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Nutritional and therapeutic potential of *Waltheria indica* linn: A review

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Abstract

In food and pharmaceutical industries the bioactive compounds are the frontline sellers. Recently, the bioactive compounds of plants are gaining more significance to formulate as nutraceutical. *Waltheria indica* is an herb that is used in traditional medication to diverse illnesses such as cough, dysentery, diarrhoea, bladder disorder, haemoptysis, inflammations, neuralgia, wounds, and ulcers. Both the crude plant and purified compounds of this plant recorded pharmacological effects like antioxidant, analgesic, sedative and act against bacterial, fungal, parasitic diseases. The phytochemical profile and traditional usage highlights the efficacy of this plant for microbial infections and inflammatory diseases. Yet, more scientific research is required for its conventional use. Molecular mechanism of *W. indica* to treat the different diseases like anti cataract, anti diabetics and anti cancers is to be explored. Hence this article reviews on the scientific efficacy of *W. indica* plant.

Keywords: *Waltheria indica*, bioactive compounds, phytochemistry, traditional medicine, pharmacological effects

Introduction

World Health Organization address plants are the best hotspots for acquiring a wide assortment of medications (Sardi *et al*, 2013) [66]. Only few plant species are accessible worldwide to experimentally read up for its likely use in medical care (Leonti *et al.*, 2001; Cragg, 2002) [42, 15]. Around 330,000 species found on the tropical areas and islands are generally likely to get wiped out (Ledford, 2019) [40]. Because of globalization and urbanization, traditional information on plants is likewise crumbled (Srithi, 2009) [71]. Customary utilization and therapeutic property of each plant species and their items for better comprehension by rustic networks and new medication are in advancement (Ishikawa *et al.*, 2008; Mathabe *et al*, 2006) [34, 45]. Consequently along these lines, this paper surveys on pharmacological and therapeutic properties of *Waltheria indica*.

Waltheria indica, ordinarily known as tired morning, is dispersed generally in tropical locales of the world and 60 species were incorporated under this family (Saunders, 2007) [67]. Fosberg (1975) [22] expressed that *W. indica* and *W. americana* are accounted for at the same time. The thick furry type of *W. indica* var. *indica*; var. *americana* and slender pubescent type of var. *indica* was proposed by Robert Brown (Zongo *et al.*, 2013) [84]. Consequently, *W. indica* exists in numerous nearby structures that are particular from different characters, without impacting ordered recognizable proof (Fosberg, 1975) [22].

It is an erect lasting shrub, followed leaves with edges shallowly and sporadically toothed (Van Wyk *et al.*, 1998) [76]. Its blossoms are yellow and happen in clusters. The plant has harsh, cool to cold and astringent property; consequently, it is utilized to clear sodden hotness, poison and to cool blood. It is additionally used by local populaces in various districts of the globe to treat a few obsessive conditions. The supplement constituents like coffee corrosive, flavonoids, alkaloids, sugar, and tannins are distinguished in the entire plant separates that add to the clinical applications (Fosberg *et al.*, 1975) [22].

Geographical distribution

W. indica, is dispersed significantly in subtropical and equatorial jungle areas of scour backwoods, damp deciduous timberlands, plain meadows or forests, rough slopes, gravelly soil, moist sandy soils, mud soils, riverbanks, savannahs, and in upset or devastated soils. The plant is natively dispersed in East Africa (Kokwaro, 1976) [38], West Africa (Traoré, 1983), Northern piece of South Africa covering Namibia and Botswana

(Mathabe, *et al.*, 2006, Verdoorn, 1981; Abbott and Shimazu, 1985) [45, 78, 1], South America (Olajuyigbe *et al.*, 2011, Dimayuga *et al.*, 1987) [59, 19], jungles, and subtropics of the old and New World covering Florida and Texas to Brazil (Dick, 2001, Nelson, 1996, Texas, 2001) [18, 56, 74]. In India, the plant is generally dispersed in Punjab, Gujarat, Maharashtra, Assam, Odisha, Andhra Pradesh, Tamil Nadu, and Kerala (Sharma *et al.*, 1991, Harihar, 2014) [68, 30]. The plant is restricted to the mineralized ground with a high convergence of zinc, copper, manganese, rubidium, strontium, sodium, and potassium (Gandhi *et al.*, 1975) [23].

Traditional uses

All parts of this plant are utilized for therapeutic purposes in Africa and the plant is utilized customarily against hemorrhoids, syphilis, paleness, hack and Spanish fly (Hussain and karatel *et al.*, 1989, Sabo *et al.*, 2017, Gnanavel *et al.*, 2013) [32, 64, 26]. In South Africa, leaves of *W. indica* are cooked as a verdant vegetable while the Shangaan lady additionally utilized the plant for fruitlessness (Magwede *et al.*, 2018). Mongalo *et al.* (2012) [49] studied the utilization of the roots, leaves and entire plant to battle physically sent contaminations, urinary lot diseases just as assortment of baby ailments in Limpopo. *W. indica* is used in Sudan to treat ulcer, the runs, diabetic injury contamination, tooth and stomach throbs, ailment, just as a tonic (Elegami *et al.*, 2001) [20]. Also, it is privately utilized as a mitigating specialist in Paraguay (Saunders, 2007) [67], as against jungle fever in Burkina Faso (Jansen *et al.*, 2010), in Mexico for the treatment of looseness of the bowels (Leonti, *et al.*, 2001) [42] and in Boussou for the treatment of epilepsy (Sugiyama and Koman, 1992) [72]. Malignant growths, barrenness, bladder afflictions, erectile brokenness and ineptitude, looseness of the bowels, skin ulcer, seizure, conjunctivitis and gum disease was treated by this plant (Leonti *et al.*, 2001, Graham *et al.*, 2000, Rojas *et al.*, 2010, Zailani *et al.*, 2010, Zongo *et al.*, 2013) [42, 27, 63, 83, 84].

It is applied for skin sicknesses like skin ejections (Aguilar and van., 2001), wounds, ulcer, and disease (Olajuyigbe *et al.*, 2011) [59]. In Turks and Caicos Islands, the spice tea and the plant extricates are utilized as remedial for female sterility. Previously, the fibre from the plant was utilized for creating ropes, terminating, shoes, and cushioning (Borokini *et al.*, 2012). The stems are utilized as a bite stick (Musa *et al.*, 2016) [52]. In Hawaii, to ease sore throat, the root is bitten (Wagner *et al.*, 1999) [79]. The root bark decoction and the entire plant are utilized as an unpleasant tonic for grown-ups against asthma (Nacoulma, 1996) [53]. Stems and leaves are utilized as a blood tonic, a safe promoter, and for reinforcing little youngsters (Burkill, 1985). Root fluid concentrate of this plant for treating inside discharge, syphilis, and soothing torments and hurts. It is likewise utilized as a remedial specialist during the works of gathering by the Yorub (Mohammed *et al.*, 2005, Bala *et al.*, 2011) [47, 8].

The entire plant battles different newborn child ailments; explicitly, the yellow blossoms and buds are utilized for babies during getting teeth in northern Nigeria. The plant is additionally utilized as an abortifacient in Ghana (Burkill, 1985), emollient in Haiti (Vardhana, 2008), laxative in South Africa (Khare, 2008) [37], and sudorific in Venezuela (Saunders, 2007) [67]. In the Kalrayan slopes of India, the plant is utilized to fix diabetes mellitus (Kannan *et al.*, 2016) [35].

Bio constituents

Alkaloids, flavonoids, saponins, tannins, anthraquinones, terpenoids and phenols, steroids in *W. indica* (Petrus, 1990) [62]. The presence of phytochemicals in *W. indica* indicates it as a possible therapeutic plant (Chandekar *et al.*, 2017) [14]. Subjectively, the bounty of steroids in *W. indica* upholds its uses as a Spanish fly and body invulnerability (Gbadamosi *et al.*, 2012) [25]. The higher rate of flavonoids in plants contrasted with other optional metabolites support its movement in GC-MS studies (Borokini Omotayo, 2012, Kesava, *et al.*, 2016)

The bioactive compound from ethanolic leaf extract of *W. indica* has pharmacological activities. The compounds present in the leaf of *Waltheria indica* Linn was identified by Gas Chromatography-Mass Spectrometry (GC-MS) analysis by ethanol extract. The GC-MS analysis showed 27 bioactive compounds. The major compounds identified are 2,3-Dihydro-3,5-Dihydroxy-6-methyl-4h-pyran-4-one, tetradecane, nonadecane, tetracosane, phytol and squalene. (Banakar *et al.*, 2018) [9]. In a mass spectrum, each compounds were identified based on their retention time and peak area. Pharmacological activities of these compounds indicated that the compounds present in the leaf can be used as a crude drug and be used to develop a novel drug.

In any case, the phytochemical examinations on the species are scant (Correa, 1974) [73]. A fundamental phytochemical screening has recognized the presence of triterpenes, steroids, phenolic mixtures and Saponins in the rough ethanol concentrate of *W. viscostissima* (Cragg, Newman, 2002 and Vasques, 1999) [15, 77] and one triterpenes additionally has been identified (Soares, 1998) [69]. Phytochemistry explores unified to organic tests have raised the expected employments of plant separates or disengaged phytoconstituents as insect poisons as well as larvicides, with many examinations confirming the efficacy of these regular items (Santiago *et al.*, 2005, Santos *et al.*, 2015, Lakshmi *et al.*, 2018) [39]. These insect poisons or potentially larvicides are particularly applicable in tropical nations, where mosquitoes add to the event of serious viral sicknesses, like yellow fever, dengue, and Zika (Fernandes, 2018, Sowmya *et al.*, 2005) [21, 70].

Around 10gms of dried and coarsely powdered leaves were exposed to extraction with ethanol (250 ml) utilizing Soxhlet contraption. The concentrate was exposed to GC-MS examination (Dandekar *et al.*, 2015) [17]. The GC-MS examination uncovered the 27 substance compounds. The tetradecane (18.21%) is the most elevated synthetic compound and 5,5 Diethylheptadecane (0.34%) as the least substance compound. The compound 2,3-Dihydro-3,5-Dihydroxy-6-methyl-4H-pyran-4-one, tetradecane, Hexadecane, 2-Hexadecen-1-ol, 3,7,11,15-Tetramethyl- (R*(R*-)-E), showed pharmacological action (Nandagopalan *et al.*, 2015) [54], Marsilea quadrifolia (Karikalan *et al.*, 2014) [36] and *Gymnema sylvestre* (Thirunavukkarasu *et al.*, 2016) [75]. Additionally, phytol and squalene likewise showed the different organic exercises as revealed for *Coldenia procumbens* (Kesava *et al.*, 2016).

Analgesic and calming activity

Analgesic activity of *W. indica* was studied by Mohammed *et al.*, (2005) [47] and stems additionally showed portion related hindrance of intense and ongoing irritation in Carrageenan prompted edema. The impact might be because of hindrance of histamine, serotonin, bradykinin, prostaglandin, and

cyclooxygenase (Youbare-Ziebrou *et al.*, 2016, Chandekar *et al.*, 2017)^[82, 14] and (Owemidu *et al.*, 2018)^[61]. Critical decrease in the pellet weight of cotton pellet granuloma test models was additionally seen after treatment with methanol leaf separates (Owemidu *et al.*, 2018)^[61]. Atomic element (NF- κ B), a vital participant in aggravation instigated cancer arrangement, was ended up being repressed by Waltherione An and C acquired from the decoction of the elevated parts (Monteillier *et al.*, 2017)^[50]. The assessment of the calming movement *in vivo* was directed utilizing the model of carrageenin-actuated paw edema (Winter *et al.*, 1962). Carrageenan actuated paw edema in a biphasic peculiarity (Swingle *et al.*, 1974; Owemidu *et al.*, 2008)^[73, 61]. The underlying mechanism includes histamine, serotonin and bradykinin while the late stage is described by invasion of leukocytes and prostaglandins biosynthesis (Posadas *et al.*, 2004).

Lipoxygenase is a critical compound in the biosynthesis of leukotriene from arachidonic corrosive and play in the physiology of a few fiery infections (Rackova *et al.*, 2007 and Werz *et al.*, 2007)^[80]. *In vitro* study showed that the fluid concentrate of *Waltheria indica* repressed Lipoxygenase action with a level of hindrance of 94.63%. The hindrance of Lipoxygenase by the fluid concentrate of stems with leaves of *W. indica* has obstructed the development of leukotriene by means of arachidonic corrosive. Stems with leaves of *W. indica* would have decreased the incendiary reaction.

Pain relieving and narcotic effect

Conventional therapeutic plants with pain relieving properties are utilized these days (Owemidu *et al.*, 2018)^[61]. *W. indica* is used as a pain relieving, against convulsion and insect nociceptive specialists. The concentrates of *W. indica* had altogether pain relieving impacts ($p \leq 0.05$) and portion subordinate with hindrance rates from 36.27 to 54.12%. Paracetamol incited security 50.40% against the withdrawals actuated by acidic corrosive. The pain relieving impact of concentrates of *W. indica* at 300 mg/kg bw) was more prominent than the paracetamol (150 mg/kg bw). The assurance of *W. indica* in torment is affirmed by crafted by many creators. (Rao *et al.* 2005) detailed that the pain relieving impact of plant separate was connected cytokines (TNF α , IL-12) hindrance. The pain relieving impact of *W. indica* concentrate could be identified with the restraint of the arbiters associated with nociception gadget including cytokines.

Different concentrates of the leaf portion conditionally postponed the spasm beginning, seizure passing, and furthermore diminished the quantity of spasm each moment (Igwebuike *et al.*, 2017, Mundo *et al.*, 2017)^[33, 51]. Mundo *et al.*, (2015) showed that in mouse cerebral cortex, the wild plant and cell suspension societies of *W. Yankee* folklore expanded the arrival of Gamma amino butyric corrosive, the synapse that might force a constructive outcome on neuronal problems like nervousness, wretchedness, and dementia.

Antibacterial activity

W. indica has dynamic mixtures like tannins, flavonoids, alkaloids terpenoids, steroids, and saponins and leaves had the most elevated action against *Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella typhi* contrasted with the stem that might be because of the presence of cardiovascular glycosides in leaves (Zailani *et al.*, 2010, Garba *et al.*, 2014)

^[83, 24] Ethanol, methanol, and CH_3CO removes were tried against *Bacillus pumilus*, *Enterococcus faecalis*, *E. coli*, *Shigella dysenteriae*, *Staphylococcus aureus*, and observed fluid concentrate had great insignificant restraint fixation (MIC), and the zones of hindrance were portion subordinate (Mongalo *et al.*, 2012; Mongalo, 2014)^[49, 48]. The leaf removes in various polar solvents corrosive, base, unbiased polar, non-polar and root extricates ethyl acetic acid derivation, chloroform, and chloroform: methanol showed the zones of hindrance between 24–28 mm and 24–25 mm, individually, against *S. pneumonia*, *S. aureus*, *K. pneumonia*, *S. pyrogens*, and not many *Candida* species (Petrus, 1990; Olakunle *et al.*, 2017)^[62, 60].

Enterococcus spp., *P. aeruginosa* were accounted for to contribute 8.5 and 10.7% of diseases in clinics, individually (Hryniewicz *et al.*, 2001; Dhanendra *et al.*, 2015)^[31]. Such diseases might prompt expansion in opposition among urinary lot microorganisms to ordinary medications and is a significant wellbeing concern. These protections might prompt neighbourhood networks depending on restorative plants. *S. viridans* is for the most part predominant in oral cavity, it might dwell in the upper respiratory plot and can prompt dangerous illnesses which incorporate endocarditis and pneumonia (Tunkel *et al.*, 2002; Neda *et al.*, 2004; Refoua, 2005)^[55]. Methanol remove showed huge action against chosen human microorganisms and this might be ascribed to the presence of solvent phenolic and polyphenol compounds (Igbinsosa *et al.*, 2009). Ethanol extricate at 20 mg/ml showed best movement against every one of the chose organic entities, thus expansive range. There were no zones of restraint in bad controls; *K. pneumonia* is the most powerless gram negative microscopic organisms. For the most part, *W. indica* represses an assortment of bacterial strains in a portion subordinate way and comparative example has been accounted for somewhere else (Pandey *et al.*, 2011; Swingle, 1974)^[73].

Antifungal activity

Flavonoids from chloroform concentrate of *W. indica* leaf and quinolone alkaloids from the roots restrained the development of *Candida albicans*, *Candida krusei*, *Candida tropicalis*, *C. glabrata*, *C. parapsilosis*, *Trichophyton mentagrophytes*, and *Aspergillus niger* (Petrus, 1990)^[62], (Ragasa *et al.*, 1997). The outcomes consequently support ethno clinical uses of *W. indica* as hostile to parasitic specialist (Cretton *et al.*, 2015).

Antiviral activity

Plants contain different bioactive mixtures give them remedial strength. The high commonness of viral diseases leads to the improvement of drugs from therapeutic plants (Mundo *et al.*, 2017)^[51]. Anti-microbial in controlling numerous diseases relies upon prudent use to limit the occurrence of safe structures (Danso, 2002; Maregesi *et al.*, 2008)^[43]. In non-industrial nations, because of the expense of effective antimicrobials, an enormous extent of the populace uses therapeutic plants for the treatment of irresistible sicknesses (Alonso-Paz *et al.*, 1995)^[4]. The hydro alcoholic and watery concentrate of the plant was examined against rotavirus, the causative specialist of gastroenteritis, on its initial replicative cycle and saw that the concentrates diminished genomic RNA and viral protein amalgamation (Loaiza Gutiérrez, 2014). The fluid and methanol removes showed huge hindrance on human immunodeficiency infection (HIV 1) protease

(Miyashiro *et al.*, 1994). The water-methanol shoot separate likewise hindered HIV 1 and HIV 2 strain (Maregesi *et al.*, 2008, Maregesi *et al.*, 2010) [43]. Herpes simplex infection, Semliki woods infection, vesicular stomatitis infection, and Coxsackie infection were not hindered by the plant removes (Zongo *et al.*, 2013) [84]. The counter popular property might be because of the presence of 1-Docosanol, a wide range viral specialist dynamic against lipid wrapped infections that were recognized in the ethanol concentrate of the plant (Banakar *et al.*, 2018) [9].

Hematinic activity and cataract potential

Iron deficiency is described by a decrease in red platelets, haemoglobin, and haematocrit in fringe blood that influences individuals. The frequency of pallor is higher because of helpless nourishment, neediness, and jungle fever (Asuquo *et al.*, 2013; Basiru *et al.*, 2014) [6, 11]. For the oxidative pressure intervened age-related eye infirmities; Rats actuated with naphthalene cataract had been handled with *W.indica* ethanol leaf extract that restored superoxide Dismutase, malondialdehyde, catalase, and glutathione *S transferase* to everyday levels; additionally, it not on time the cataract onset and progression. The plant is likewise located to deal with ophthalmic, conjunctivitis, and night time blindness (Kokwaro, 1976) [38]. Maintenance of antioxidant enzymes, reduced MDA levels, or retardation of sulfhydryl corporations in lens epithelium is probably accountable for anticataract function. Evaluation of anticataract potential of *Waltheria indica* in albino rats was carried by Atif *et al.*, (2014) [7]. Still, molecular research to apprehend the mechanism of anti-cataractogenic potential of the *W. indica* need to be analyzed.

Anti oxidant activity

The antioxidant compounds can neutralize unfastened radicals (Meda *et al.*, 2013; Anthony *et al.*, 2013) [46, 5]. DPPH technique used to assess the antioxidant potential of the aqueous extract of stems with leaves of *W.indica*. Inhibition of ROS prevents oxidation of membrane lipids results in the manufacturing of arachidonic acid (Garba *et al.*, 2012) [24]. The antioxidant impact of the extract of *W. indica* contribute its anti-inflammatory homes. The antioxidant interest of aqueous extracts of *Waltheria indica* has been additionally evaluated through the inhibition of lipid peroxidation (Garba *et al.*, 2012) [24]. Model of infection prompted through carrageenan to accelerate the manufacturing of peroxidised lipids (Tanas *et al.*, 2010). Lipid peroxidation changed into stated as complicating the inflammatory process (Uzkeser *et al.*, 2012). The aqueous extract of *W. indica* inhibited the lipid peroxidation of rat liver homogenate *in vitro*. These outcomes recorded that this plant possessed antioxidant and anti inflammation (IPCS, 2002). The phytochemical screening confirmed that the aqueous extract powder of stems with leaves of *Waltheria indica* contained tannins, flavonoids, saponins, triterpenes and sterols and anthocyanosides. Several authors indicated the presence of the compounds of this plant causes anti-edematous, analgesic, anti inflammatory, anti-oxidant effect (Bruneton, 2009).

Anti-cancer activity

Phytochemicals are located to withstand the invasion of those viral dealers and inhibit the interest of viral oncoproteins (Nirmala *et al.*, 2019) [57]. The root, leaf, and department extracts of *W. Americana* had been used for most cancers

remedy (Graham *et al.*, 2000) [27]. Nuclear factor- κ B (NF- κ B) induces infection-mediated most cancers advertising and progression. Thus, the plant compounds provide chemoprevention against cancers (Monteillier *et al.*, 2017) [50]. Tannins can also additionally selectively inhibit HIV replication, and are widely recognized to make timber and shrubs a hard meal for caterpillars because of its astringent taste (Ishikawa *et al.*, 2008; Ban, 2007) [34, 10]. Furthermore, tannins can also additionally act on microorganisms through precipitating microbial protein and making dietary proteins unavailable (Prasad *et al.*, 2008). Moreover, it could hasten the recuperation of wounds and infected mucous membrane (Njoku Akumefula, 2007) and saponins serve for heart diseases (Abukakar, 2008; Ngbede *et al.*, 2008) [2].

Biological uses

Inhibition of *Trypanosoma brucei* was recorded by extracts from *Waltheria indica* (sleepy morning) (Bala *et al.*, 2011; Cretton *et al.*, 2015) [8]. The root bark decoction and the whole plant are used as a bitter tonic for adults against asthma (Nacoulma, 1996) [53]. Stems and leaves are used as a blood tonic, an immune booster, and for strengthening young children. 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 (Mohammed *et al.*, 2005; Hryniewicz *et al.*, 2001) [47, 31].

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 (Nirmalaand, 2021) [58]. The plant is also used as an abortifacient in Ghana, emollient in Haiti, purgative in South Africa (Khare, 2008) [37], and sudorific in Venezuela (Saunders, 2007) [67]. In the Kalrayan hills of India, the plant is used to cure diabetes mellitus (Kannan, 2016) [35]. The aqueous extracts of root, stem, and leaves of *W.indica* had an intraperitoneal lethal dose (LD₅₀) 141 mg/kg body weight in mice. The aqueous ethanol extract from aerial parts showed LD₅₀ of 875 mg/kg body weight in mice (Hamidu, 2008) [29]. 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 (Blanpin, 1963) [12]. 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 (Sharma and Patk, 2010). 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 (Leonard *et al.*, 2010; Wilmott *et al.*, 2004) [41, 81]. Standardization and evaluation of anticonvulsant activities of leaf extract and fractions of *Waltheria indica* was done by Igwebuikwe *et al.* (2017) [33].

Conclusion

Waltheria indica is the reservoir of bioactive compounds of nutrients and it has potential role in phytotherapy. *W. indica* utilized in numerous traditional treatments and is a promising herbal antimicrobial agent in pharmaceutical industry for controlling the pathogenic bacteria. The ethanol leaf extract of *W.indica* has 27 exclusive compounds that have exclusive pharmacological activities such as anti-inflammatory, analgesic, sedative, anti-microbial, and anti-viral. Mechanism for the anti-cataract, anti-diabetics, asthma, anti-anaemic and

anti-most cancers are to be investigated for the plant. Research is to be extended for the molecular and pharmacological efficacy of this plant in order to improve the plant based drugs.

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