Holoptelea integrifolia (Roxb.)Planch- a review

Nadella Durga, Padmaa M Paarakh*.

Dept of Pharmacognosy, The Oxford College of Pharmacy, Hongasandra, Bangalore, Karnataka

Summary

Holoptelea integrifolia (Roxb.) Planch (Ulmaceae) commonly had known as Indian Elm, Kanju. It is a large deciduous tree, commonly found throughout the greater part of India. In traditional system of medicine, bark and leaves are used as bitter, astringent, acrid, thermogenic, anti-inflammatory, digestive, carminative, laxative, anthelmintic, depurative, repulsive, urinary astringent and in rheumatism. The present study gives the detailed literature search on pharmacognosy, phytochemistry and pharmacological activities of the plant.

Key words: *Holoptelea integrifolia*, Pharmacognosy, Phytochemistry, Pharmacological activities, review.

***Corresponding author:padmaparas@hotmail.com;durga_9@yahoo.co.in;**09880681532

Correspondence address:
Dr. Padmaa M Paarakh
Principal and HOD
Department of Pharmacognosy
The Oxford College of Pharmacy
6/9, I Cross, Begur Road
Hongasandra
Bangalore 560068

Introduction

Holoptelea integrifolia (Roxb.)Planch. [Ulmaceae] commonly known as *Ulmus integrifolia* .It is a large spreading glabrous tree, commonly found throughout the greater part of India[1,2]. In traditional system of medicine, bark and leaves are used as bitter, astringent, acrid, thermogenic, anti-inflammatory, digestive, carminative, laxative, anthelmintic, depurative, repulsive, urinary astringent and in rheumatism[3,4] etc. The aim of the present review is to highlight the traditional uses, pharmacognostical, phytochemical and pharmacological investigation carried out on the plant.
Plant profile

Synonyms
Ulmus integrifolia

Common Names[5,6,7]:
Sanskrit: Chirbilva, pootikaranja.
English: Indian elm, Kanju,
Hindi: Kanju, Papri, Chilbil, Begana.
Telugu: Thapasi, Nemali, Pedanevili.
Kannada: Tapasigida, Rasbija, Kaladri.
Tamil: Aya, Ayil, Kanci, Vellaya.
Malayalam: Aval.
Oriya: Duranja, Turuda.
Punjabi: Rajain, Khulen, Arjan
Marathi: Vavli, Papara.
Gujrathi; Kanjho, Waola
Kumaon: Papar, Kanju
Burmese: myaukseik, pyaukseik
Bengali: nata karanja
Nepalese: sanapangro
Konkani: vamvlo28

Taxonomical /Scientific Classification

Domain: Eukaryota
Kingdom: Plantae
Subkingdom: Viridaeplantae
Phylum: Tracheophyta
Subphylum: Euphyllophytina
Infraphylum: Radiatopses
Class: Magnoliopsida
Subclass: Dilleniidae
Superorder: Urticanae
Order: Urticales
Family: Ulmaceae
Genus: *Holoptelea*
Specific epithet: *integrifolia* - Planch.

Fig1: Whole plant of *H. integrifolia*

Fig* 2: Stem bark of *H. integrifolia

Fig 3: Dried fruits of *H. integrifolia*

Fig 4: Fresh fruits of

Fig 5: Stem bark of *H. integrifolia*

Fig 6: Fresh leaves of H.integrifolia

Classical Names[7]

Chirabilva, Hastivaruni, Vayasi, Karanji, Karabhanjika

Botanical Description[8,9]

It is a large deciduous tree, commonly found throughout the greater part of India up to an altitude of 660 m, lower ranges of Himalaya from Jammu to Oudh, Rohilkhand, forest of Dehra Dun, Saharanpur, Orissa, Chota Nagpur, Bihar, West Bengal, Hill of Deccan, Eastern slopes of Western Ghats and North Circas. A large spreading glabrous deciduous tree, which grows from 15 to 18 m height with grey, pustular bark that is smooth when young, exfoliating in corky scales on older trees. Leaves elliptical-ovate, acuminate, base rounded or subcordate. Flowers greenish yellow, in short racemes or fascicles on the leafless branches. Fruit sub-orbicular samara with membraneous wing. Seeds flat.

Climate, Soil and Propagation

Habitat moisture and shady area is favourable for survival. The tree is not frost hardy. It coppices well. The leaves are not readily browsed by goats and cattle. It can be grown by both nursery technique and direct sowing technique. Fruits are plucked off the felled branches, cleaned and dried in the sun. Seeds donot retain their viability more than 7 to 8 months.

Nursery Technique[1,11,12]

The fresh seeds soon after collection are sown on the primary bed during April to May covered with a thin layer of soil. Stiff soil should be avoided and regular weeding and loosening of the soil should be carried out. Overhead shade is necessary. Seedlings are transplanted into the polybags in June to July. One year old seedling is planted out.

Direct sowing: The fresh seed is sown in April-May in the field at the distance of 2 seeds per stake in lines 3 m apart. The seed is lightly covered with soil. Weeding and loosening of the soil in the lines are necessary. At the time of weeding at the close of monsoon rains, the seedlings may be spaced 30-50 cm apart. Mulching and lateral shade is provided to seedlings to combat the hot dry season. Plantation areas are also protected against fire and grazing.

Seed collection and Storage: Fruits are plucked off the felled branches, cleaned and dried in the sun. Seeds do not retain their viability more than 7 to 8 months. Pre-treatment: Not essential Seed Biology: No. of seeds per Kg: 25,000 to 28,500; Germination percentage: 70 to 80 Plant percent: 60 No. of seedlings per Kg. of seed: 15,000 to 17,000.

Plantation Techniques: The seeds should be sown fresh as their viability is low. The seeds can be sown in nursery beds in April- May. The raised seed beds should contain soil and red soil in the ratio of 2:1. The nursery beds should be made in the shade. The seeds germinate within 10 to 15 days. Loosing of the soil, regular weeding and watering everyday are essential during the first 3 months. The seedlings can be transplanted in to polythene bags after 2 months.

Stump planting: The stumps can be made from 12 month old seedlings; they should contain 10-20 cm of shoot and 20-25 cm of roots, trimmed at the sides. Field planting the seedlings can be transplanted into the fields after 12 months Field plantation should be done keeping a distance of 3 m x 3 m between plants during the rainy season. The growth of the seedling is fast in the first year the stumps can be planted into the field during the rainy season.

Rate of growth: The growth of seedlings is slow, but steps up after the second year. The annual diameter growth rate averages about 1 cm up to about 50 years of age, when the height attained may be about 30-35 m. Pest and Diseases: The tree is reported to be attacked by wood-borers of *Bostrychidae, Buprestidae, and Cerambycidae and Plalypodidae* families.

Pharmacognostical Studies

Macroscopical Characteristics[13,14,15]

Leaves: 8-13 cm long and 3.2-6.3 cm wide. alternate, elliptic-ovate, glabrous, margins entire, apex acute or acuminate, base rounded or cordate, main nerves 5 to 7 pairs; stipules lanceolate.
Flowers: Usually male and hermaphrodite mixed, small, greenish-yellow to brownish, pubescent, borne in short racemes or fascicles at the scars of fallen leaves; sepals often 4, pubescent. Sepals often four, pubscent, 1.5 to 2.5 cm long. Stamens 4 to 8. Filaments are glabrous; anthers are pubscent, 1-celled, stalked.
Fruit: An orbicular samara, 2.5 cm in diameter, with membranous, reticulately veined wings; seed flat. The crushed bark and leave emit an unpleasant odour. Flowering: January to February. Fruiting: April to May.
Bark: flat or somewhat curved in shape, 2 to 5 cm in width and 1 to 1.5 cm in thickness, outer surface rough, grayish brown in color, warty due to rounded protuberances of the lenticels, finely longitudinally or obliquely cracked, often exhibiting blackish brown adherent patches of rhytidoma, inner surface tough, longitudinally striated yellowish. Odour characteristics, taste astringent and some what bitter.

Microscopical Characteristics[13,14,15,16]

Fruit: It shows single layered epicarp having numerous, pointed, unicellular hairs; mesocarp composed of 3-5 layered, oval to polygonal, elongated parenchymatous cells; a few vascular bundles and tannin cells found scattered in this region; endocarp consisting of 2-3 layered, round to oval, sclerenchymatous cells with striations and narrow lumen; perisperm in seed composed of single layered, parenchymatous cells filled with reddish-brown content; endosperm and embryo composed of colorless cells containing oil globules.
Bark: The outermost multilayered periderm consists cork cambium and secondary cortex. The cork layer is interrupted at many places due to the presence of lenticels. The cortex is multilayered consists of parenchymatous cells. The primary phloem remains as patches of crushed tissue. The secondary phloem consists of sieve tubes, companion cells, phloem parenchyma and phloem rays. Vessels are present in broken conditions and crushed form. The xylem is represented by both primary and secondary xylem tissue. It consists of vessels and tracheids. The primary xylem towards pith. The secondary xylem consists of large vessels and xylem parenchyma. Xylem is found in the form of continuous medullary rays. The pith is large and remains to the central part of the stem. It consists of thin walled parenchymatous cells having many intercellular spaces. The pith regions have oil droplets. The vascular bundle is collateral and open endark.

Powder Characteristics

Fruit: Powder - Reddish-brown shows fragments of thin walled, oval to polygonal parenchymatous cells of endosperm, tanniniferous oil globules, unicellular hairs, thickwalled, polygonal, sclerenchymatous cells and polygonal cells of testa in surface view.

Bark: STONE CELLS: U-shaped, lignified structures; PHLOEM FIBRES: lignified, tapering ends, narrow lumen; CORK CELLS: thin walled, few colorless and few are with yellowish brown matter. CALCIUM OXALATE CRYSTALS: micro-prisms of calcium oxalate crystals with dark colored parenchyma; OIL CELLS: in phloem parenchyma, isolated and fragmented; STARCH GRAINS: minute, few, simple and compound.

Physico-Chemical Parameters

Table 1: Physical constants of Bark

Physico-chemical parameters	**% w/w**
Water soluble extractive	8.8 ± 0.05
Alcohol soluble extractive	2.6± 0.057
Loss on drying	7 ± 1.7
Total ash	11 ± 1.15
Acid insoluble ash	2 ± 0.3
Water soluble ash	4 ± 0.05

Important Marketed Formulations[7]

Chirabilvadi kvatha, Chirabilvadi churna, Chirabilvadi lepa, Kushthanashana rasa, Agarvadi taila. Piyhushavalli Rasa, Gandharvahastadi Kvatha Churna

Doses[7]

Decoction: 50 to 100 ml.

Traditional uses[3,11]

Plant part used: Bark, leaf, seed.

Bark and leaves: bitter, astringent, acrid, thermogenic, anti-inflammatory, digestive, carminative, laxative, anthelmintic, depurative, repulsive, urinary astringent, in inflammations, acid gastritis, dyspepsia, flatulence, colic, intestinal worms, vomiting, wounds, skin disease, vitiligo, leprosy, filariasis, diabetes, haemorrhoids and in rheumatism.

Seeds: in infected ulcers, as deodorant for foul smell of the body.

Ayurvedic Medicinal Properties[7]

Rasa: Tikta, Kashaya
Guna: Lakhu, Rooksha
Virya: Ushna
Vipaka: Katu
Doshaghnata: Kaphapittashamaka
Rogaghnata: Kaphapattikavikara Shotha, Agnimandya, Chhardi.
Karma: Pittahara, Stambhaka, Shothahara, Deepana, Anulomana.

Phytochemical Studies

Stem bark: Two triterpenoid fatty acids esters holoptelin A and B[17,18], 2-amino napthaquinone, friedelin,epifriedelin,β-sitosterol and its -D-glucose[19].

Heart wood: β-sitosterol, 2, 3-dihydroxy olean-12-en-28 oic acid and hederagenin[20,21].

Leaves: Hexacosanol, octacosanol, β-sitosterol and α–amyrin[22].

Seeds: Carbohydrate pigments, oil, acids, glycosides, sterols, tannins, proteins, free amino acids. Major fatty acids are palmitic acid, oleic acid, myristic, stearic, linoleic, linolenic acid and steroids-β-sitosterol and stigma sterol; β-amyrin, friedelin, epifriedelinol, friedel-1-en-3-one, lupeol, α-sitosterol, β -sitosterol- O-D-glucoside and stigmasterol[23,17].

Pollens: Histamine and 5-hydroxy tryptamine[17].

Root: 24-Ethyl-cholest-22-en-3α-ol[24].

Seed oil: Lauric acid 0.2%, myristic acid 3.5%, palmitic acid 35.1%, stearic acid 45%, arachidic acid 1.1%, behenic acid 0.4%, hexadonic acid 1.9% and oleic acid 53.3%[25].

Pharmacological Studies

Holoptelea integrifolia is said to possess many therapeutic activities according to traditional claims. However some of them have been proved scientifically by various investigations, some of them are discussed below.

Antiobese Activity:
The present invention discloses the extracts of *H. integrifolia* in combination with one or more known anti-obesic agents useful for the purpose of inhibition, amelioration or prevention of adipogenesis and lipolysis involved diseases. The invention further discloses a method for

treating or preventing obesity and adipogenesis and lipolysis involved diseases using the compositions containing the extracts of purified fractions of *H. integrifolia*[26].

Antidiarrhoel Activity:

The ethanol extract of the leaves of *H. integrifolia* was studied for its antidiarrhoel potential in experimental diarrhoea induced by castor oil and magnesium sulphate in mice. At the doses of 250 and 500 mg/kg p.o, the ethanol extract showed significant and dose-dependent antidiarrhoeal activity in both models. The extracts also significantly reduced the intestinal transit in charcoal meal test when compared to atropine sulphate (5 mg/kg; i.m.). The results showed that the ethanol extract of leaves of *H. integrifolia* have a significant antidiarrhoeal activity and supports its traditional uses in herbal medicine[27].

Antidiabetic Activity:

The leaf extracts of *H. integrifolia* was tested at a dose of 200 mg/ kg body weight orally for antidiabetic activity using alloxan induced diabetic rats on acute and prolonged treatment. The extracts showed significant antidiabetic results. The results of preliminary phytochemical investigation showed the presence of steroids, triterpenoids in ethanol, aqueous and chloroform extracts. Tannins and phenolic compounds were present. The results obtained were comparable with the standard drug Glibenclamide[28].

Antimicrobial Activity:

The most important mechanism of the beta-lactam antibiotic resistance is the destruction of the antibiotics by the enzyme beta-lactamase. Use of beta-lactamase inhibitors in combination with antibiotics is one of the successful antibacterial strategies. The inhibitory effect of a phytochemical, 1, 4-naphthalenedione, isolated from the plant *H. integrifolia* on beta-lactamase is reported here. This compound was found to have a synergistic effect with the antibiotic amoxicillin against a resistant strain of *Staphylococcus aureus*. An assay showed that the compound can inhibit the enzymatic activity of beta-lactamase. Modeling and molecular docking studies indicated that the compound can fit into the active site of beta-lactamase. Hence, the compound can serve as a potential lead compound for the development of effective beta-lactamase inhibitor that can be used against beta-lactam-resistant microbial strains[19,29].

The aqueous extract of leaves of *H. integrifolia* (Ulmaceae) was evaluated for antimicrobial activity against various bacteria viz. *Streptococcus pyogenes, Staphylococcus aureus Escherichia coli, Pseudomonas aeruginosa* and *Salmonella typhi.* The antibacterial activity of aqueous extract of *H. integrifolia* in different concentration was evaluated where zone of inhibition was observed against all most resistant bacterial strains.

In an another study, the antimicrobial property of the *Holoptelea* was studied against the six bacterial and five fungal strains using the agar well diffusion method and minimum microbicidal concentration and minimum inhibitory concentration were determined for each strain, in which

methanolic extract of stem bark has shown bigger zone of inhibition than methanolic extract of leaves[30].

Antibacterial activity of the extract of aerial parts of *H. integrifolia* was determined in the present study. The leaf and stem powder extracts of four different solvents and water extracts were checked against four different randomly selected bacteria by disc diffusion method. It was found that the methanol and benzene leaf extract was strongly effective against all the chosen bacteria[31].

The antibacterial activity of different extracts of *H. integrifolia* at various concentrations were evaluated where zone of inhibition was compared with the standard drug i.e. ampicillin. Chloroform extract was found to be very effective against all the test microorganisms used; petroleum ether extract was only effective against *P. aeruginosa*; benzene extract was effective against *E.coli* and *B.subtilis*; methanol extract was effective against *E.coli* and aqueous extract was effective against *S.aureus* and *E.coli*, respectively when compared to standard drug ampicillin. The minimum inhibitory concentration for chloroform extract was found to be 50,300,25 and 100 µg/ml against *S.aureus, B. subtilis, E. coli* and *P. aeruginosa* ; for petroleum ether extract was 100 µg/ml (*P.aeruginosa*); for benzene extract was 100 µg/ml(*E.coli*) and 25 µg/ml (*B.subtilis*); for methanol extract was 100 µg/ml (*E.coli*) and for aqueous extract was 50 µg/ml (*S.aureus)* and 25 µg/ml(*E.coli)* respectively suggesting the antibacterial activity of *H. integrifolia*[32].

Antitumour Activity:

The antitumour activity of the ethanol extract of leaves of *H. integrifolia* (EHI) was evaluated against Dalton's ascitic lymphoma (DAL) in Swiss albino mice at the dose of 250 and 500 mg/kg, body weight. The extract was administered orally for 14 consecutive days to tumour bearing group of animals. The extract increased the life span of DAL treated mice and restored the hematological parameters as compared with the DAL bearing mice in a dose-dependent manner. The study revealed that the ethanol extract of *H. integrifolia* showed significant antitumour activity in tested animal models49. In *in vivo* study the extract at 100mg/kg was effective in reversing all the parameters in EAC and DLA inoculated mice[33].

Antioxidant Activity:

The anti-oxidant activity was evaluated by DPPH free radical scavenging activity using HPLC method. Antioxidant activity of alcoholic extract of *H. integrifolia* was tested in three well established methods. Extracts showed significant *in vitro* antioxidant activity. The free radical scavenging potential of the extract was evaluated by two different antioxidant methods; ferric thiocyanate and thiobarbituric acid method. The ethanol extract was found to exhibit good antioxidant property[34].

Wound Healing Activity:

In excision wound model, more than 90% wound healing was recorded in treated groups by 14 days of post surgery, where as only 62.99% was observed in the control group. In incision

model, higher breaking strengths and higher hydroxyproline content in treated groups suggested higher collagen re-deposition than the control group. Finally, histopathology studies conformed wound-healing activity of *H. integrifolia*[31].

Antiemetic Activity:

The effects of ethanolic extract of leaves of *H. integrifolia* Planch on cisplatin-induced nausea using a rat model were investigated. Cisplatin at 3 mg/kg (i.p) induced significant pica accompanied by reduced food intake, suggesting the presence of nausea. Hence, this cisplatin dose was selected for testing the antinausea activity of extract. Cisplatin-induced pica decreased significantly when animals were pretreated with *H. integrifolia* extract at doses of 250 mg/kg p.o and 500 mg/kg p.o[35].

Anti-inflammatory Activity:

The purpose of the present study was to investigate the anti-inflammatory properties of aqueous extract of the leaves of *H. integrifolia,* Planch. The hind paw edema was produced in rats by sub planter injection of carrageenan. The aqueous extract of *H. integrifolia*, Planch at dose (250 and 500 mg/kg) caused % inhibition of paw edema which were comparable with indomethacin (10 mg/kg) used as a reference drug. The extract administered orally at doses of 250 and 500 mg/kg produced a significant dose dependent inhibition of edema formation[36,37].

Anthelmintic Activity

The present study was carried out to investigate the anthelmintic activities of different extracts of benzene, chloroform, methanol and aqueous extracts of the stem bark of *H. integrifolia* against adult earth worm *Pheretima posthuma*. The time taken for each worm for paralysis and death were determined. The results were compared with the results of standard i.e. Piperazine citrate. Methanolic and aqueous extracts both were found to possess significant anthelmintic activity in comparison to the standard drug. Both the extract showed dose dependent anthelmintic activity. Chloroform and benzene extracts at 20 mg/ml concentration did not show any activity in comparison with piperazine citrate at dose of 40 and 60 mg/ml[38,39].

Adaptogenic Activity

The present work was planned to compare adaptogenic activity of ethanolic extracts of *H. integrifolia* (ETHEHI 250 mg/kg and ETHEHI 500 mg/kg) with *Withania somnifera* (ETHEWS 100 mg/kg) using forced swimming endurance test and chronic cold restraint stress models. Based on the results, it can be concluded that both 250 mg/kg and 500 mg/kg doses of ethanolic extract of *H.integrifolia* showed adaptogenic activity and this activity was closer to the activity of 100 mg/kg of *Withania somnifera*. The adaptogenic activity was dose dependent in ethanolic extract of *H.integrifolia*. These effects may be due to the presence of tannins, saponins, alkaloids, phenolics, flavonoids in the extract of bark of *H. integrifolia*[40].

Antigenic and Allergenic Activity

Antigenic extracts prepared from pollen samples collected at weekly intervals during the same season did not exhibit significant variation in protein concentration. Stored pollen samples from different years, however, showed highly significant variations in protein concentration. Protein content of samples from different ecozones of India also varied (CV =± 32%). The IEF and SDS-PAGE patterns were almost identical in samples from the same season, but were variable in the samples stored from different years and different parts of India. IgE binding proteins from different samples also varied depending on the overall protein profiles. Almost all the patients, however, showed IgE binding to four proteins at 50, 60, 66 and 70 kD, indicating the important allergenic components of *H. integrifolia*[41].

Analytical Methods:

HPTLC method was developed for estimation of friedelin in powdered drug using Toluene: Ethyl acetate: 9.5: 0.5 as solvent system followed by spraying with anisaldehyde sulphuric acid reagent; densitometer scan at 584 nm[42].

Acknowledgement

The authors are grateful to Chairman and Executive Director, Children's Education Society, Bangalore, Karnataka for providing necessary facilities.

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