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Holoptelea integrifolia: A review of its ethnobotanical and medicinal properties

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Abstract

Study of indigenous medicine is the new horizon of medicine. Backed by effectiveness of secondary metabolites, plant extracts of *Holoptelea integrifolia* have been used since ages in curing routine maladies of skin and pain management. Also known as Indian elm tree or jungle cork tree, it is widely distributed along Sino-India and Indo-Myanmar region.

Pharmacological studies indicate the effectiveness of isolated secondary metabolites like terpenoids, sterols, tannins, saponins, alkaloids and other biomolecules in treating alleviating symptoms of various skin infections, rheumatism and cancer. Although, studies are still required to trace the biochemical interactions of these molecules and target tissues along with toxicity assessment, it sure is a potential candidate in preventative medicine.

Key Words – indigenous, secondary metabolite, rheumatism, toxicity assessment.

Introduction

Holoptela integrifolia (Planch) is an ornamental road side tree and known as Indian Elm Tree. It is distributed over tropical and temperate region of northern hemisphere (Parrot 2001). H. integrifolia is considered to be native to Asian –Tropical region including India, Nepal, Srilanka, Cambodia, Laos, Myanmar, Vietnam and China (Bambhole et al 1985)

Plants have been an abundant source of medicinal agents for centuries, with a long history of use in various traditional systems of medicine, such as Ayurveda, Unani, Siddha, and Chinese medicine (Ganie &Yadav 2014) These plant species have provided a rich source of anti-infective agents that are cost-effective and have fewer side effects. In fact, the World Health Organization estimates that 60% of people worldwide rely on herbal medicines for some aspects of their health.

It is well documented from ancient times that the active principles from plant origin have been used as medicines for various diseases and microbial infections. These active principles from plant origin have provided numerous crucial molecules in the search of new drug medicine (Borris, 1996). Only 2,500 plant species are used in the preparation of herbal drugs, highlighting the immense potential of untapped resources.

With the rise of health consciousness among individuals, there has been a notable surge in the examination and analysis of plant-derived products. This heightened interest has spurred extensive research efforts focused on uncovering the possible health advantages that these products may provide. However, a vast proportion of the available higher plant species have not yet been screened for biologically active compounds. Thus, drug discovery from plants remains an essential component in the search for new medicines.

Purpose of review

The review of *H. integrifolia* aims to provide a comprehensive update on the botany, phytochemistry, and pharmacological activities of the plant, bridging the gap between traditional uses and in vitro pharmacological/biological studies. This review is based on gathered information from various sources, including scientific databases, recognized books, abstracts, conference proceedings, and non-indexed journals. The review highlights the traditional uses of the plant in Indian system of medicine, secondary metabolites/phytoconstituents isolated from various parts of the plant with proven biological activity, different biological activities reported on various extracts and fractions of different plant parts. The information provided in the review may be useful for scientists and researchers to discover new entities responsible for therapeutic activity of *H. integrifolia*.

Ethnobotany of *H. integrifolia*- Uses in Indian Medicine

Distribution:

Holoptelea integrifolia, commonly known as Indian elm, jungle cork tree, monkey biscuit tree, or Indian beech tree, is a large deciduous tree that originated from Pacific Islands. It is widely distributed in temperate and tropical areas of northern hemispheres, particularly in Asia, including India, Nepal, Sri Lanka, Indo-China, Cambodia, Laos, Myanmar, Vietnam, Burma, and China. In India, it is found in the outer Himalayan region from Jammu eastward up to 1,800 meters extending to Assam and Burma, and southwards from Bengal to Central, Western, and South India to the dry region of Ceylon. It is used for various medicinal purposes in traditional medicine.

Vernacular Names-

Language	Vernacular name
Hindi	Papri, Chilbil, Kanju, Cilbil, Poothigam, Chirabil
Sanskrit	Chirivilva, Pootikaranja, Vayasi, Karanji, Chirabilwa
English	Indian Elm, Jungle cork tree, Monkey Biscuit Tree
Punjabi	Rajain, Khulen, Arjan
Malayalam	Aavil, Aval
Telugu	Nemilinara, Nali, Thapasi, Nemali, Pedanevili
Kannada	Kaladri, Nilavahi, Rahubija, Rasbija
Tamil	Aya, Ayil, Kanci, Avil, Pattai
Bengali	Nata Karanja
Marathi	Ainasadada, Vavala, Vavli, Papra, Bawal
Gujarati	Charal, Charel, Kanjo, Chirbil, Chirmil
Oriya	Dhauranjan, Turuda, Karanja
Konkani	Vamvlo
Burmese	Myaukseik, Pyaukseik
Nepali	Sano pangro
Siddha	Iya

Table 1: Vernacular names of *Holoptelea integrifolia* (Taken from Ganie & Yadav, 2014)

Taxonomy:

The plant's taxonomic classification is as follows:

Domain - Eukaryota
Kingdom – Plantae
Division - Magnoliophyta
Class - Magnoliopsida
Order – Urticales
Family – Ulmaceae

Genus – *Holoptelea*
Species - *integrifolia*

Morphological features:

It is a deciduous tree with a height of up to 20 meters. The bark is white-grey in colour and smooth, with pubescent branchlets. The leaves are simple, alternate, and ovate or elliptic-ovate in shape, with acuminate tips. The tree produces small greenish-purple flowers that are polygamous and found in short racemes or axillary fascicles. Male flowers have eight stamens, while bisexual flowers have four. The ovary is superior, unilocular, compressed, and stalked, and the style is very short with a bi-lobed stigma. The fruit is a one-seeded samara that is obliquely elliptic or orbicular, light brown, and stalked, with wings that are 1.2-3.4 cm long and 0.3-0.5 cm wide.

Figure (1A)

Figure (1 B)

Figure (1A) and (1 B) showing fresh and dry fruiting bodies of *Holoptelea integrifolia*

Ethnomedicine:

Holoptelea integrifolia is a plant that has been used traditionally for various medicinal purposes. The bark and leaves of the plant have been used for their anti-inflammatory, digestive, and carminative properties. The plant has also been used as an anthelmintic, repulsive, and urinary astringent.

The bark of *H. integrifolia* is known to contain a significant amount of mucilage, which has various medicinal properties. It has been used to treat rheumatic swellings, and the paste of the stem bark is applied externally to treat the inflammation of lymph glands, ringworm, and scabies. A decoction of the leaves is believed to help regulate fat metabolism and to have therapeutic effects on ringworm, eczema, and other cutaneous diseases.

The stem bark of the plant has been used as an anti-inflammatory agent, specifically for the eyes. An external application of stem bark paste on the forehead is a traditional remedy for treating common fever. The bark and leaf paste of the plant is applied externally on the white patches or leucoderma, and bark boiled in coconut oil and mixed with garlic is applied externally to eczema.

A common traditional remedy using *Holoptelea integrifolia* bark is to apply a paste made from the bark on the affected area as a treatment for herpes simplex infection. Similarly, tying a piece of bark cut in the shape of a coin on the left arm below the shoulder is believed to be a remedy for malaria.

To treat hair loss caused by an infection, a mixture of leaf buds and lime juice is applied externally to the affected area. A paste made from grinding the bark of *Holoptelea integrifolia* with lemon juice is commonly used to alleviate weakness. The seeds of the plant are traditionally used to treat ringworm, while the dried fruit is used to manage polyuria and urinary disorders.

Pharmacological Constituents -

Holoptelea integrifolia possess many phytochemicals that have very important medicinal properties. The plant species originated from Pacific Island (Singh 2012). These constituents are found in different parts of the plant such as the stem bark, heartwood, leaf, seed, pollen, and root.

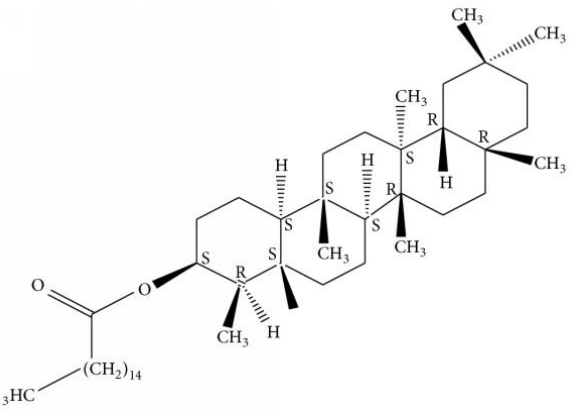

Figure 2. Holoptelin A

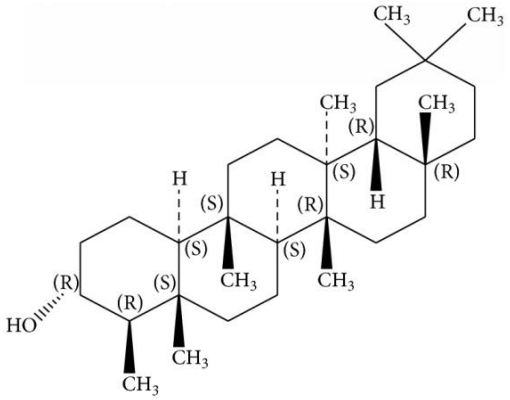

Figure 3. Holoptelin B

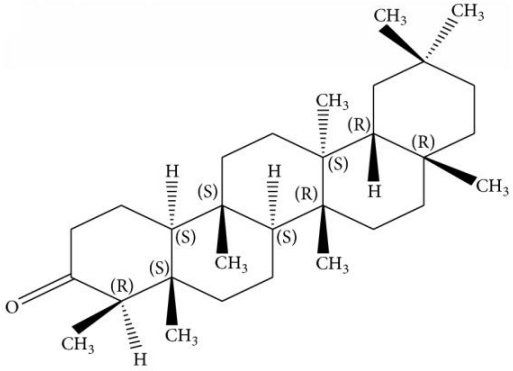

Figure 4. Friedlin

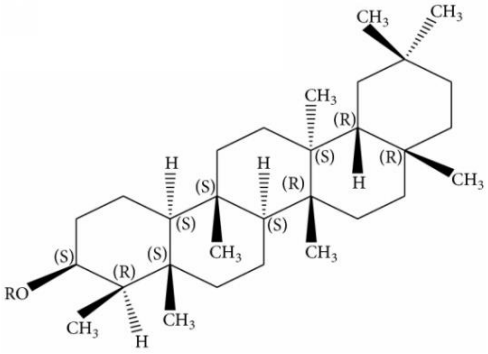

Figure 5. Epifredlin

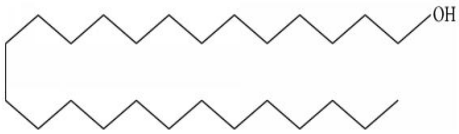

Figure 6. Hexacosanol

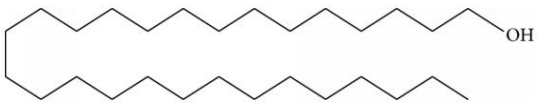

Figure 7. Octacosanol

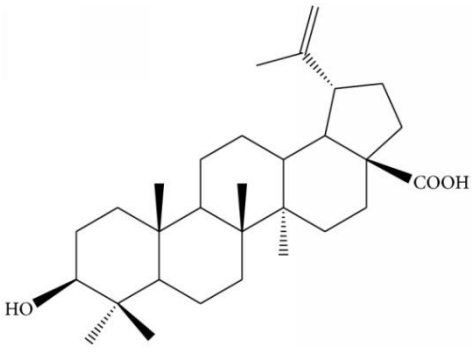

Figure 8. Betulinic Acid

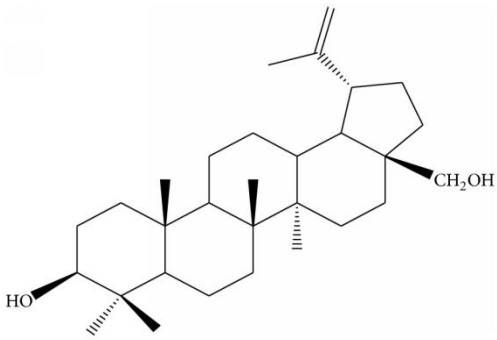

Figure 9. Betulin

Diagram courtesy- (Showkat & Yadav, 2014)

Stem bark contains Holoptelin-A and B, 2-amino naphthoquinone, friedlin, epifriedlin, β-sitosterol, β-D-glucose, β-amyrin, betulin, and betulinic acid. Heartwood contains 2,3-dihydroxyolean-12-en-28 oic acid and hederagenin.

Leaf contains hexacosanol, octacosanol, 1,4-naphthalenidione, α-amyrin, and a new phytosterol 17-(6-diethylamino) decan-3-yl)-10,13-dimethyl-12,13-dihydro-10H-cyclopenta[a]phenanthren-3-ol. The seeds of *Holoptelea integrifolia* are a notable source of various fatty acids, including palmitic acid, myristic acid, stearic acid, linoleic acid, and linolenic acid. and steroids like stigmasterol, α and β-sitosterol, β-amyrin, friedel-1-en-3-one, lupeol, and β-sitosterol-D-glucoside. Pollen grains contain histamine and 5-hydroxy tryptamine, while roots contain 24-ethyl-cholest-22-en-3α-ol.

Pharmacological Activities -

- **Antibacterial Activity** -Studies have reported the antibacterial activity of various extracts of *Holoptelea integrifolia* against different strains of bacteria. The diethyl ether extract of the plant's leaves showed the highest antibacterial activity against lactam-resistant strains of Staphylococcus aureus. The active compound responsible for the antibacterial activity was identified as 1,4-naphthoquinone, with a minimum inhibitory concentration of 4 mg/mL. The chloroform extract of the stem bark of the plant was found to be the most effective against various test microorganisms, including *S. aureus*, *Bacillus subtilis*, *Escherichia coli*, and *Pseudomonas aeruginosa*, with a minimum inhibitory concentration ranging from 50 to 1366 µg/mL.
- **Wound-healing Property**- Wound healing is a complex process of repairing damaged skin or tissues. The methanolic extracts of both stem bark and leaves at a concentration of 50 mg/550 mm2 of wound area were found to possess wound healing potential on albino rats in incision and excision wound model (>90% wound healing recorded) (Reddy , Reddy & Naidu 2008) The antimicrobial activity of the extracts was evaluated against six bacterial and five fungal strains, and the minimum inhibitory concentration and minimum microbicidal concentration were determined for each strain. The stem bark extract showed a larger zone of inhibition than the leaf extract.
- Wound healing is a complex phenomenon, including proliferation of both parenchymal and connective tissue cells, synthesis of ECM (extra cellular matrix proteins), remodelling of connective tissue and parenchymal components and acquisition of wound strength (Ramzi, Vinay and Stanley 1994). This study suggests that *Holoptelea integrifolia* has potential as a natural wound-healing agent with antimicrobial and antioxidant activity.
- **Antioxidant Activity**- The antioxidant activity was evaluated using the DPPH free radical scavenging assay, and the stem bark extract had a lower IC50 value than the leaf extract. In the excision wound model, the treated groups showed more than 90% wound healing by day 14 post-surgery, compared to 62.99% in the control group. The treated groups in the incision model had higher breaking strengths and higher hydroxyproline content, suggesting increased collagen re-deposition compared to the control group.
- **Antiviral Property**-A study by Tyagi et al. evaluated the methanolic and aqueous extracts of *Holoptelea integrifolia* bark against two viral systems in vitro, Herpes simplex and influenza virus. The study found that the plant was considerably effective against the Herpes simplex virus. This research suggests that *Holoptelea integrifolia* may have potential as a natural treatment for viral infections. (Rajbhandari, 2001)
- **Anthelminthic Activity**- This activity is responsible to expel parasitic worms by killing or stunning them. The first report on anthelminthic activity of H. integrifolia was provided by Nadella and Paarakh (Nadella and Paarakh ,2011).
- To further understand the mechanism of action and identify the potential phytoconstituents responsible for the anthelmintic activity, it would be interesting to conduct isolation studies. This would involve the extraction and purification of individual compounds from the plant extracts and evaluating their individual effects on the anthelmintic activity. Additionally, mechanistic studies could be conducted to understand how these compounds exert their effects on the earthworms. These studies could provide insight into the development of natural anthelmintic agents for the treatment of parasitic infections.

- **Antidiabetic Activity** -Anti-diabetic activity on ethanolic and petroleum ether extract of the leaves of *H. integrifolea* has been evaluated against alloxan induced diabetes in male Wistar rat which was comparable with standard drug Glibenclamide. (Sharma et al 2010). The alloxan-induced diabetic rats showed a high mortality rate, and various parameters such as blood glucose level, body weight, and lipid profile were estimated. The results showed a gradual decrease in the blood glucose level in the animals treated with the bark extract (250 mg/kg b.w. and 500 mg/kg b.w., orally), and a statistically significant decrease was observed after 15 days of treatment at the dose level of 500 mg/kg. Moreover, the prevention of body weight loss in diabetic animals was found to be significant on day 15 in both treatment groups.
- **Anticancer Activity**- The effect of H on Dalton's ascitic lymphoma in Swiss albino mice was reported by Lakshmi et al. (Lakshmi et al 2010). Recently, Guo et al. (Guo & Wang 2013) observed antineoplastic (anti-cancer /antitumor) activity of butanol, hexane, ethyl acetate, and chloroform bark extracts of *Holoptelea integrifolia*. The effect was studied on small cell lung cancer, breast, prostate, and colorectal and hepatocellular cancer cell lines. The findings of the study showed that hexane and ethyl acetate extracts had significant cytotoxic effects on breast and prostate cancer cells.
- **Allergenic Activity**- It has been a major cause of allergic rhinitis and asthma during the onset of pollen season in Northern India. A study conducted in two sites of Allahabad during 2006-2007 showed predominance of *H. integrifolia* pollen load in air (Sahney and Chaurasia, 2013). Huge pollen load released by anemophilous *H. integrifolia* coincides with spike in cases of nasobronchial allergy during the months of February, March and April. The pollen dispersal mechanism and frequency of this plant is also strategic. A study conducted in Jaipur; Rajasthan confirmed an intradiurnal pattern of *H. integrifolia* pollen release in air. Average study during March showed that the pollen count dipped between 4-6 am, followed by a gradual increase that peaked between 2-4 pm. After that the pollen count gradually reduced (Dimple Singh *et al*., 2013). Apart from causing seasonal allergy, pollen sensitivity was also reported to be responsible for sensitizing 10% of atopic individuals in Delhi (Sharma *et al*., 2005). *H. integrifolia* and *Parietaria judaica* share cross reactive protein which renders significant population of *H. integrifolia* sensitized people to be positive for skin test towards *P. judaica* pollen extract (Ghosal and Gupta-Bhattacharya, 2015).
- **Adaptogenic Activity** – Many plants have adaptogenic activity due to having various chemicals. To be an adaptogen a plant must possess three basic characteristics. It is non-toxic when taken in normal doses. It helps your body cope with stress. It allows your body to return to balance (homeostasis). These effects may be due to the presence of tannins, saponins, alkaloids, phenolics, flavonoids in the plant. Extract of bark of *Holoptelea integrifolia* as flavonoids, tannins, and phenolics are mainly responsible for adaptogenic activity (Shakti et al 2011).

Conclusion

With fresh technological advancements, it would be possible to extract and study in-vivo and in-vitro biochemical interactions of various actives found in *Holoptelea integrifolia.* Proper evaluations of deleterious as well as medicinal effects of these actives will present an array of opportunities of integrating the pharmaceutical findings into ethnomedicine, resulting in greater reach and treatment potential.

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