Rich Diversity & Potential Medicinal Value of Endemic Sri Lankan Plant: *Jeffreycia zeylanica*

ABSTRACT

The genus *Jeffreycia* consists of about 109 species to have medicinal properties. *Jeffreycia zeylanica* (Family: ASTERACEAE) is commonly referred to as “Heen-botiya, Papula or Pupula in Sinhala and Kappilay or Kuppilay in Tamil”. It is an endemic herbaceous plant in Sri Lanka. Synonyms of *Jeffreycia zeylanica* are *Cacalia zeylanica Kuntze*, *Eupatorium zeylanicum* L., *Gymnanthemum zeylanicum* (L.), *Vernonia zeylanica* (L.). This plant can create secondary metabolites that may have substantial bioactivity. Extracts from leaves, stems and aerial parts are rich in alkaloids, flavonoids, steroids, triterpenoids, polyphenols, and saponins. These bioactive compounds lead to various pharmacological properties of *Jeffreycia zeylanica*. It is utilized in both Ayurvedic and folk medicine in a variety of methods to treat various illnesses, such as bone fractures, eczema, asthma, diarrhea, wound, and abscesses also as an anti-venom. Several studies have been carried out on this plant, including the evaluation of anti-inflammatory activity, antinociceptive activity, antioxidant activity, and anti-tumor activity. The lack of considerable toxicity associated with the plant *Jeffreycia zeylanica* makes it a choice for future development of therapeutic products, with the combination of traditional and novel technologies. A significant number of presently used antioxidant, anti-inflammatory, anthelminthic, and antitumor agents are compounds isolated from plants or their synthetic or semisynthetic derivatives.

Keywords: Jeffreycia zeylanica; Vernonia zeylanica; endemic plant; Asteraceae; Sri Lanka.

1. INTRODUCTION

Over 1,600 genera and 2,500 species make up the ASTERACEAE family, one of the largest flowering plant families in the world [1,2]. ASTERACEAE family members have been employed in food and medicine [3]. They have been used to treat a variety of disorders for millennia in folk medicine [4]. Plants of the *Jeffreycia* genus (ASTERACEAE) occur in different habitats from desert regions to freezing regions, from marshes to savannahs to dry plains to tropical woods [5]. Plants of the genus *Jeffreycia* are widely used in ethnomedicine. There are 109 different species of *Jeffreycia* that have been widely employed in traditional societies' everyday medical practices [6]. The World Conservation Monitoring Centre has nominated Sri Lanka as a ‘hotspot’ concerning its biodiversity [7].

According to reports, there are 3771 different species of flowering plants grown in Sri Lanka. About 927 (24%) of them are endemic to Sri Lanka. Additionally, 1430 species are thought to have therapeutic benefits. A total of 174 (12%) of these medicinal plants are native to Sri Lanka [8]. *Jeffreycia zeylanica* (Family: ASTERACEAE) is commonly referred to as “Heen-botiya, Papula, or Pupula in Sinhala and Kappilay or Kuppilay in Tamil. This review focuses primarily on the plant which is endemic to Sri Lanka *J. zeylanica.* This plant was mostly known as *Vernonia zeylanica*, however, recent data suggest that the scientific name *Vernonia zeylanica* has been changed to *Jeffreycia zeylanica* and it was mentioned in the National red list of Sri Lanka [9].

Because of their capacity to produce secondary metabolites with potential biological action, plants have long played a vital role in the development of medicine [10-17]. Plants materials with various concentrations of biologically active compounds may affect the efficacy and safety of medicine [18]. From the plant, a variety of phytochemicals have been isolated. According to studies,

alkaloids, flavonoids, steroids, triterpenoids, polyphenols, and saponins were detected during phytochemical screening of the plant's aqueous stem extract. These phytochemicals and bioactive compounds with antioxidant activity have a positive effect on human health and could diminish the risk of numerous diseases [19-22]. Alkaloids are well-known therapeutically as anesthetics, cardioprotective, and anti-inflammatory agents, and they also have an impact on the nervous system [23]. Plants are known to produce flavonoids, which are hydroxylated phenolic compounds that can act as antioxidants. Flavonoids have the capacity to activate the body's natural defense mechanisms, making them beneficial against a wide range of viral and bacterial infections as well as cardiovascular, cancerous, and other age-related disorders [24,25]. Phytosterols, also known as plant steroids, decrease cholesterol levels in people and are frequently used as dietary supplements. And have anti-cancer properties [26]. One of the most abundant and diverse groups of plant natural products, saponins, is involved in the defense mechanism of plants. Saponins offer a wide range of therapeutic benefits, including anti-viral, anti-cancer, anti-fungal, and anti-parasitic actions [27]. Triterpenoids are employed as anti-inflammatory, cardiotonic, and anti-tumor agents [28]. Polyphenol-containing compounds can be used as antioxidants. They provide defense against the onset of cancer, heart disease, diabetes, osteoporosis, and neurodegenerative disorders [29]. Extracts of the plant, *J. zeylanica,* have been utilized in a variety of folk medicines as therapies for cancer, microbial infections, and inflammation, and for treating wounds, bone fractures, and snake venom [30]. Only a few research has been done so far about *J. zeylanica*. So, future efforts should focus on *in vitro* and *in vivo* studies, as well as clinical trials should be implemented, to validate traditional knowledge [31].

1.1 Morphology of *Jeffreycia zeylanica*

An herbaceous plant is native to Sri Lanka. It exhibits a variety of ethnomedical traits. It is a

Fig. 1. Flowers, fruits, and leaves of *J. zeylanica* [34]

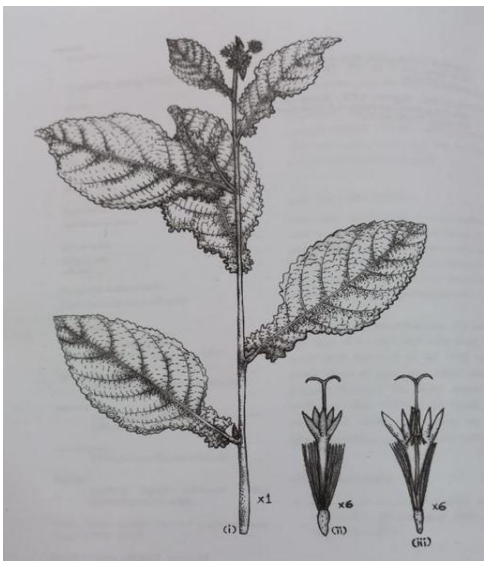

Fig. 2. Schematic diagram of *J. zeylanica* [33]

Fig. 3. Photograph of *J. zeylanica* whole plant

Fig. 4. *J. zeylanica* whole plant [39]

member of the family ASTERACEAE. *J. zeylanica* is a small under shrub (0.5-) 1 - 2.5 m tall with many strangling, divaricate, cylindrical branches that are finely tomentose when young [32-35].

1.1.1 Leaves

Easy, alternative White with fine wool beneath, 3.7-8.5 cm long, 1.7-3.5 cm wide, fiddle-shaped auriculate at base, obtuse or subacute at apex, strongly crenate and undulate, delicately tomentose above, and stiff and thick. Petioles are short and tomentose, with reticulate, pellucid, conspicuous veins beneath them [32].

1.1.2 Flower

Flower heads are small, numerous, irregularly corymbose, frequently 2-4 cm in size, and have short stalks (; new flowers are bone on the tip while the older ones are at the base.). Flowers are all tubular, bisexual, very pale violet, 6–8 to a head, wide spreading with the corolla being curved outwards, and a pappus of hairs erect in the center of the head. Sepals have been reduced to hairy bristles almost if the corolla tube. Involucre bracts are 1.5–2.5 mm long, oblong oval, apiculate, closely imbricate slightly floccose. united petals formed a 3.5–4 mm long tube. Stamens 5 united to corolla tube, filaments free, anthers fused into a tube round the style, anther cells acute, not tailed; lobes linear or triangular, 1.5 mm long, acute spreading at the extremities; inferior ovary with 1.5 mm long hairy, unilocular basal ovule, 6 mm long style with subulate limbs. March, September, and October are flowering months [32-34].

1.1.3 Fruit

The fruit is brown in color and is an achene with a slightly 5-ribbed pubescence and a yellowish-white pappus. The outer row is sparse and very short. Wind helps disperse seeds [34].

1.2 Synonyms and Other Names

Homotypic synonyms

Eupatorium zeylanicum L.
Gymnanthemum zeylanicum (L.) [36]

Heterotypic synonyms

Cacalia Zeylanica kunteze
Vernonia zeylanica

Common names in Sri Lanka

Sinhala name - Pupula, Hin-botiya, Papula, Wail Pupula
Tamil name – Kuppilay

1.3 Taxonomic Classification

Kingdom – Plantae, Subkingdom – Tracheophytes, Division- Angiosperms, Class – Eudicots, Subclass- Asterids, Order- Asterales, Family – Asteraceae, Genus- *Jeffreycia* or

Vernonia, Species – *Jeffreycia zeylanica,* Subspecies - *Jeffreycia zeylanica* Less [37].

1.4 Geographical Distribution

Jeffreycia zeylanica is endemic to Sri Lanka and shows a native distribution in the dry-wet zone. Common in Chena cultivation and home gardens in the dry zone. It can be seen in Madawacchiya; Wawnia district, Trincomalee district, Hanthana in Kandy district, Peradeniya, Kurunegala district, Wilpatthu National Park, Patangala, Maussakalee in Mathalee district [32]. Due to recent road development projects, this plant has been removed considering it is a weed showing a high growth rate. The National Red List of Sri Lanka is the record that has information about the conservation status of the fauna and flora in Sri Lanka. According to this record, *Jeffreycia zeylanica* is listed as LC (Least Concerned) [38].

2. ETHNOMEDICAL INFORMATION

Jeffreycia zeylanica is used to treat fractures because it encourages bone fusion. It is applied as an oil that is prepared by using the extractions of bark and leaves. A poultice made of ground roots is used to treat fractures. To encourage suppuration, the leaves are blended into a paste and applied to boils. With beneficial results, they are applied to leg eczema after being toasted with turmeric. Internally the extraction of leaves is used for the treatment of asthma. It is also useful emetic. Juice of the whole plant in high doses is used in emetic. Juice of the whole plant in high doses is used, particularly in case of food poisoning. Other than diarrhea and dysentery this plant can be used for wounds and abscesses, and as an anti-venom agent [30-33,40]. *J. zeylanica* has been identified as an endemic and economically viable medicinal plant that promotes immunity and is used to treat various diseases in folk medicine [41].

3. PHYTOCHEMISTRY

The chemistry of Asteraceae has been reviewed and some of the plant constituents of several species of the genus, *Jeffreycia* have been reported.

3.1 Whole Plant

Mainly triterpenoids and steroids are present in the whole plant, and it was detected by the Liebermann-Burchard test. Triterpenoids are mostly found in plants. These triterpenoids are mainly two types, tetracyclic and pentacyclic triterpenoids. Tetracyclic triterpenoids are categorized into dammarane and tirueallane while pentacyclic triterpenoids are categorized into six groups friedelane, lupane, urasane, oleanane, serratane, and taraxastane. Steroids are found in plants animals and micro-organisms. Plants contain a lot of steroids, and out of the steroids, sitosterol is known to be the comments secondary plant metabolic [42].
Extraction of crude plant material with non-polar solvent followed by purification was used for the isolation of triterpenoids. Purification was done by precipitation, column chromatography regarding silica gel, and preparative thin layer chromatography (TLC). *Jeffreycia zeylanica* mainly consists of lupane, which is a type of triterpenoid. In Sri Lankan plants at least 25 subtypes of lupanes were identified and out of them, *J. zeylanica* indicates the presence of lupanol (which is known to be the type of lupane) [42].

J. zeylanica indicates the presence of stigmasterol which is a steroid. Out of 111 investigated Sri Lankan plants stigmasterol dehydrositosterol is occur in only three species they are *Elephantopus scaber*, *Vernonia cinaria,* and *Jeffreycia zeylanica*. These steroidal compounds are essential for plant growth, reproduction, and responses to various abiotic and biotic stress [42-44].

3.2 Leaves

Starch, sugar, phenol/tannins, saponins, glycosides, steroids, terpenoids, and alkaloids were found. Cyclohexane, dichloromethane, and methanol were used to obtain leaf extracts. Steroids are mainly contributed to the growth, reproduction, and response to stress, flavonoids and phenols are important for antioxidant activity [45,46]. Alkaloids are known to be important in anti-nociceptive activity and anticoagulant activity [47,48].

3.3 Stem

The plant's aqueous stem extract (ASE) was utilized to research the substances found in the stems of *J. zeylanica*, including alkaloids, flavonoids, steroids, triterpenoids, polyphenols, and saponins. The ASE was treated to reverse-phase column chromatography, then fractions indicating similar spots under UV light were again subjected to thin-layer chromatography (TLC). Alkaloids often play a key role in anti-nociceptive

action, while flavonoids and phenols play a key role in antioxidant activity. [45,46,49].

3.4 Aerial Parts

Aerial parts of *J. zeylanica* crude material were used to obtain hexane, dichloromethane, ethyl acetate, and methanol extracts. Ethuliacoumarin (67.0%) and stigmasterol (73.5%) were present in aerial parts. The presence of stigmasterol was confirmed by the H-NMR and C-NMR data and the presence of Ethuliacoumarin was confirmed by NMR spectroscopy. These compounds are beneficial for enhanced cell migration activity which may contribute to wound healing activity. This ethuliacoumarin is a coumarin, plant-derived natural phenolic product that may contain meditative effects such as anti-inflammatory, anticoagulant, antibacterial, antifungal, anticancer, antioxidant, and neuroprotective effects [50,51].

There was no reported previous research on the phytochemistry of other plant parts (flowers, roots, fruits, bark)

4. BIOACTIVITY

4.1 Antinociceptive Activity

Aqueous stem extract (ASE) of *J. zeylanica* was used to investigate the antinociceptive activity. Rats were used for the study. Hot-plate and tail flick tests were used to determine the nociceptive activity, also various concentrations were used (750, 1250, 2500 mg/kg). When compared to the control significant prolongation of the reaction time in the hot-plate test was indicated by the 1500 mg/kg dose of ASE while there was no remarkable variation in the tail-flick reaction time with any of the ASE-treated rats compared with the control rats. In conclusion, ASE has a significant antinociceptive activity when evaluated in the hot-plate test but not with the tail flick test. It indicates that the stem of *J. zeylanica* owns moderate oral antinociceptive activity, which is perhaps helpful as an herbal pain-relieving factor [49].

4.2 Antioxidant Activity

An antioxidant is a chemical that guards against free radical damage to cells (unstable molecules made by the process of oxidation during normal metabolism). Cancer, cardiovascular disease, stroke, and other aging-related disorders may all be impacted by free radicals. Beta-carotene, lycopene, vitamins A, C, and E, as well as other organic and synthetic compounds, are examples of antioxidants. Medicinal plants consist of this proprietary which is important to lower the risk of a variety of illnesses (including heart disease and certain cancers). Antioxidants remove free radicals from the body's cells and stop or lessen oxidation-related damage. Antioxidants' protective effects are still being researched globally due to their importance [52-54].
Different concentrations: of 15, 20, 30, and 125 µg/ml of aqueous stem extract of the plant were used. Thiobarbituric acid reactive substances assay (TBARS) was used for the detection of antioxidant properties. Temperate antioxidant activity in the stem of the plant was detected, compared with the controls. (Butylated hydroxytoluene, vitamin E, and Ascorbic acid) [49].

Leaves, bark, and stems of *Jeffreycia zeylanica* were used. DPPH scavenging assay was used for the evaluation of the results. The radical scavenging activity of the methanolic extract was 90± 1%. This study summarizes that *J. zeylanica* has a low radical scavenging activity relative to other endemic plants [55].

The powdered plant material of *J. zeylanica* was used to determine the antioxidant activity. Polysaccharides were obtained from the plant material using hot water and alkali (NaOH) extraction methods and FTIR was used to confirm the presence of polysaccharides. DPPH radical scavenging activity assay and OH scavenging activity assay was used to determine the antioxidant activity. Significant scavenging abilities on hydroxyl radicals (IC_{50} 4.832 mg/mL) were indicated by NaOH extraction of *J. zeylanica*, while hot water extraction showed significant scavenging abilities on DPPH radicals (IC_{50} 9.594 mg/mL) [56].

4.3 Anti-inflammatory

Methanol/ dichloromethane (MDE) extract of *J. zeylanica* leaves was used to detect the anti-inflammatory activity by using *in-vivo* inhibition of rat paw-edema, *in-vitro* inhibition of the production of nitric oxide (NO) and superoxide and inhibitory effect on inducible nitric oxide synthase (iNOS) gene expression. *In-vivo* inhibition of rat paw-edema, rats were treated with the obtained plant extract at 1500mg/kg indicated remarkable inhibition of paw-edema from 1^{st} – 5^{th} hour, compared to the control, Indomethacin was used as the reference drug, and its peak inhibition was 98.3±7.1% at 4^{th} hour.

Similarly, MDE indicated inhibition of 94.5±5.28% at the 5th hour. *In-vitro* NO inhibitory property was determined using the MDE of *J. zeylanica,* the inhibitory concentration (IC_{50}) for mouse macrophages (RAW) was 105µg/mL and for rat-peritoneal cells (RPCs) was 80µg/mL, this NO inhibitory properties indicated remarkable dose-dependency. *In-vitro* inhibition of superoxide production of activated RAW cells was decided by the quantitative Nitroblue Tetrazolium (NBT) assay. N-monomethyl-L-arginine acetate (NMMA) was used as the positive control for the detection of *in-vitro* inhibition of the production of NO and Diphenyleneiodonium chloride (DPI) for the inhibitory activity of superoxide production. MDE concentration of 250µg/mL indicated 55% inhibition of ROS production in RAW cells, whereas NMMA showed 78% inhibition of NO production for RAW cells and 70.1% for RPCs. In the meantime, DPI indicated 61% superoxide inhibitory activity with RAW cells. The MDE of *J. zeylanica* showed NO inhibitory activity on RAW cells and it was verified by the remarkable reduction (99.1%) in iNOS gene expression. The reverse transcriptase polymerase chain reaction (RT-PCR) method was used to identify the inhibitory effect on mRNA expression. In conclusion, those results indicate the potent anti-inflammatory activity of MDE of *J. zeylanica*. Further studies should be done to detect the anti-inflammatory effect on other plant parts [30,57].

4.4 Antimicrobial Activity

Plant extracts are considered natural sources of antimicrobial agents, regarded as nutritionally safe and easily degradable. The antibacterial compounds from medicinal plants may inhibit the growth of bacteria, fungi, viruses, and protozoa by different mechanisms than those of presently used antibacterial and may have a significant clinical value in the treatment of resistant bacterial strains [58].

Antibacterial activity was investigated against *Staphylococcus aureus, Klebsiella spp., Escherichia coli, Proteus spp., Pseudomonas spp., and Serratia spp*. Using agar well diffusion method. Cyclohexane, dichloromethane (DCM), and methanol were used to obtain the leaf extract. As the study suggests *S. aureus* was highly sensitive to the dichloromethane (DCM) extract of *J. zeylanica* (35.30±2.61 mm). Cyclohexane extract of *J. zeylanica* indicated a relatively higher percentage of inhibition against *Proteus spp.* (14.14±0.198 mm). And almost all the bacterial strains used were sensitive (clear zone of inhibition) for the methanolic extract of *J. zeylanica*. And the standard antibiotic Streptomycin was used as the positive control [59,60].

Petroleum ether, Ethyl acetate, Ethanol, and water were used to acquire the leaf extracts of *J. zeylanica*. The plant *J. zeylanica* appears to have a lower yield for ethyl acetate extraction and a higher yield for water extraction. *S. aureus* and *E. coli* were used as microorganisms and the agar well diffusion method was used for the analysis. The aqueous (water) extract of *J. zeylanica* manifested a significant inhibition against *E. coli*, but not with *S. aureus*. And in ethyl acetate and ethanolic extract of the plant showed inhibition zones against both bacteria. Streptomycin (30µg/mL) was used as the positive control [61].

Antibacterial activity was investigated using the powdered plant material of *J. zeylanica.* Polysaccharides were obtained from the plant using hot water and alkali (NaOH) extraction methods, and FTIR was used to confirm the presence of polysaccharides. Phenol sulfuric acid method and agar well diffusion method was used against *Staphylococcus aureus* and *Cladosporium cladosporoides* to detect antibacterial property. NaOH extraction of polysaccharides from *J. zeylanica* showed significant antimicrobial activity against *S. aureus* [56].

4.5 Anti-tumor Activity

The free radical scavenging, metal ion chelating, and antioxidant properties of flavonoids and phenolic compounds are considered to be responsible for many of their biological effects. In the method of chemoprevention, which refers to using chemical substances of natural or synthetic origin to reverse, slow down, or delay the multistage carcinogenic process, antioxidant and phenolic agents have been implicated. Sesquiterpene lactones and flavonoids are the phytochemicals that are the most abundant compounds in crude extracts and fractions isolated from genes *Jeffreycia*. Those are the compounds with the greatest interest antitumor potential within *Jeffreycia* species [62,63].

Due to their various modes of action, natural compounds have attracted much attention in the research for possible anti-Breast Cancer agents [64,65]. Possible cytotoxic chemicals from *J. zeylanica* extract in chloroform and ethyl acetate were identified in this study using bioactivity-guided isolation, and their anti-proliferative

effects were evaluated in three breast cancer phenotypes (MCF -7, MDA-MB-231, SKBR-3). In the isolated study, a new sesquiterpene lactone was found (vernolactone). Using mass spectroscopy, the structure of an isolated chemical was clarified. The chemical has significant cytotoxic effects on breast cancer cell lines SKBR-3 and MDA-MB-231, but not on cells from the normal mammary epithelium MCF-7 or MCF-10A. Morphological changes, DNA fragmentation, increased caspase 3/7 activity, up-regulation of p53 and Bax, and down-regulation of Surviving were used to validate the drug's apoptotic effects. Both the MDA-MB-231 and SKBR-3 breast cancer cells displayed a substantial reduction of HSP complex-related genes. Overall findings suggest that vernolactone can mediate its harmful effects through apoptosis and HSP complex modulation [66].

In this work, the effects of the plant-derived vernolactone on the development, apoptosis, autophagy, and antioxidant activity of human embryonic carcinoma cells were investigated (NTERA-2, a cancer stem cell model). NTERA-2 cells and human peripheral blood mononuclear cells (control cells) were used to measure the antiproliferative effects of vernolactone using the Sulforhodamine B (SRB) assay and the WST-1 antiproliferative assay, respectively. Vernolactone's antiproliferative effect was investigated further using the colony formation technique. Vernolactone's effects on apoptosis were investigated using phase contrast light microscopy, fluorescence microscopy, caspase 3/7 expression, and real-time PCR of the apoptosis-associated genes p53 and surviving. Vernolactone's influence on NTERA-2 cell migration was seen in a wound-healing experiment. Vernolactone's impact on autophagy-related gene expression was evaluated using real-time PCR (LC3, Beclin 1, PI3K, Akt, and mTOR). The 2,2-Diphenyl-1-2,2-diphenyl-picrylhydrazyl (DPPH), 2,2-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), and ferric reducing antioxidant power (FRAP) assays were used to measure the antioxidant activity of vernolactone further. According to the complete study's findings, vernolactone has very little antioxidant activity but can limit cell proliferation, cause apoptosis and autophagy, and reduce NTERA-2 cell migration in a dose- and time-dependent way. [67,68].

4.6 Sedative Activity

The sedative activity was investigated using two groups of rats. One group was administered 1500 mg/kg aqueous stem extract (ASE) of *J. zeylanica*, and the other group was administered distilled water. The rat-hole board test was used to evaluate the sedative activity. The frequency of rears, frequency of head dips, and locomotion were monitored. ASE 1500 mg/kg treated rats showed significantly impaired results in comparison to the control. The frequency of rearing was impaired by 46%, while locomotion and frequency of head dips were impaired by 38% and 45% respectively in the rat-hole board test. It indicates that the plant has considerable sedative activity [49].

4.7 Allelopathic Effects of *J. zeylanica*

Allelopathy is a biological condition that can occur in different plant sections. Allelopathy is the process by which chemicals emitted from one plant directly affect the growth and development of another plant. These substances are allelochemicals, which are biologically active compounds [69]. Allelochemicals have been regarded as a feasible drug development technique for ecologically favorable biological herbicides because of their ability to either stimulate or suppress plant germination, occurrence, growth, and succession [70].

The Asteraceae family includes the herbaceous, long-lasting, deep-rooted shrub *J. zeylanica.* It is a prominent endemic weed species that is common in tropical coconut (*Cocous nucifera* L.) crops and spreads quickly. The study was implemented to determine the speed of germination of *J. zeylanica* under different circumstances. Higher osmotic potential did not result in the germination of *J. zeylanica* seeds on some species in bioassay testing (-0.9MPa). Softwood cuttings produced the species' highest sprouting percentage. The extremely phytotoxic aqueous leaf extract drastically reduced all evaluated bioassay species' germination and seedling growth. All examined species' root and hypocotyl development rates were greatly slowed down by full-strength (33.3gL-1) aqueous leaf extracts. The results have been emphasizing that leaf extract of *J. zeylanica* and its rhizosphere-contaminated soil can suppress seed germination, seedling growth, and seedling emergence of certain plant species, indicating a possible allelopathic effect. The inhibitory effects were prevalently concentration-dependent [71].

4.8 Wound Healing Ability

In several ways, natural substances promote tissue regeneration and healing. Numerous phytoconstituents, including polyphenols, triterpenoids [72], and alkaloids have antioxidant and anti-microbial properties as well as the ability to support one or more pathways of the repair process [73]. Herbs are frequently used as external remedies in conventional and folk medicine to treat wounds [74].

To conduct the study, classic *ola leaf* scrolls that describe various herbal treatments for wounds were consulted. Some commonly used herbs have been considered for scientific validation [75]. Evidence from modern literature, Since *J. zeylanica* is an endemic plant, only a few reported works of literature were available, according to the available data, it is used to alleviate wound complications via exhibiting its anti-inflammatory activity and antinociceptive potential. Among the different preparations recommended for wound healing, *J. zeylanica* (20 remedies) is found in *ola leaf* manuscripts [75].

Evidence from ayurvedic literature, Ayurvedic medicine, and folk medicine has remedies based on their, knowledge, observations, and experiences over centuries. Due to their "*Vrana shothahara"* (anti-inflammatory) and "*Raktasthambhana"* (hemostatic) action in the inflammatory phase, they promote wound healing. On the other hand, they act on the fibroblast proliferation phase since they have "*krimighna"* (anti-microbial), "*Raktashodhaka"* (blood clarifying), and "*Vrana shodhaka"* (wound contraction with increased capillary formation) properties. In the remodeling phase, their "*Vrana ropana"* (promote healing) and "*Rasayana"* (free radical scavenging activity) properties enhance and complete the wound healing process [76]. *J. zeylanica* which is an endemic herbaceous plant in Sri Lanka has proven antinociceptive efficacy and may be prescribed as an herbal pain-relieving agent for wounds in ayurvedic medicine [49].

Another study was done to investigate the wound-healing ability of the aerial parts of *J. zeylanica* using hexane, dichloromethane, ethyl acetate, and methanol extracts. Each extract was assayed for its cell migration enhancement ability by scratch wound assay (SWA) [77,78] at a concentration of 20 mg/L on Madin-Darby Canine Kidney (MDCK) cells. Out of these four extracts, the hexane extract of the aerial portions of *J. zeylanica* with the greatest mean percent-guided fractionation yielded a fraction with improved cell migration activity (90.3%) at a concentration of 10 mg/L [79].

4.9 Brine Shrimp Lethality Assay

To investigate the lethal concentration (LC_{50}) freeze-dried powder of *J. zeylanica,* aqueous stem extract (ASE) was used. Brine shrimp (*Artemia salina* Leach) eggs were placed on a petri dish with seawater for 48 hours and 4, 20, and 100 µg/mL concentrations were used for the study. For each concentration, 60 shrimps were used. Result analysis was done considering any shrimp that was moving but not making forward progress was considered as dead. Linear regression analysis was used to determine the LC_{50} value, and the percentage of deaths at each dose was calculated. The percentage of deaths for the concentrations 4, 20, and 100 µg/mL were 1, 2, and 4 respectively and for the control, it was 0. It indicates that the effect depended on the dose and the LC_{50} value was found to be 1429.6 µg/mL which was non-toxic because in this study LC_{50} value of less than 1000 µg/ mL was considered toxic [49].

4.10 Toxicity

Subchronic treatment with aqueous stem extract (ASE) of *J. zeylanica* did not show any visible signs of toxicity, stress, or adverse behavior. No deaths occurred among the treated rats during the study period and there was no significant change in the rectal temperature. It indicates that sub-chronic treatment with ASE was well tolerated and did not produce visible signs of clinical toxicity (diarrhea, yellowing of hair, posture abnormalities, impairment of food and water intake and body weight) hepatotoxicity, nephrotoxicity, and hematotoxicity. It was indicated by no alteration in enzymes; SGOT, SGPT, creatinine, urea, or hematological parameters that were investigated [49].

4.11 KU 812 Cells Effect

The purpose of the current investigation was to ascertain whether the methanol-dichloromethane extract (MDME) of *J. zeylanica* and its solvent fractions (hexane, ethyl acetate, and methane) have any modulatory or inducing effects on human basophils, specifically KU 812 cells. Cell-starvation therapy alone for 6 days in full medium or a 21-day hydrocortisone treatment for KU 812 cells was used to achieve maturity. Based on the findings, starvation treatment was chosen for additional trials because it produced an 8–12% greater yield of mature basophils than

hydrocortisone therapy did. Calcium ionophore (A23187) and phorbol-12-myristate-13-acetate were used to induce mature KU 812-derived basophils (PMACI). Human basophil degranulation assay, Fura-2 AM indicator, and RT-qPCR were each used to determine the impact of *J. zeylanica* on non-IgE mediated degranulation, intracellular calcium concentration, and IL-8 expression. The MDME of *J. zeylanica*, together with its hexane and methanol fractions, significantly inhibited the non-IgE mediated degranulation of mature basophils generated from KU 812 (r= 0.91-0.96; p 0.05). No discernible inhibition was seen in the ethyl acetate fraction. But when treated with MDME and its three solvent fractions, [Ca] influx (35.74-47.01%; p0.05) and IL-8 expression both increased (0.38-1.80-fold change). These findings suggest that *J. zeylanica* affects mature basophils generated from human KU 812 in both an inhibitory and an inciting manner. Additionally, the strength of its inhibitory effects could not directly depend on the two molecular factors examined in a non-IgE mediated route. To identify specific therapeutic lead candidates for allergic-inflammatory indications, more research is required on the characterization of MDME and its solvent fractions of *J. zeylanica* as well as the isolation of active components [80].

5. CONCLUSION

This review specifies the ethnomedicinal, phytochemical, and pharmacological properties of *J. zeylanica* endemic to Sri Lanka. There are many articles on the *Jeffreycia* genus, but very little research has been conducted on *J. zeylanica.* So, there's still a need for more research on this plant. This plant can be used to treat various occasions like bone fractures, boils, diarrhoea and dysentery, asthma, and many more with further modifications. This plant has an anti-tumor activity which is also important, further studies should be done to evaluate its anti-tumor potency. The significant therapeutic potency of this plant can be used to develop novel drugs in the future.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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