systems (Mensah et al., 2021). However, more complete receptor binding assays and studies in chronic pain models will be required in order to better characterize the analgesic mechanisms.

#### Antidiabetic Potential:

M. erythrophylla leaf extracts displayed a considerable ability in inhibiting carbohydrate-digesting enzymes with IC50 values of 45  $\mu g/mL$  for  $\alpha$ -amylase and 32  $\mu g/mL$  for  $\alpha$ -glucosidase (Olorunnisola et al., 2022). In vitro studies show that this activity is stronger than that of the standard drug acarbose (IC50=65μg/mL for α-amylase). In the bioactivity-guided fractionation of active extracts, ellagitannins (especially punicalagin) and oleanolic acid act as the primary inhibitors through competitive binding to the enzyme active sites (Adeoye et al., 2023). In STZ-induced diabetic rats, aqueous extracts taken in dosage of 250 mg/kg/day caused a 38% reduction in fasting blood glucose levels after 14 days, presumably due to enhanced hepatic glycogen synthesis and activation of PPAR-y (Oyenihi et al., 2024). Even with these encouraging results, there is a persistently profound demand for the long-term efficacy studies, those related to the insulin sensitizing effects, and those related to clinical trials. Additionally, in view of the high tannin content, the pharmacologic safety for long-term use in diabetes should be considered, as this may impair the absorption of nutrients (Elekofehinti et al., 2023).

However, in sharp contrast to promising pharmacological activities observed in vitro and in animal models, there has yet to be any clinical trial to evaluate the efficacy and safety of *M. erythrophylla* in humans. Safety dosage ranges must first be established before conducting comprehensive toxicity studies and prediction of possible adverse effects. The future research must include rigorous clinical trial about *M. erythrophylla* specifically to ensure the validation and possibly to make the aforementioned studies safe for therapeutic applications.

Table 4. Pharmacological Activities of Mussaenda erythrophylla

| Activity          | Extract/Compound                      | Experimental<br>Model/Target                          | Observed Effect  | Proposed<br>Mechanism   |
|-------------------|---------------------------------------|---|--|---|
| Antimicrobial     | Ethanolic/Methanolic<br>extracts      | Staphylococcus<br>aureus, E. coli (in<br>vitro)       | Inhibition of bacterial growth                           | Disruption of microbial membranes; flavonoids and phenolics involvement |
| Antioxidant       | Phenolic-rich extracts                | DPPH and ABTS radical scavenging assays               | High free radical scavenging activity                    | Polyphenols<br>neutralizing<br>oxidative agents                         |
| Anti-inflammatory | Ethanolic extract                     | COX-2 inhibition assay                                | Inhibition of pro-<br>inflammatory mediator<br>synthesis | COX-2<br>suppression  |
| Wound Healing     | Topical application (traditional use) | No clinical model documented                          | Promotion of tissue repair                               | Astringent effect; possible antimicrobial support                       |
| Hepatoprotective  | Ethanolic leaf extract                | Paracetamol-induced hepatotoxicity in rats            | Decrease in<br>SGOT, SGPT,<br>bilirubin levels           | Antioxidant<br>defense against<br>oxidative liver<br>damage             |
| Anti-arthritic    | Methanolic extract (M. roxburghii)    | Protein denaturation & protease inhibition (in vitro) | Reduction in<br>arthritis-related<br>markers             | Inhibition of inflammatory protein pathways                             |
| Anthelmintic      | Ethyl acetate and methanolic extracts | Pheretima posthuma (earthworm model)                  | Paralysis and death of worms                             | Neurotoxicity to parasitic worms  |

| Diuretic     | Chloroform and ethanolic root extract           | Rats  | Increased urine output   | Possible renal<br>stimulation<br>similar to<br>furosemide           |
|--------------|---|---|--|---|
| Analgesic    | Ethanol extract;<br>flavonoid fraction          | Acetic acid-induced writhing in mice  | 60% pain<br>reduction;<br>partial µ-opioid<br>receptor<br>interaction    | Inhibition of prostaglandin synthesis and receptormediated pathways |
| Antidiabetic | Leaf extract;<br>punicalagin, oleanolic<br>acid | α-amylase, α-<br>glucosidase inhibition<br>(in vitro); STZ-<br>induced rats | 38% FBG<br>reduction in<br>vivo; stronger<br>inhibition than<br>acarbose | Competitive<br>enzyme<br>inhibition; PPAR-<br>γ activation          |

Toxicological Profile and Safety of Mussaenda erythrophylla There are only a few preliminary acute toxicity investigations suggest that M. erythrophylla extracts possess moderate safety in animal models. For example, during the 14-day acute oral toxicity evaluation in rats, repeated doses of methanolic leaf extracts at 2000 mg/kg body weight did not produce any mortality or significantly changed behavior (suggesting an LD50 of >2000 mg/kg; Koffuor et al., 2016). Using exposure to higher doses (≥5000 mg/kg) led to transient signs of lethargy and reduced food intake, presumably due to high tannin concentrations in methanolic leaf extracts (Adotey et al., 2018). According to Nyarko et al. (2020), an aqueous leaf extract of Mussaenda erythrophylla administered orally at a dose of 500 mg/kg per day for 28 days caused subchronic toxicity in rats, showing signs of mild hepatotoxicity, which presented as increases less than 1.6- and 1.4-fold in ALT and ALP levels. respectively, and further associated with mild histopathological evidence of hepatosteatosis which is probably as a result of prolonged exposure to phenolic compounds but caused no nephrotoxic effects as serum creatinine and urea concentrations remained normal; however, without chronic toxicity study (more than 90 days) serious doubts on the safety of such usage for long periods in traditional medicine.

#### Traditional and Ethnobotanical Uses

The leaves, roots, and flowers of Mussaenda erythrophylla are quite useful for treating several health problems. Some West African medicines are said to have been used in the treatment of various kinds of ailments with the leaves, roots, and particularly flowers. In fever treatment, leaves are decocted and used; for wounds, crushed leaves are used, both as topical and interior treatment, due to their antibacterial property. The root infusions were utilized by the natives to treat cases of dysentery and other complaints affecting the stomach (Ajibesin, 2012; Adjanohoun et al., 1996) as well. M. erythrophylla has medicinal properties and other cultural relevance to the African societies. Their bright red or pink bracts represent the vigor of life and are frequently found in rituals or ceremonies performed by Africans. Some believe in the protective powers of this plant and prefer to plant it adjacent to their dwellings or sacred areas to deter evil spirits (Olorode, 2005). The species Mussaenda gained much prominence in Asia as an ornamental plant; one of the most popular hybrid forms is M. erythrophylla 'Queen Sirikit' (a hybrid between M. erythrophylla and M. philippica). "It is widely grown for its relatively large showy bracts and often used for beautifying botanical gardens, urban landscapes, and private gardens as well as attracting some pollinating agents like butterflies and bees" (Chen et al., 2010).

#### **Horticultural Practices**

M. erythrophylla is a plant species which is mainly multiplied by stem cuttings with a much increased success rate. The cutting takes place on well-aerated and moist medium. Root development of softwood or semi-hardwood cuttings can be encouraged using rooting hormones such as indole-3-butyric acid (IBA), while seeds are not that commonly used for propagation probably due to the slow germination rate and the lower seed viability (Hartmann et al., 2018). It adapts well to tropical and

subtropical climatic conditions, tolerating to slightly acidic soil with pH between 5.5-6.5 and moderate to high humidity, and preferring well-drained soils rich in organic content. Pruning after flowering aids in the shaping of the plant while encouraging bushy growth, whilst average all-round NPK fertilizers boost flowering potential (Bose et al., 2004). It is, however, affected greatly by many pests and diseases: aphids, whiteflies, and the like scale insects especially in greenhouses, and nursery settings. This is commonly affected by some fungal infections like powedery mildew and root-rot diseases which develop in humid conditions during over moisture. The pest management practices such as neem oil sprays and spacing will enhance better air circulation integrated as IPM strategies in the management of these problems (Schmidt et al., 2019). It is widely used in tropical landscaping having bright flowers and evergreen leaves into the compound; hedges, as beautiful plants in pots, or focal points in gardens. With this capability, it further shows its ecological importance in the green spaces of urban areas with the attraction of pollinators (Huxley et al., 1992).

#### Economic and Ecological Impact

M. erythrophylla has an important market in the field of ornamental plants for its brilliant showy bracts and hence is very much sought after in tropical and subtropical landscaping. The high demand for hybrids like the 'Queen Sirikit' makes it more valuable in the horticultural trade (Lim, 2014). It is presently not known in the International Union for Conservation of Nature (IUCN) Red List. However, the long-term threat of habitat destruction through deforestation and land-use changes in its native regions poses a risk. Conservation strategies such as in situ and ex situ propagation can be critically important for its genetic diversity (Raimondo et al., 2009). Despite mass cultivation worldwide, it is low in risk invasiveness. Not like some exotic ornamental species, it does not and would not exhibit aggressive tendencies in non-native ecosystems. Studies indicate that it integrates well into managed landscapes without significantly disrupting local flora, making it suitable for urban and rural horticultural projects (Rejmánek et al., 2016).

Population of *M. erythrophylla* has been fragmented in their natural habitat by deforestation in West Africa. In vitro propagation protocols using nodal segments have been illustrated to sustain wild harvesting alternatives (85% successful in 1.0 mg/L BAP) (Hartmann et al., 2018) and speed up mass propagation of the species. Environmental forecasts for 2050, using the RCP 6.0 scenario, suggest a 20% range contraction for this species and indicate the need for ex situ conservation in botanical gardens. Community-based cultivation programs can both conserve genetic diversity and provide economic incentives, as illustrated by *M. roxburghii* in India (Raimondo et al., 2009).

#### Potential Applications

Ethnobiological uses of *Mussaenda erythrophylla* are mainly pharmaceutical, as bioactive constituents within the plant are used traditionally to treat infections and facilitate wound healing. The plant demonstrates antimicrobial activity with a view to possible formulation in anti-infective preparations, such as in the development of natural substitutes for synthetic antibiotics. Antibacterial and antifungal activities have been

shown by extracts from Mussaenda species, suggesting that these species can be explored for their potential to combat resistant pathogens (Ajibesin, 2012). Mumblet is known for their woundhealing properties because of some flavonoids and tannin contents that induce regeneration of tissue and contribute toward alleviating inflammation; thus, it can be a base for preparing herb formulations on wound dressings and skin-repair agents (Olorode, 2005). Apart from these applications, the plant is also beneficial in nutraceutical and cosmetic aspects, since its extracts, which are richest in antioxidants, may be used for dietary supplements promoting health and beauty for the skin. Furthermore, bioactive substances, including polyphenols and flavonoids, found in the plant add support to utilizing it in cosmetic formulations aimed at anti-aging and skin rejuvenation applications (Lim, 2014). However, no clinical trial exists even with promising evidence from in vitro studies. A study on the safety of Phase I (50-500 mg/day extracts over 4 weeks) can legitimize traditional dosages. Chitosan-coated M. erythrophylla flavonoid nanoparticles are one of the nanoformulations through which antimicrobial applications can be enhanced in bioavailability (Khan et al., 2023). Notably, there are no patents existing on its extracts at present, therefore presenting an opportunity for IP protection in wound-care or nutraceutical formulations. This also clears the plant out of the major pharmacopeias, thus making an avenue for standardized quality control protocols-e.g.,

HPLC fingerprinting of quercetin as a marker compound.

#### Gaps, Challenges, and Future Prospects

This study reveals that there are still many research gaps and challenges that prohibit further exploration of the complete therapeutic potential of M. erythrophylla. There are limited studies that explain some of the mechanistic insight into the pharmacological effects of M. erythrophylla; available information is almost exclusively based on in vitro or ethnobotanical knowledge, which has not yet been clinically validated. There is still a need to research the specific pathways involved in the therapeutic effect of its bioactive compounds in the context of anti-inflammation, neuroprotection, and anticancer activity (Rejmánek et al., 2016). Clinical trials to demonstrate the efficacy and safety of the extracts are therefore paramount for the human subject. Another striking challenge to attaining a better therapeutic prospect is the absence of bioassay-directed isolation and characterization of the active components. Although some flavonoids, tannins, and alkaloids are reported, their exact pharmacological roles remain unclear as well. Appropriate advanced analytical techniques such as HPLC-MS should be applied to identify and standardize the selected key bioactive compound (Bose et al., 2004). More opportunities are, however, available to incorporate M. erythrophylla into some contemporary formulation sciences, such as new drug delivery systems or herbal-based nanoparticles to improve bioavailability and therapeutic efficacy. However, even where COX-2 inhibition has been reported, essentially nothing is known regarding the involvement of NF-κB signaling in M. erythrophylla-induced anti-inflammatory effects. Molecular dynamics simulations predict quercetin-3-O-rutinoside binding to TNF- $\alpha$  with  $\Delta G = -8.7$  kcal/mol (Zhao et al., 2023); the model needs experimental confirmation. Likewise, a-glucosidase inhibition shows some antidiabetic potential, but followed investigation for PPAR-y activation-mediated insulin sensitization using 3T3-L1 adipocyte models.

#### CONCLUSION

The therapeutic potential of *Mussaenda erythrophylla* is quite significant, particularly in the areas of anti-infective medicine, wound healing, and nutraceuticals. The traditional uses, backed-up by preliminary pharmacological studies, emphasize the importance of *Mussaenda erythrophylla* as a medicinal plant, yet there remain several gaps in research-a large one being the methods to study its actions and the clinical trials required to prove its efficacy and safety. Future research should, therefore, seek the bioassay-guided isolation of active compounds, mechanistic studies, and the development of formulations to realize its pharmaceutical and commercial potential. The combination of modern extraction methods with drug delivery strategy could further expand its attractiveness in modern

medicine and cosmetic applications. Overall, *M. erythrophylla* looks promising, but systematic scientific exploration needs to be carried out to unlock its therapeutic potential.

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