

REVIEW

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Ethnobotanical, phytochemistry, and pharmacological property of *Waltheria Indica* Linn

C Nirmala*  and M Sridevi

Abstract

Background: In modern therapeutics, various human pathological disturbances were treated with the plant-based products. *Waltheria indica* Linn, a perennial herb, was commonly used in traditional medicine worldwide against various ailments such as cough, dysentery, diarrhea, bladder disorder, hemoptysis, inflammations, neuralgia, wounds, and ulcers.

Main body: The shrub was majorly distributed in tropical, subtropical regions and exists in many distinct local forms. Both the crude extracts and purified compounds from the whole plant and its parts showed wide pharmacological properties like antioxidant, analgesic, sedative, anti-bacterial, anti-fungal, and anti-parasitic. The phytochemical profile and traditional usage highlight the potency of the plant in the treatment of microbial infections and inflammatory diseases. Yet, additional studies are required for the confirmations of its traditional uses against other diseases. More detailed understanding of anti-cataract, anti-diabetics, asthma, anemia, and anti-cancer mechanism has to be explored. Though many research articles on the proposed plant are available, there has been a rising concern in the therapeutic property, especially on the alkaloids and flavonoids from this plant for drug design.

Conclusion: This article aims in a systematic and updated review on distribution, botany, traditional uses, phytocompounds, and relevant biological activities from each part of the plant. The information was collected from databases like PubMed, ScienceDirect, Web of Science, Google Scholar, books, dissertation, and reports via academic libraries that included more than 100 articles published since 1937. This ethnopharmacological study of the plant may create new insight into drug discovery to develop important novel leads against various biological targets.

Keywords: *Waltheria indica*, Distribution, Traditional uses, Phytochemicals, Pharmacological activities

Background

In both developed and developing nations, the majority of the population relies on plant-based traditional medicine to overcome high resistant pathological conditions and new emerging diseases [1]. Plants contain various bioactive compounds that give them therapeutic

potency. According to the World Health Organization (WHO), plants represent the best sources for obtaining a wide variety of drugs that could benefit a large population [2]. Only 10% of plant species available worldwide have been scientifically studied for its potential use in healthcare [3]. About 330,000 species found on the tropical regions and islands are most probable to get extinct [4]. Due to globalization and urbanization, traditional knowledge of plants is also disintegrated [5]. It is imperative to document traditional usage and medicinal property of every plant species and their products for

* Correspondence: nirmalabt@gmail.com

Department of Biotechnology, Vinayaka Mission's Kirupananda Variyar Engineering College, Vinayaka Mission's Research Foundation (Deemed to be University), Sankari Main Road (NH-47), Periyaseeragapadi, Salem, Tamilnadu 636 308, India

better understanding by rural communities and new drug development.

Waltheria indica, a medicinal plant commonly known as sleepy morning, is distributed widely in tropical regions of the world. The plant has bitter, cool to cold, and astringent property; hence, it is used to clear damp heat, poison and to cool blood. It is also utilized by native populations in different regions of the globe to treat several pathological conditions. The nutrient constituents like caffeic acid, flavonoids, alkaloids, sugar, and tannins are identified in the whole plant extracts that contribute to the medical applications [6].

Based on the etic approach, evidence on the pharmacological property of *W. indica* are available [6–9]. Still, anti-cataract [10], anti-diabetics [11], asthma [6], anemia [12], aphrodisiac [13], and anti-cancer activity [14] have to be evaluated for a detailed understanding of its mechanism and to utilize them in new drug designing process. This review aims to present an updated overview of the conventional use, medicinal properties of crude extract, and isolated phytochemicals from *W. indica*. The article also reviews the emic perspective of local and traditional uses of *W. indica* at different parts of the world. The growing interest in the curative properties of the plant evoked to review the previous studies on the plant extracts and its bioactive compounds for novel pharmacological preparations. This discussion may justify future research opportunities for this plant to promote the development and expansion of plant-based medicine.

Main text

Research data extraction criteria

The data acquainted for the study was browsed from PubMed, ScienceDirect, Web of Science, Google Scholar, books, dissertation, and reports via academic libraries. The data were retrieved using the terms *Waltheria*, pharmacological property of *W. indica*, and *W. americana* that was published since 1937. The search was solely performed on data reporting pharmacological, chemical, and experimental studies on in vitro and in vivo models, using the isolated compounds and crude extracts from the proposed plant. To grant reliability on data publications information from peer-reviewed journals are alone chosen.

Geographical distribution

The shrub, *W. indica*, is distributed majorly in subtropical and tropical zones of scrub forests, moist deciduous forests, plain grasslands or woodlands, rocky hills, gravelly soil, humid sandy soils, clay soils, riverbanks, savannahs, and in disturbed or impoverished soils. The plant is indigenously distributed in East Africa [15], West Africa [16], Northern part of South Africa covering

Namibia and Botswana [7, 17], Hawaii [18, 19], South America [8, 20], tropics, and subtropics of the old and New World covering Florida and Texas to Brazil [21–23]. In India, the plant is widely distributed in Punjab, Gujarat, Maharashtra, Assam, Odisha, Andhra Pradesh, Tamil Nadu, and Kerala [24, 25]. The plant is confined to the mineralized ground with a high concentration of zinc, copper, manganese, rubidium, strontium, sodium, and potassium [26].

Taxonomic classification

Domain: Eukaryota

Kingdom: Plantae

Phylum: Spermatophyta

Subphylum: Angiospermae

Class: Dicotyledonae

Order: Malvales

Family: Sterculiaceae

Genus: *Waltheria*

Species: *Waltheria indica* Linn

Synonym: *Waltheria americana*

Waltheria, the genus name was given in credit to Augustin Friedrich Walther (1688–1746), the German anatomist, botanist, and physician and 60 species were included under this genus [27]. Fosberg and Sachet [28] stated that *W. indica* and *W. americana* are reported simultaneously. The dense hairy form of *W. indica* var. *indica*; var. *americana* and thin pubescent form of var. *indica* was proposed by Robert Brown [29]. Hence, *W. indica* exists in many local forms that are distinct from other characters, without influencing taxonomic identification [28].

Vernacular names

The plant is commonly known as velvet leaf, monkey bush, marsh-mallow, boater bush, buff coat, and leather coat [30]. The epithet *indica* links the species with India, hence known as 'Nallabenda' in Telugu, 'Shengali-poondu' in Tamil [31]. In northern Nigeria, the plant is locally called as '*kafafi*' in Fulani, '*hankufah*' or '*hankubah*' in Hausa, '*efu-abe*' in Nupe, '*korikodi*' in Yoruba [32, 33], '*matum kevel*' in Wolof [34], '*kiaza*' or '*kerza*' in Bissa [35] '*yar-yamde*' in Moore [36], and '*Mokhutesela*' in Limpopo province in South Africa [37]. Also, it is named '*güinar*,' '*manrubio* o '*tapacola*' in Mexico [34], '*hierba de soldado*' in Panama, '*barulad*' in the Philippines [38], '*hi'aloa*,' '*uhaloa*,' '*kanakaloa*,' '*mauvegris*,' '*motobranco*,' '*fulutafu*,' and '*kafaki*' in Hawaii [39]. The Spanish common names of the plant are '*basoriprieta*,' '*escobillo blanco*,' and '*malvavisco*' [40]. Though the plant has many local names, the scientific research and reports are presented in two Latin names *W. indica* and *W. americana*.

Botanical description

W. indica, a flowering plant species (Fig. 1) in the Malvaceae family, was placed previously in family Sterculiaceae. It grows in areas receiving annual rainfall of about 750–1800 mm and at 400 m (1300 ft) elevations from sea level. It is an erect, hardy, short-lived, spreading subshrub reaching 2–7 m height with a stem diameter of 2 cm. The plant develops a brown, flexible, weak tap root, strong lateral roots, and enormous fine roots. It has a strong, single stem that often branches near the ground. The grayish-green leaves of the plant are alternate, egg-shaped, and narrowly ovate with a round to heart-shaped base, zigzag serrate edges, and rounded to pointed tip [41]. The stalks are 0.5–3.3 cm long; the blades are 2–12 cm long and 1–7 cm broad. Thick inflorescence clusters are found in leaf axils, which contain fragrant, yellow to orange flowers that appear throughout the year. The flowers have 3 bracts and a cup-like green calyx of 2–4 mm long that become brown on aging. Five yellow petals of 4–5 mm long fused at their base with 5 stamens that turns reddish-brown at maturity. Each 2 mm capsule of the fruit encloses one tiny, black, obovoid seed in the calyx cup until becoming



Fig. 1 *Waltheria indica* Linn

brown and dry. This shrub species have 1 locule ovary that differentiates from other species of Malvaceae that have 2 or more locules [42].

Phytochemical screening

The phytochemical analysis of the perennial plant *W. indica* showed the presence of different chemical groups like flavonoids, alkaloids, terpenes, sterols, tannins, cardiac glycosides, saponins, anthraquinones, and carbohydrates (Table 1) at various degrees in the whole plant [9, 11, 43, 53].

The pharmacological activity of the plant relies on the presence of various bioactive compounds (Fig. 2). Pais et al. [54, 55] identified and named alkaloids in the leaves and roots as adouetins X, Y, Y1, and Z which were considered as the first reported cyclopeptide alkaloids in plants. From the whole plant, flavonoids like epicatechin, kaempferol derivatives, tiliroside, and quercetin were reported [51, 56, 57]. 5,2',5'-trihydroxy-3,7,4'-trimethoxyflavone and 5,2'-dihydroxy-3,7,4',5'-tetramethoxyflavone were isolated from leaves [59]. 2,3-Dihydro-3,5-Dihydroxy-6-methyl-4h-pyran-4-one, tetradecane, tetracosane, nonadecane, squalene, and phytol are the major bioactive compounds identified in the ethanolic extracts of leaves [60]. From the dichloromethane extract of aerial parts, polyhydroxymethoxy flavonoids such as vitexicarpin, flindulatin, oxyanin A, chrysosplenol E, 5-hydroxy-3,7,4'-trimethoxyflavone, and quinolone alkaloids, like Waltheriones A, C, E-L, M-Q (2, 7, 8, 10, 11), and 5(R)-vanessine were identified. Novel compounds like Methyl (2R,3R)-3,4-dihydro-3,8-dihydroxy-2-methyl-(4-methylpent-3-en-1-yl)-2H-1-benzopyran-6-carboxylate, Methyl(R)-2,3-dihydro-7-hydroxy-2-[(S)-2-hydroxy-6-methylhept-5-en-2-yl]-2H-1-benzofuran-5-carboxylate, Methyl(R)-2,3-dihydro-7-hydroxy-2-[(2R,5S)-5-(2-hydroxypropan-2-yl)-2-methyltetrahydrofuran-2-yl]-2H-1-benzofuran-5-carboxylate, (2S)-2-[(1S)-1-(5,5-Dimethyltetrahydrofuran-2-yl)-1-hydroxyethyl]-2,3-dihydro-2H-1-benzofuran-5-carboxylic acid, and Methyl (2S,4aR,10aS)-2,3,4,4a,10,10a-hexahydro-6-hydroxy-2-(2-hydroxypropan-2-yl)-4a-methyl-pyrano[3,2-b][1]benzopyran-8-carboxylate were also identified in aerial parts of the plant [14, 52, 61].

Traditional uses

Each part of the plant and its infusions are traditionally used for the treatment of cough [15], eye baths [15], ulcers [20], hemoptysis [8], bladder ailments [38], neuralgia [43, 62], and lung infections [62]. It is applied externally to cure skin diseases like skin eruptions [38], wounds [34], abscess, and leprosy [8]. The plant is also used to medicate diarrhea [47], rheumatism [20], epilepsy [34], aphrodisiac, impotence [46], malaria, typhoid fevers [63], and tiredness [48]. In Turks and Caicos Islands, the herb tea and the plant extracts are used as

Table 1 Phytochemical constituent in different parts of *W. Indica*

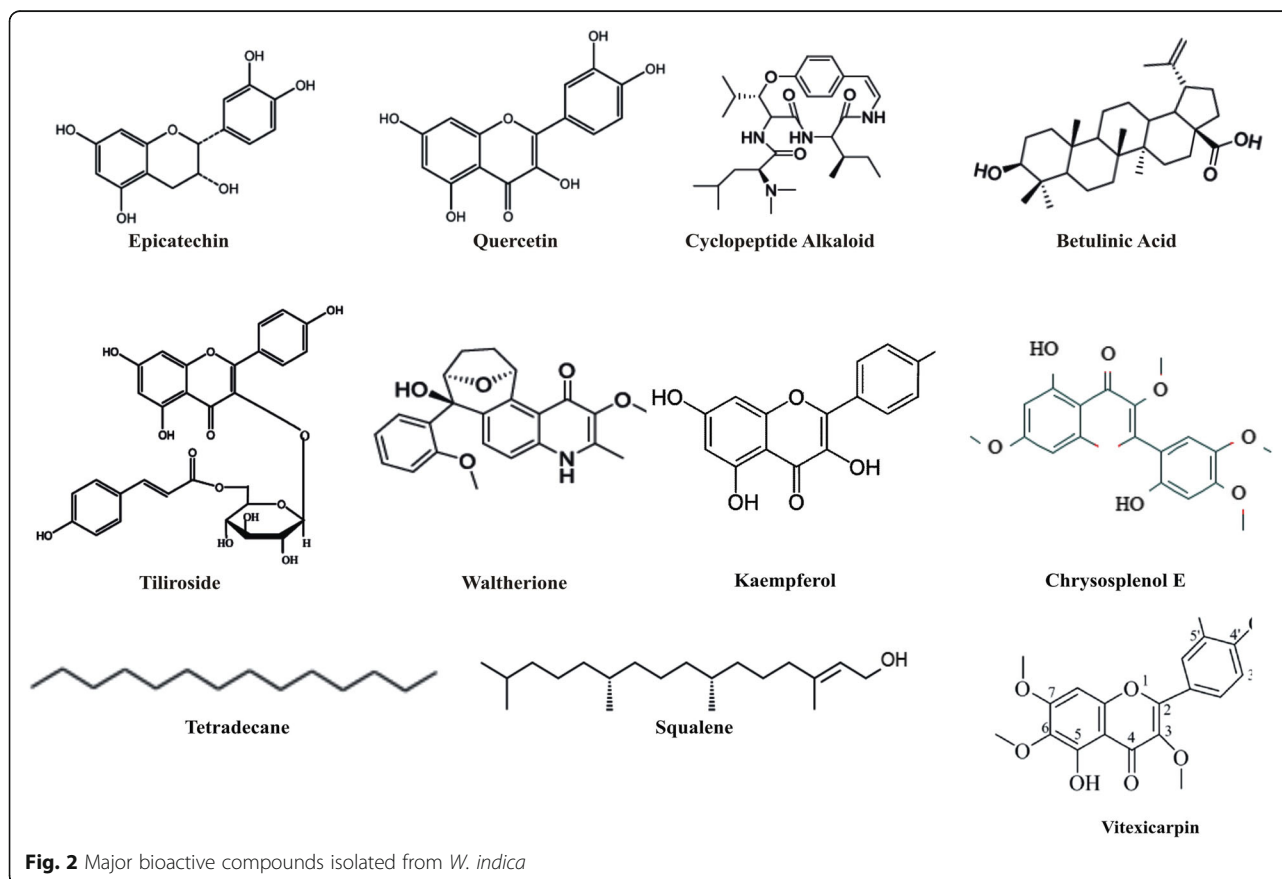
S. no.	Plant parts	Phytochemical constituents	References
1.	Roots	Alkaloids, carbohydrates, cardiac glycosides, saponins, steroids, tannins	[8, 43–46]
2.	Stem	Alkaloids, carbohydrates, cardiac glycosides, saponins, steroids, tannins	[8, 39, 43, 44, 46, 47]
3.	Leaves	Alkaloids, carbohydrates, cardiac glycosides, phenolic acids, saponins, steroids, tannins, terpenoids	[8, 43–50]
4.	Flowers	Alkaloids	[39]
5.	Aerial parts	Caffeic acid, flavonoids	[51, 52]
6.	Whole plants	Alkaloids, anthraquinones, carbohydrates, cardiac glycosides, flavonoids, mucilage, saponins, sterols, tannins, terpenes	[8, 9, 11, 43, 44, 46, 47, 53–58]

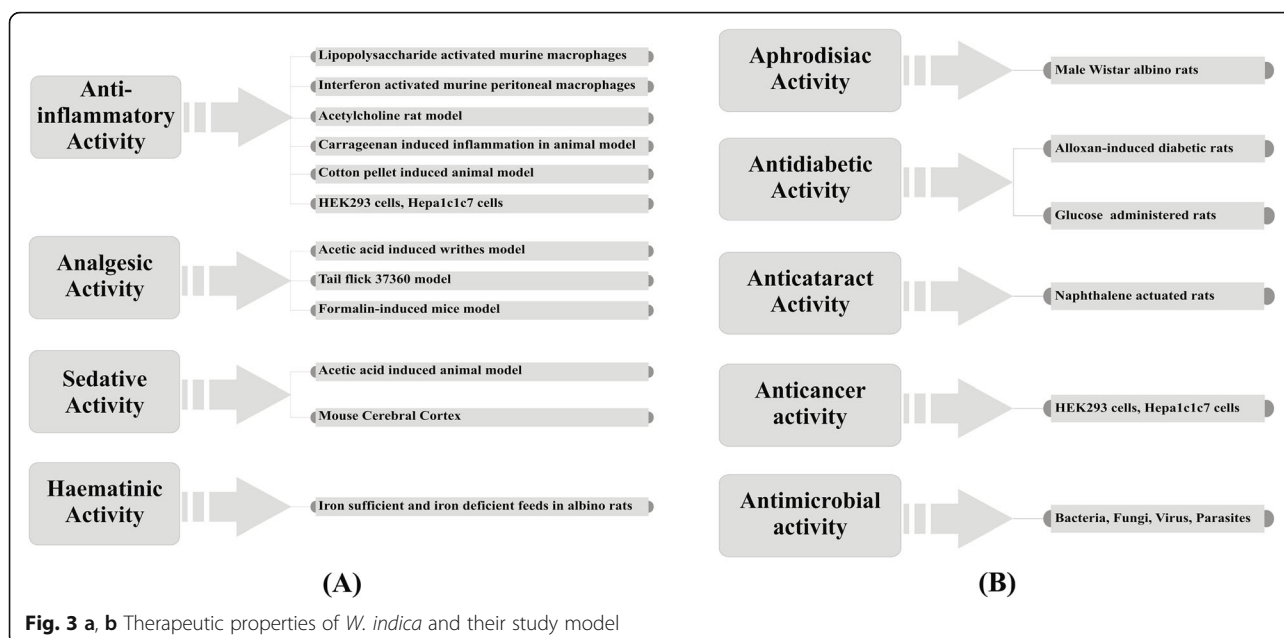
curative for female sterility. Formerly, the fiber from the plant was used for producing cords, sacking, sandals, and padding [43]. The stems are used as a chew stick [58]. In Hawaii, to ease sore throat, the root is chewed [64]. The root bark decoction and the whole plant are used as a bitter tonic for adults against asthma [36]. Stems and leaves are used as a blood tonic, an immune booster, and for strengthening young children [30]. The Fulani group uses the root aqueous extract for treating internal hemorrhage, syphilis, and relieving pains and aches. It is also used as a restorative agent during the labors of harvesting by the Yorub [46, 65].

The whole plant combats various infant illnesses; specifically, the yellow flowers and buds are used for infants during teething by Hausas community in northern Nigeria. The plant is also used as an abortifacient in Ghana [30], emollient in Haiti [66], purgative in South Africa [67], and sudorific in Venezuela [27]. In the Kalrayan hills of India, the plant is used to cure diabetes mellitus [11].

Therapeutic properties

On literature review, the suggested plant was found to have various pharmacological properties. Figure 3a, b

**Fig. 2** Major bioactive compounds isolated from *W. indica*



enumerates the therapeutic activities of the plant and their study model reported till date.

Anti-inflammatory activity

Inflammation is a complex biological response of body tissues for self-protection against irritants or pathogens. Flavonoid derivatives such as tiliroside, (-)-epicatechin, and quercetin obtained from sequentially fractionated ethanol whole plant extract were evaluated by Rao et al. [56] in lipopolysaccharide and interferon activated murine peritoneal macrophages. The results showed the inhibition of the inflammatory mediator cytokines, tumor necrosis factor (TNF)- α , nitric oxide (NO), and interleukin (IL)-12, dose independently, without any cytotoxicity. Among the three flavonoids, quercetin exhibited high activity that may be due to its inhibitory effect of iNOS enzyme expression. Quercetin also inhibited protein tyrosine kinase that suppresses the cell signalling kinase Cdk2 [68]. Zongo et al. [6] interpreted that root extract and (-)-epicatechin isolated from root extract showed inhibition of smooth muscle contraction phosphodiesterase-4A1 (PDE4A1 α), lipoxidase and phospholipase A2. The root extract also reduced the contractions induced by acetylcholine on isolated rat trachea. At the second phase of carrageenan inflammation in rats, high inhibition of edema is induced by the hydro alcoholic extract (1 g/kg) of the whole plant of *W. indica* than phenyl butazone [69]. Pet ether, methanol leaf extracts of the *W. indica*, and aqueous extract of stems with leaves also showed dose-related inhibition of acute and chronic inflammation in Carrageenan induced edema. The effect may be due to inhibition of histamine, serotonin, bradykinin, prostaglandin, and cyclooxygenase

(COX) products [9, 70, 71]. Significant reduction in the pellet weight of cotton pellet granuloma test models was also observed after treatment with methanolic leaf extracts [71]. Nuclear factor (NF- κ B), a key player in inflammation-induced tumor formation, was proved to be inhibited by Waltherione A and C obtained from the decoction of the aerial parts [14]. Hence, the property of selected plant in traditional treatment of inflammatory diseases is validated in both in vitro and in vivo studies.

Analgesic activity

Anti-inflammatory drugs are used as analgesics for pain treatment, but due to its side effects, traditional medicinal plants with analgesic properties are used nowadays. The analgesic property of *W. indica* aqueous root extract significantly reduced the abdominal constrictions in Swiss albino mice induced by acetic acid writhes than the stem extracts [46]. Hamidu et al. [72] conferred the highest protection in acetic acid induced-writhes by aqueous ethanolic plant extract (69%) than N-butanol (54%), acetone (50%), and aqueous residue (38%). The extract fraction protected the animal from death by increasing the amylobarbitone sleeping time. Yougbare-Ziebrou et al. [9] showed that different concentrations of plant extracts had significant analgesic effects and dose-dependent inhibition percentages at 300 mg/kg by weight of extract that was greater than the paracetamol (150 mg/kg by weight). The anti-nociceptive activities were also analyzed in tail-flick, formalin-induced paw licking, and acetic acid-induced writhing tests in mice using methanol leaf extracts of the plant that indicated the reduction in the mean of the number of abdominal constrictions in the test groups compared to the control

group [71]. Thus, these studies support the use of *W. indica* as an analgesic, anti-convulsant, and anti-nociceptive agents.

Sedative activity

Phytomedicine is found to be a better alternative for neurological disorders that acts harmlessly compared to conventional psychotropic drugs. General screening of *W. indica* revealed the presence of certain flavonoids and caffeic acid, which acts as a central nervous system sedative, medulla stimulant, and used to treat neuralgia. Blanpin et al. [73] explored that adouetin Z have sedative effect in mice with a reduction of spontaneous motor activity. The aqueous ethanol extract of the plant exhibited anti-convulsant and sedative actions by blocking leptazole-induced convulsion. The sleeping time of amylobarbitone sodium increased dose-dependently ($p < 0.05$) and decreased exploratory activity in mice [72]. Various extracts of the leaf dose-dependently delayed the convulsion onset, convulsion death, and also reduced the number of convulsion per minute [74, 75]. Mundo et al. [76] showed that in mouse cerebral cortex, the wild plant and cell suspension cultures of *W. americana* increased the release of Gamma amino butyric acid (GABA), the neurotransmitter that may impose a positive effect on neuronal disorders like anxiety, depression, and dementia. Thus, the studies prove the neuropharmacological activity of plant extracts.

Anti-bacterial activity

Microorganisms contribute to various infectious diseases in humans like respiratory illness, diarrhea, and dysentery. A series of in vitro studies using different extracts of the same parts and different parts of *W. indica* were performed on the same and different microbial species. Diverse inhibitory properties were observed on the same microbial species based on the solvent extracts and plant parts. This may be due to variation in the presence of active compounds such as tannins, flavonoids, alkaloids terpenoids, steroids, and saponins in different solvent extracts. The leaves had the highest activity against *Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella typhi* compared to the stem that may be due to the presence of cardiac glycosides in leaves [47, 77]. While the ethanol extracts from the leaf, stem, and root were active against both Gram-negative and Gram-positive organisms in the order of root extract > stem extract > leaf extract. This antiseptic activity may be due to the presence of phenolic compounds and their derivatives [8]. The aqueous, ethanol, methanol, and acetone extracts were tested against *Bacillus pumilus*, *Enterococcus faecalis*, *E. coli*, *Shigella dysenteriae*, *Staphylococcus aureus*, and found aqueous extract had good minimal inhibition concentration (MIC), and the zones of inhibition were dose-

dependent [37, 58, 78]. One hundred milligrams per milliliter of root methanolic extract had 91.7% anti-bacterial activity against the clinical isolates (*Klebsiella pneumonia*, *P. aeruginosa*, *S. aureus*, *Staphylococcus epidermidis*) obtained from diabetic wound infection [79]. The leaf extracts in different polar solvents (acid, base, neutral polar, and non-polar) and root extracts (ethyl acetate, chloroform, and chloroform: methanol) showed the zones of inhibition between 24–28 mm and 24–25 mm, respectively, against *S. pneumonia*, *S. aureus*, *K. pneumonia*, *S. pyrogens*, and few *Candida* species [50, 80]. The anti-bacterial activity of the plant extract against *Chlamydiae* and *Mycoplasma* known to be used in treatment of conjunctivitis [29]. The mechanism of the anti-bacterial spectrum thus aligns with the bouquet of phytoconstituents in the plant. Hence the findings support that the plant can be used to treat urinary tract infection [78] and as an anti-bacterial, anti-diarrheal agent [81].

Anti-fungal activity

The frequency of multidrug-resistance fungal infections especially in immune-compromised patients is increasing with a mortality rate greater than 50% despite the development of new drugs. Flavonoids (5,2',5'-trihydroxy-3,7,4'-trimethoxy flavone and 5,2'-dihydroxy-3,7,4',5'-tetramethoxy flavone) isolated from chloroform extract of *W. indica* leaf and quinoline alkaloids isolated from the roots inhibited the growth of *Candida albicans*, *Candida krusei*, *Candida tropicalis*, *C. glabrata*, *C. parapsilosis*, *Trichophyton mentagrophytes*, and *Aspergillus niger* [50, 59, 80]. The anti-fungal activities were pH-dependent that may be due to the changes in the fungal environment or protonation of the phyto molecules that facilitate their import into the fungal cells [82]. The results thus support the indigenous claim for the ethnomedical applications of *W. indica* as anti-fungal agents.

Anti-viral activity

The high prevalence of viral infections and the constant evolution of resistant viral strains lead to the development of novel anti-viral agents from medicinal plants. The hydro alcoholic and aqueous extract of the plant was analyzed against rotavirus, the causative agent of gastroenteritis, on its early replicative cycle and observed that the extracts decreased genomic RNA and viral protein synthesis [83]. The aqueous and methanol extracts showed significant inhibition on human immunodeficiency virus (HIV 1) protease [84]. The water-methanol shoot extract also inhibited HIV 1 (strain IIIb) and HIV 2 (strain ROD) [85, 86]. Herpes simplex virus, Semliki forest virus, vesicular stomatitis virus, and Coxsackie virus were not inhibited by the plant extracts [29]. The anti-viral property may be due to the presence of 1-

Docosanol, a broad-spectrum anti-viral agent active against lipid enveloped viruses that were identified in the ethanolic extract of the plant [60]. These results suggest evidence for the anti-viral activity of the plant.

Anti-parasitic activity

The emergence and spread of drug-resistance parasites attributed to the increasing prevalence of diseases. Phytoconstituents are now directed for the development of broad, chemically diverse anti-parasitic agents. Dichloromethane extract from roots and aerial parts of *W. indica* exhibited moderate anti-plasmodial activity [63]. Maregesi et al. [86] reported that the water-methanol (80%) shoot extract showed anti-plasmodial activity with IC_{50} between 125 and 250 $\mu\text{g/mL}$ [6]. Bala et al. [65] found the inhibitory activity of polar ethanolic whole plant extract against *Trypanosoma brucei brucei* (*T. b. brucei*) was higher than nonpolar petroleum ether extracts. Cretton et al. [61, 82] tested dichloromethane root extract against *T. cruzi*, *T. b. brucei* STIB 427 strain and *T. brucei rhodesiense* STIB 900. The highest activity was against *T. cruzi* with IC_{50} of 0.74 $\mu\text{g/mL}$ and a good selectivity index value of 35. Waltherione C, an alkaloid fractionated from this extract exhibited low cytotoxicity (IC_{50} -101.23 μM), anti-trypanosomal activity towards *T. cruzi* (IC_{50} -1.93 μM) and a selectivity index value of 52.

The mechanism of trypanocidal action is not clearly known, yet the presence of quinolone alkaloid, oleanane skeleton, and pentacyclic triterpenes from the plant extracts may lead to anti-trypanosomal activity. The activity of the extracts may be due to the interference in the redox balance of the parasites [65]. Thus, more studies on the mechanism of crude extract and compounds isolated from the plant on parasites are required to strongly exemplify the anti-parasitic activity.

Hematinic activity

Anemia is characterized by a reduction in red blood cells, hemoglobin, and hematocrit in peripheral blood that affects people of all ages. The incidence of anemia is higher due to poor nutrition, poverty, and malaria [87]. Oladiji et al. [12] evaluated the hematinic potential of *W. indica* root (aqueous extract) on Albino rats tended on iron sufficient and iron deficient feeds. They observed a significant increase in hemoglobin count, packed cell volume, red blood cells, liver body weight rate, and mean corpuscular hemoglobin. The oral administration of aqueous extract of leaf increased the count of red blood cells, white blood cells, and the values of alanine and aspartate aminotransferase, creatinine, and blood urea nitrogen in male albino rats [88]. The increase in white blood cells is to defend microbial infection that may be linked to the anti-microbial activity of cardiac glycosides in the leaves. Hence, the anti-anemic property of the

plant is reported, yet more detailed mechanism has to be evaluated to prove its traditional use.

Aphrodisiac activity

Aphrodisiacs are substances that stimulate sexual desire in humans. Male impotence affects the sexual life of millions of men worldwide. There was a growing need to search for herbal or natural plant aphrodisiacs with fewer side effects. The aqueous root extract of *W. indica* showed a dose-dependent increase in mounting frequency, intromission frequency, anogenital sniffing, and genital grooming, and a decrease in mount latency and intromission frequency as compared to control sildenafil citrate in male Wistar albino rats [13, 46]. Though the aphrodisiac activity of the plant is studied, the area is open for more investigation in the mechanism of action and targets of the plant extracts/compounds.

Anti-diabetic activity

Diabetes mellitus is a metabolic disorder of carbohydrates, fat, and protein metabolism that leads to insulin deficiency, insulin resistance, and hyperglycemia [89]. In alloxan-induced diabetic rats, the methanol extract of *W. indica* showed a dose-dependent decrease in blood sugar level at 4th, 7th, and 14th days of analysis [11]. The hydro alcoholic root extract (250 mg/kg, 500 mg/kg) showed a significant reduction in the hyperglycemic peak in glucose (2 g/kg) administered rats that was comparable to the effect detected with metformin. The regulation of blood glucose level is correlated with the presence of flavonoids and total phenols in plant extracts [90]. Thus, the study shows evidence for the traditional use of plants to cure diabetes. Detailed pharmacological studies on diabetic animal models, toxicological studies, and elucidation of active constituents present in the plant extracts are still required to understand the utility of these plants to control diabetes.

Anti-cataract potential

Formation of a visual lens cataract leads to difficulty in seeing for the majority of visually impaired individuals. For the oxidative stress-mediated age-related eye ailments; medications with prophylactic or cataract healing impacts are lacking. Rats actuated with naphthalene cataract were treated with *W. indica* ethanolic leaf extract that restored superoxide Dismutase (SOD), malondialdehyde (MDA), catalase, and glutathione S transferase to normal levels; also, it delayed the cataract onset and progression. The plant is also found to treat ophthalmia, conjunctivitis, and night blindness [15, 34]. Maintenance in the activity of antioxidant enzymes, decreased MDA levels, or retardation of sulfhydryl groups in lens epithelium might be responsible for plant anti-cataract function [10]. Still, molecular studies to

understand the mechanism of anti-cataractogenic potential of the *W. indica* have to be analyzed and extended.

Antioxidant activity

Free radicals like reactive nitrogen, oxygen, and chlorine species are produced from various harmful chemicals, biochemical reactions, unhealthy foods, and stress. Hyperglycemic condition is also linked with the oxidative and nitrosative stress that induces tissue damage, over production of superoxide, lipid membrane oxidation, and DNA damage. This oxidative stress leads to the development of cardiovascular and neurological disorders. Mongalo et al. [37] showed antioxidant activity of methanol extract of *W. indica* roots at a concentration of 65.71 ± 2.32 mg/100 ml by inhibiting 2,2-diphenyl-1-picrylhydrazyl (DPPH). The aqueous leaf extract also inhibited in vitro lipid peroxidation in rat liver homogenate [9]. DPPH inhibition was dose-dependent in liver and kidney tissues of alloxan-induced diabetic rats when treated with methanolic extract of the whole plant [11]. Garba et al. [77] analyzed that 1.0 mg/mL of hexane leaves extract had 92.8% antioxidant activity higher than ascorbic acid and α -tocopherol that had 90.2% and 15.4%, respectively. Hydro alcoholic root extract inhibited hemolysis of erythrocytes induced by 2, 2'-azobis 2 amidino propane dihydrochloride (AAPH) dose-dependently. The reducing power of the extract inhibited the production of nitric oxide thus exhibiting antioxidant property [90]. The phenolic compounds specifically the flavonoids and tannins present in the plant extract act as free radical scavengers that corresponds to the antioxidant potential of the plant.

Anti-cancer activity

There was an exponential increase in cancer that is caused by long-term exposure to mutagens or certain viral proteins. Phytochemicals are found to resist the invasion of these viral agents and inhibit the activity of viral oncoproteins [91]. The root, leaf, and branch extracts of *W. americana* were used for cancer treatment [20, 92]. Nuclear factor- κ B (NF- κ B) induces inflammation-mediated cancer promotion and progression. Monteillier et al. [14] isolated Waltheriones A and C from the decoction of the aerial parts of *W. indica* and confirmed their ability to induce phase 2 enzyme activity in Quinone reductase induction assay and NF- κ B inhibition. Thus, the plant compounds offer interest in the field of cancer chemoprevention, yet the research against various cancer targets has to be explored and expanded.

Other biological activities

The aqueous extracts of root, stem, and leaves of *W. indica* had an intraperitoneal lethal dose (LD₅₀) of 69 mg/kg, 363 mg/kg, and 141 mg/kg body weight in mice

[46]. The aqueous ethanol extract from aerial parts showed LD₅₀ of 875 mg/kg body weight in mice [72]. The cyclopeptide alkaloid, adouetin Z sulfonate also showed an intraperitoneal LD₅₀ of 52.5 mg/mL in mice and a minimal lethal dose of 75 mg/ml [73]. The leaf extracts at high doses became hepatotoxic thus diffused hydropic degeneration of hepatocytes and induced cellular infiltration in the periportal region of the liver [88]. Though toxicity data and its related effects for specific organs are least available, the plant at high doses should be used with caution especially during pregnancy [62, 93, 94].

Patented products from *W. indica*

Herbal compositions containing the key ingredients of *W. indica* for various applications have been patented. Some of the patented products include acne-removing cleanser [95], Cosmetic for skin whitening [96], lymphatic slimming [97], cosmetic preparation [98], and topical application [99].

Conclusion

Recently, medicinal plants are found to be the reservoir of secondary metabolites, and phytotherapy has attained a new era as natural drugs. This study emphasizes information on the current state of the art on *W. indica*, a medicinal plant used in several ethnomedical treatments. The phytoconstituents in each part of the plant is widely explored and related to the biological activities they execute. The pharmacological studies such as anti-inflammatory, analgesic, sedative, anti-microbial, and anti-viral are extensively studied while the anti-cataract, anti-diabetics, asthma, anti-anemic, aphrodisiac, and anti-cancer activity have to be investigated more to identify the phytochemical attributing to the property and the mechanism of action in drug design and development. The study of diversity of endophytes in the proposed plant and the synthesis of silver nanoparticles from them are under progress. Also, the efficacy of synthesized nanoparticles as anti-cancer agent is under study to expand the pharmacological potency of the plant. Thus, the study will be a promotion for the development and expansion of plant-based medicine by conscious exploitation of biodiversity.

Abbreviations

TNF: Tumor necrosis factor; PDE4A1: Phosphodiesterase-4A1; NF- κ B: Nuclear factor kappa-light-chain-enhancer of activated B cells; GABA: Gamma aminobutyric acid; MIC: Minimal inhibition concentration; HIV: Human immunodeficiency virus; IC₅₀: Half maximal inhibitory concentration; SOD: Superoxide dismutase; DPPH: 2,2-diphenyl-1-picrylhydrazyl; AAPH: 2,2'-azobis 2 amidino propane dihydrochloride

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Plant authentication

The plant material was authenticated at Botanical Survey of India, Southern Regional Centre, Coimbatore with identification no. BSI/SRC/5/23/2020/TECH/562.

Authors' contributions

CN had collected all the study material, analyzed, and prepared the complete manuscript. MS has critically reviewed the article for improvement. All authors have read and approved the final manuscript.

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