

Holoptelea Integrifolia: An Overview

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Abstract: Natural products have evolved as a source of bioactive compounds and possess a potential for developing novel therapeutic agents. Medicinal plants which are found on earth have renowned medicinal significance and their usages are increasing day by day in our daily life. Different researches are going on to explore the beneficial, pharmacological and medicinal properties of herbal drugs. Systematic and detailed pharmacognostical studies have been performed on an important medicinal plant, *Holoptelea integrifolia* (Roxb.) (Ulmaceae). Various parts of *Holoptelea integrifolia*, a roadside plant, are indicated by Charaka Samhitha Sushruta and other traditional systems for the treatment of inflammation, acid gastritis, Dyspepsia, Flatulence, Colic, Intestinal Worms, Vomiting, Wounds, Vitiligo, Leprosy, Filariasis, Diabetes, Hemorrhoids, Dysmenorrhoea and Rheumatism. According to literature survey, the plant *Holoptelea integrifolia* (Roxb.) exhibits a wide range of biological activities which have been reported by many workers. These all activities are subjected to further studies aimed at developing a promising pharmaceutical candidate for preclinical and clinical trials. This review presents a detailed survey of the literature on pharmacognostical and various medicinal properties of *Holoptelea integrifolia*.

Key words: *Holoptelea integrifolia* • Phytochemical investigation • Pharmacological activity
• Traditional uses

INTRODUCTION

Holoptelea integrifolia belongs to the family Ulmaceae, having 15 genera and about 200 species, distributed over tropical and temperate regions of Northern hemisphere including Indian peninsula to Indo China and Srilanka [1]. The common vernacular names of the plant in India are Chirabilva, Putigandha (Sanskrit), Papri (Urdu), Karanj, Putikaranj (Oriya) [2]. Kanjho, Waola (Gujarati), Kanju, Papri, Banchilla, Chilbil, Dhamna, Begana (Hindi), Thavasai, Rasbija, Kaladri, Nilavahi (Kannada), Aval (Malayalam), Vavli, Papara (Marathi), Dauranja, Rajain, Khulen, Arjan (Punjabi); Aya, Ayil, Kanci, Vellaya (Tamil), Thapasi, Nemali, Pedanevili (Telugu) [3]. It is commonly known as Indian Elm Tree. *Holoptelea integrifolia* is a large deciduous tree distributed throughout the greater part of India up to an altitude of 2,000 feet. It is an important pollen allergent plant of India [4]. Bark of the tree remains grey, pustular, exfoliating in somewhat corky scales. Leaves are elliptic-ovate, acuminate, base rounded or subcordate in shape,

flowers greenish yellow, polygamous and found in short racemes or fascicles. Fruits are sub-orbicular with membranous wing. The flowering time of the tree is January to February, whereas, fruiting is seen in April to May [5]. The plant *Holoptelea integrifolia* is used traditionally for the treatment of inflammation, gastritis, dyspepsia, colic, intestinal worms, vomiting, wound healing, leprosy, diabetes, hemorrhoids, dysmenorrhoea and rheumatism [6]. Bark and leaves are used as bitter, astringent, thermogenic, anti-inflammatory, digestive, carminative, laxative, anthelmintic, depurative, repulsive, urinary astringent and in rheumatism [7]. The plant is being used by tribal people for their medicinal properties. The mucilaginous bark is boiled and the juice squeezed out and applied to rheumatic swellings [8]. Decoction of the bark used oxytocic in pregnant ladies. Paste of the stem bark is externally applied to treat the inflammation of lymph glands, common fever and ringworm and scabies. Decoction of the leaves is used to regulate fat metabolism, treat ringworm eczema and cutaneous diseases [9]. Stem bark acts as an anti-

inflammatory agent specifically for eyes. Bark and leaf paste of the plant are applied externally on the white patches or leucoderma. Bark boiled in coconut oil with that of *Pongamia glabra* Vent and garlic and is applied externally to eczema [10]. For treatment of herpes simplex infection, bark paste applied over the affected part until it disappears. Bark cut in the shape of a coin tied on left arm below the shoulder for treatment of malaria, patient advised not to use cow's milk curd and sour foodstuffs [11]. It is also used for treating intestinal cancer [12]. Leaf bud mixed with lime juice and applied externally to affected area for treatment of hair loss by infection and treatment of herpes infection [13]. A handful of bark and leaves ground with 15 pepper seeds, one bulb of garlic in rice washed water. Half liter of plant extract given to cattle, daily once for 1–2 days for treatment of cold and cough and bark ground with jaggery and lemon juice and made into paste is used for weakness [14]. Seeds used topically on ringworm and dried fruit used in polyurea and urinary disorders [15].

Phytochemical Constituents: Preliminary phytochemical investigations on stem bark of ethanolic extract of *Holoptelea integrifolia* revealed the presence of alkaloids, flavonoids, tannins, saponins, glycosides, phenols and reducing sugars. The stem bark contains the triterpenoidal fatty acid esters, holoptelin-A (epi-friedelinol palmitate) and holoptelin-B (epi-friedelinol stearate), friedelin and epi-friedelinol. β -sitosterol and stigmasterol are isolated from dried seed. Histamine and 5-hydroxytryptamine are isolated from pollens [15]. 2-aminonaphthoquinone, Friedlin, β -sitosterol, β -D-glucose, are also isolated from stem bark [16].

The leaves of *Holoptelea integrifolia* ethanolic extract showed the presence of terpenoid, steroids, tannins, saponins, carbohydrates and protein. 1,4-naphthalenedione has been isolated from leaves of *Holoptelea integrifolia* and is reported to possess

antibacterial activity against *Staphylococcus aureus* [17], hexacosanol, octacosanol, β -sitosterol, β -amyrin are isolated from leaves. β -sitosterol, 2 α ,3 α -dihydroxyoelan-12-en-28 oic acid and hederagenin are isolated from heartwood [18]. The leaves contain friedelin or friedelin-type compounds has been considered for treatment of cancer of bladder, convulsions, inflammation, topical ulcers, rheumatic inflammation, fever and dysentery [19].

Pharmacological Activity

Anti-Inflammatory Activity: A significant % inhibition of paw edema by the aqueous extract of leaves of *H. integrifolia* Planch and it's almost nearby same % inhibition with indomethacin suggest its usefulness as an anti-inflammatory agent [20]. The ethanolic extract of the leaves of *Holoptelea integrifolia* Planch showed significant anti-inflammatory effects in various animal models. Results revealed that administration of ethanolic extract inhibited the oedema starting from the first hour and during all phases of inflammation, which is probably inhibition of different aspects and chemical mediators of inflammation [21].

Antioxidant Activity: The ethanol crude extracts of stem bark of *Holoptelea integrifolia* Planch showed antioxidant property which is comparable to the standard vitamin E. Thus ethanol extract exhibited significant *In vitro* antioxidant activity by inhibiting the oxidation of linoleic acid in both FTC and TBA methods. The activity was comparable with standard vitamin E [22]. The antioxidant activity was evaluated by DPPH free radical scavenging activity using HPLC method [23].

Antimicrobial Activity: Antimicrobial property of the methanolic extracts of *Holoptelea integrifolia* (Roxb.) was studied against the six bacterial and five fungal strains using the agar well diffusion method and minimum microbicidal concentration and minimum inhibitory

Table 1: Preliminary phytochemical screening of *Holoptelea integrifolia* [9]

S. No	Solvent	Plant part	Reducingsugar	Protein	Phenol	Alkaloid	Steroid	Triterpinoid	Flavones	Cathacin	Anthroquinone	Tannin	Amino acid	Saponin
1.	Petroleum Ether	Leaf	+	+	-	-	+	-	+	-	-	+	+	-
		Stem	-	-	-	-	+	-	-	+	-	+	-	-
2.	Benzene	Leaf	-	-	-	-	+	-	+	+	-	+	-	-
		Stem	-	+	-	-	+	-	+	-	-	+	+	-
3.	Chloroform	Leaf	-	+	-	-	+	-	-	-	-	-	+	-
		Stem	-	+	+	-	+	-	+	-	-	-	+	-
4.	Methanol	Leaf	-	+	-	+	+	-	+	-	+	-	+	-
		Stem	-	+	+	+	+	+	-	+	+	+	+	-
5.	Distilled Water	Leaf	-	-	+	-	-	+	-	-	+	+	-	-
		Stem	-	-	-	-	-	-	+	-	-	+	+	-

(+) denote present and (-) denote absent

concentration were determined for each strain, in which methanolic extract of stem bark (MSBE) has shown bigger zone of inhibition (11.3–20.4 mm) than methanolic extract of leaves (MLE) (9.6–14.9 mm) [24]. The inhibitory effect of a phytochemical, 1,4-naphthalenedione, isolated from the plant *Holoptelea integrifolia* on beta-lactamase. The studies indicate that the synergistic effect of the plant *H. integrifolia* extract with beta-lactum antibiotics is due to the presence of the compound 1,4-naphthalenedione. A number of 1,4-naphthalenedione derivatives have already been reported as having antibacterial activity [17]. The petroleum ether, benzene, chloroform, methanol and aqueous extracts of the stem bark of *Holoptelea integrifolia* were evaluated for the antibacterial activity against various microorganisms viz *staphylococcus aureus*, *Bacillus subtilis*, *E. Coli* and *Pseudomonas aeruginosa*. Disc diffusion method was adapted for assessment of *in vitro* antibacterial activity [24]. The extracts of *H. integrifolia* and *S. nuxvomica* showed better antibacterial activity against *B. cereus* [25].

Wound-Healing Activity: The methanolic extracts of *Holoptelea integrifolia* (Roxb.) leaves (MLE) and stem bark (MSBE) were studied for the wound healing potential. Both extracts possess anti-oxidant activity. Hence, the external application of these extracts on the wound prevented the microbes to invade through the wound, resulting protection of wound against their infections of the various microorganisms. At the same time, external application of the extracts entrapped the free radicals liberated from the wound surrounding cells, which are having in herent machinery to protect the cells from the microbes. Hence, the synergistic effect of both antimicrobial and antioxidant activity accelerated the wound-healing process [23].

Anthelmintic Activity: Methanolic and aqueous extracts both were found to possess significant anthelmintic activity in comparison to the standard drug. The stem bark of *Holoptelea integrifolia* extracts not only demonstrated paralysis, but also causes death of worms. The anthelmintic activities of different extracts benzene, chloroform, methanol and aqueous extract of stem bark of *Holoptelea integrifolia* against adult earth worm *Pheretima posthuma* [26]. Different extracts of *Holoptelea integrifolia* showed the presence of an array of active chemical constituents including aponins, steroids, carbohydrates, alkaloids, tannins, glycosides, flavonoids and phenols. These phytoconstituent responsible to show a potent anthelmintic activity in AQEHI and ETEHI [27].

Antiviral Activity: *Holoptelea integrifolia* exhibited considerable antiviral activity against herpes simplex virus [28].

Antidiabetic Activity: Methanol, Petroleum ether extract of leaves of *Holoptelea integrifolia* (Roxb.) was screened for Antidiabetic activity. Antidiabetic was compared with standard drug with Glibenclamide for Alloxan induced method. The methanol and petroleum ether extract showed significant antidiabetic activity [29].

Antidiarrhoeal Activity: The ethanolic extract of leaves of *Holoptelea integrifolia* successfully inhibited the castor oil-induced diarrhoea, the extract might have exerted its antidiarrhoeal action by antisecretory mechanism. This was also evident from the reduction of total number of wet faeces in the test groups in the experiment. On the other hand, magnesium sulphate has been reported to induce diarrhoea by increasing the volume of intestinal content through prevention of reabsorption of water. It has also been demonstrated that it promotes the liberation of cholecystokinin from the duodenal mucosa, which increases the secretion and motility of small intestine and thereby prevents the reabsorption of sodium chloride and water. The ethanolic extract of leaves of *Holoptelea integrifolia* was found to alleviate the diarrhoeic condition in this model [30].

Adaptogenic Activity: Ethanolic extract of *Holoptelea integrifolia* showed adaptogenic activity and this activity was closer to the activity of 100mg/kg of *Withania somnifera*. The adaptogenic activity was dose dependent in ethanolic extract of *Holoptelea integrifolia*. These effects may be due to the presence of tannins, saponins, alkaloids, phenolics, flavonoids in the extract of bark of *Holoptelea integrifolia* as flavonoids, tannins and phenolics are mainly responsible for adaptogenic activity [31].

Antitumor Activity: The antitumour effect of EHI against DAL is Swiss albino mice. A significant ($P < 0.05$) percent increase in the life span and non-viable cell count in peritoneal exudates ($P < 0.05$) was observed due to EHI treatment. To evaluate whether EHI treatment indirectly inhibited tumour cell growth, the effect of EHI treatment was examined on the viable and non-viable cell counts against tumour bearing mice [32].

Cross Reactivity: *H. integrifolia* is an important pollen allergen of India and sensitizes almost 10% of the atopic population in Delhi. The phylogenetic relationship has

been used to infer various degree of cross-reactivity among botanically related plants. The skin reactivity pattern showed that patients from India who were primarily sensitized to *H. integrifolia* pollen, as evidenced by significant skin reactivity, also showed significant skin reactivity to *P. Judaica* pollen. A high correlation between skin reactivity patterns to *H. integrifolia* and *P. Judaica* pollen allergens was observed in the Indian patients ($p < 0.001$). The *in vitro* ELISA result further demonstrated the presence of specific IgE to *P. judaica* pollen in the sera of hypersensitive patients sensitized to *H. integrifolia* pollen in the Indian patient group. Cross reactivity between *H. integrifolia* and *P. judaica*, both by *in vitro* and *in vivo* methods, as several cross reactive proteins in these two pollen allergens in the molecular range 14-95kDa have been identified [33].

CONCLUSION

Holoptelea integrifolia, the versatile medicinal plant is the unique source of various types of compounds having diverse chemical structure. A very little work has been done on the biological activity and plausible medicinal applications of these compounds and hence extensive investigation is needed to exploit their therapeutic utilities to combat diseases. A drug development programme should be undertaken to develop modern drugs with the compounds isolated from *H. integrifolia*. Although crude extracts from various parts of the plant have medicinal applications from time immemorial, modern formulations can be developed after extensive investigation of its bioactivity, mechanism of action, pharmacotherapeutics and toxicity with the help of proper standardization and clinical trials. The global scenario is now changing towards the use of nontoxic plant products having traditional medicinal use; development of modern drugs from the centuries-old knowledge on this tree should be emphasized for the control of various diseases. In fact, time has come to make good use of through modern approaches of drug development. A significant amount of research has already been carried out during the past few decades in exploring the chemistry of different parts of the plant, which generates enough encouragement among the scientists in exploring more information about this medicinal plant. An extensive research and development work should be undertaken on *H. integrifolia* and its products for their better economic and therapeutic utilization. Therefore this review might be helpful for scientists and researchers to find out new chemical entities responsible for its claimed traditional activities.

REFERENCES

1. Mahmud, S., H.M. Shareef, S. Ahmad, G.H. Gouhar and Rizwani, 2010. Pharmacognostic studies on fresh leaves of *Holoptelea integrifolia* (Roxb.). Pakistan Journal of Botany, 42: 3705-708.
2. The Ayurvedic Pharmacopoeia of India. Govt of India. Ministry of Health and Family Welfare department of ISM and H.2001; Part-1: 39-40.
3. Acharya, D., 2008. Monkey's favourite seasonal fruit: *Holoptelea integrifolia*. American Chronicle, pp: 1-5.
4. Singh, A.B. and P. Kumar, 2003. Aeroallergens in clinical practice of allergy in India: An overview. Ann Agricul Environ Medicine, 10: 131-136.
5. The Wealth of India, 1959. Council of Scientific and Industrial Research, New Delhi, pp: 109-110.
6. Warriar, P.K., V.P.K. Nambiar and C. Ramakutty, 1995. Indian Medicinal Plants a compendium of 500 species, Orient longman private Limited, 3: 162.
7. Prajapati, N.D., S.S. Purohit and A.K. Sharma, 2003. A Handbook of Medicinal Plants a Complete Source Book. Agrobias India Jodhpur, 273.
8. Nandkani, K.M., 1976. Indian Materia Medica. Popular Prakashan Pvt. Ltd. Mumbai, pp: 651-652.
9. Benjamin, J.R.K.P. and P.K.S. Christopher, 2009. Preliminary Phytochemical and Pharmacognostic Studies of *Holoptelea integrifolia* (Roxb.), Ethnobotanical Leaflets, 13: 1222-1231.
10. Harsha, V.H., S.S. Hebbar, V. Shripathi and G.R. Hegde, 2003. Ethnomedicobotany of Uttara Kannada District in Karnataka, India Plants in treatment of skin diseases. Journal of Ethnopharmacology, 84: 37-40.
11. Mahishi, P., B.H. Srinivasa and M.B. Shivanna, 2005. Medicinal plant wealth of local communities in some villages in Shimoga District of Karnataka, India. Journal of Ethnopharmacology, 98: 307-312.
12. Graham, J.G., M.L. Quinn, D.S. Fabricant and N.R. Farnsworth, 2000. Plants used against cancer –an extension of the work of Jonathan Hartwell. Journal of Ethnopharmacology, 73: 347-377.
13. Parinitham, M., G.U. Harish, N.C. Vivek, T. Mahesh and M.B. Shivanna, 2004. Ethnobotanical wealth of Bhadra wild life sanctuary in Karnataka. Indian Journal of Traditional Knowledge, 3: 37-50.
14. Rajakumar, N. and M.B. Shivanna, 2009. Ethnomedicinal application of plants in the eastern region of Shimoga district, Karnataka, India. Journal of Ethnopharmacology, 126: 64-73.
15. Khare, C.P., 2007. Indian medicinal plants an illustrated dictionary. Springer Science, 313.

16. Sharma, P.C., M.B. Yelene and T.J. Dennis, 2005. Database on Medicinal Plants used in Ayurveda. Central Council for Research in Ayurved and Siddha, Gov. of India, New Delhi, 2: 171-73.
17. Vinod, N.V., R. Shijina, K.V. Dileep and C. Sadasivan, 2010. Inhibition of Beta-Lactamase by 1,4-Naphthalenedione from *Holoptelea integrifolia*. Applied Biochemistry and Biotechnology, 160: 1752-1759.
18. Rastogi, R.P. and B.N. Mehrotra, 1991. Compendium of Indian Medicinal Plants. First edition (1970-1979). CDRI Luchnow, NISCAIR New Delhi, 2: 375.
19. Chandler, R.F. and S.N. Hooper, 1979. Review: Friedelin and Associated Triterpenoids. Phytochemistry, 18: 711-724.
20. Sharma, S., K.S. Lakshmi, A. Patidar, A. Chaudhary and S. Dhaker, 2009. Studies on Anti-inflammatory effect of aqueous extract of leaves of *Holoptelea integrifolia* Planch. in rats. Indian Journal of Pharmacology, 41: 87-88.
21. Kalpana and A. Upadhyay, 2010. Anti-inflammatory evaluation of ethanolic extract of leaves of *Holoptelea integrifolia*, Planch. Scholars Research Library Annals of Biological Research, 1: 185-95.
22. Saraswathy, A., D.S. Nandini and D. Ramasamy, 2008. Antioxidant, Heavy Metals and Elemental Analysis of *Holoptelea integrifolia* Planch. Indian Journal of Pharmaceutical Sciences, 70: 683.
23. Reddy, B.S., R.K.K. Reddy, V.G.M. Naidu, K. Madhusudhana, B. Agwane Sachin, S. Ramakrishna and P.V. Diwan, 2008. Evaluation of antimicrobial, antioxidant and wound-healing potentials of *Holoptelea integrifolia*. Journal of Ethnopharmacology, 115: 249-56.
24. Nadella, D. and P.M. Paarakh, 2011. Antibacterial activity of different extracts of *Holoptelea integrifolia* (Roxb.) Planch. International Research Journal of Pharmacy, 2: 111-113.
25. Singh, M., S. Khatoon, S. Singh, V. Kumar, A.K.S. Rawat and S. Mehrotra, 2010. Antimicrobial screening of ethnobotanically important stem bark of medicinal plants. Pharmacognosy Research, 2: 254-57.
26. Nadella, D. and P.M. Paarakh, 2010. Evaluation of Anthelmintic activity of *Holoptelea integrifolia* (Roxb.) Planch. International Journal of Research in Ayurved and Pharmacy, 1: 637-41.
27. Kaur, S., B. Kumar, S. Puri, P. Tiwari and K. Divakar, 2010. Comparative Study of Anthelmintic activity of aqueous and ethanolic extract of bark of *Holoptelea integrifolia*. International Journal of Drug Development and Research, 2: 758-63.
28. Rajbhandari, M., U. Wegner, M. Julich, T. Schopke and R. Mentel, 2001. Screening of Nepalese medicinal plants for antiviral activity. Journal of Ethnopharmacology, 74: 251-55.
29. Sharma, S., P. Khatri, A. Pandey, V. Jakheta, L. Chaturvedi and N. Dwivedi, 2010. Anti-diabetic screening leaves extract of *Holoptelea integrifolia*. International Journal of Pharmaceutical Research and Development, 2: 66-71.
30. Shrinivas, S., K.S. Lakshmi and T. Rajesh, 2009. Evaluation of antidiarrhoeal potentials of ethanolic extract of leaves of *Holoptelea integrifolia* in mice model. International Journal of Pharma Tech Research, 1: 832-36.
31. Shakti, P., K. Bimlesh, D. Jiban, T. Prashant, S. Manoj, K. Mohanjit and M. Amit, 2011. Comparative pharmacological evaluation of adaptogenic activity of *Holoptelea integrifolia* and *Withania somnifera*. International Journal of Drug Development & Research, 3: 84-98.
32. Lakshmi, K.S., S.S. Sharma, T. Rajesh and V. Chitra, 2010. Antitumour activity of *Holoptelea integrifolia* on Dalton's ascetic lymphoma in Swiss albino mice. International Journal of Green Pharmacy, 4: 44-47.
33. Sharma, S., R.C. Panzani, S.N. Gaur, R. Ariano and A.B. Singh, 2005. Evaluation of cross-reactivity between *Holoptelea integrifolia* and *Parietaria judaica*. International Archives of Allergy and Immunology, 136: 103-112.