A mini review on chemistry and biology of Holoptelea integrifolia Roxb. Planch (Ulmaceae)

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1. Introduction

Medicinal plants are part and parcel of human society to combat diseases, from the dawn of civilization[1]. Holoptelea integrifolia is well known roadside tree having a wide spectrum of biological activities. The name of plant can be simplified as ho-loh-TEE-lee-uh from the Greek holos (whole) and ptelea (elm) inte-grif-o-lee-uh meaning leaves entire (undivided). Holoptelea integrifolia (Roxb.) Planch is also known as Ulmus integrifolia Roxb. belonging to family Ulmaceae. It is commonly known as Indian Elm tree in English, Papri, Chilbil, Kanju in Hindi and Chirivilva, Poothigam in Sanskrit. Indian elm is a medium sized to large glabrous deciduous tree, with whitish or yellowish grey bark exfoliating in irregular flakes and with an offensive smell when freshly cut[2]. The family Ulmaceae, having 15 genera and about 200 species is distributed over tropical and temperate regions of northern hemisphere[3]. The native distribution of the plant can be seen in Asia–Tropical region including India, Nepal, Sri Lanka, Indo–China, Cambodia, Laos, Myanmar, Vietnam, Burma and China[4]. Various parts of the tree have been found to be useful in the treatment of bronchitis and obesity[5]. The tree has been reported to possess ovipositor deterrent and protease inhibitor activities[6]. Traditionally, the bark and leaves are used as bitter, astringent, anthelmintic and helps in treatment of inflammation, acid gastritis, dyspepsia, colic, intestinal worms, vomiting, edema, piles, wound healing, leprosy, diabetes, hemorrhoids, dysmenorrhea, diarrhoea, rheumatism, polypuria, helminthiasis, tuberculosis, fistula, flatulence, vitiligo, filariasis, and skin diseases. In Nepal, bark and leaves are applied externally on the white patches in leucoderma[7]. Many chemical constituents such as terpenoids, sterols, saponins, tannins, proteins, carbohydrates and alkaloids have been reported in this plant[8, 9].

2. Common names

Various common names of Holoptelea integrifolia are mentioned below:
Sanskrit: Chirivilva, Pootikaranja, Udakrya, Hashhivaruni,
The tree has been reported to contain various chemical constituents like terpenoids, sterols, saponins, tannins, proteins, carbohydrates, flavonoids and alkaloids\(^{(43)}\). 1, 4-naphthalenedione has been isolated from leaves whereas Holoptelin-A and B have been isolated from stem bark. Friedelin, epifriedelino\(\beta\)-D-glucose, 2-aminnaphthaquinone are reported in stem bark. Hexacosanol, octacosanol, \(\beta\)-amyrin, \(\beta\)-sitosterol are some other isolated from leaves which might be responsible for various activities shown by the tree\(^{(15)}\). Various constituents reported in various parts of the plant have been shown in Figure 1.

6. **Biological activities of plant**

6.1. **Anti-inflammatory activity**

The ethanolic extract of leaves of *H. integrifolia* showed significant percentage inhibition of paw edema as compared to standard drug, Indomethacin (10 mg/kg per oral). The ethanolic extracts were given in doses of 250 and 500 mg/kg per oral which were comparable with reference drug\(^{(15)}\). In the same manner, the aqueous extract of leaves at dose 250 and 500 mg/kg per oral was given to observe percent inhibition of paw edema which were comparable with Indomethacin (10 mg/kg per oral) used as a reference drug. The extract showed a significant dose dependent inhibition of edema formation\(^{(18)}\). It suggests the usefulness of leaves of tree in acute and chronic inflammatory conditions.

6.2. **Anthelmintic activity**

The methanolic and aqueous extracts of stem bark of *H. integrifolia*, were found to possess significant anthelmintic activity in comparison to the standard drug (Piperazine Citrate) against adult earthworm *Pheretima posthuma*. The methanol extract at various concentrations showed shortest time of paralysis and death\(^{(19)}\). In the same manner various concentrations (10, 25, 50 and 100 mg/ml) of ethanolic and aqueous extract of bark were tested against worms (*Eisenia fetida*), compared to standard Piperazine Citrate (10 mg/ml). The extracts not only demonstrated paralysis, but also caused death of worms especially at higher concentrations\(^{(20)}\). The results showed that constituents of bark could be a potent anthelmintic agent for next generation.

6.3. **Antibacterial activity**

The chloroform extract of stem bark of *H. integrifolia* was found to be very effective against microorganisms like *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, and *Pseudomonas aeruginosa* at concentrations of 50, 30, 25 and 100 \(\mu\)g/ml respectively. The antibacterial activity of extract was studied by employing Disc diffusion method where zone of inhibition was compared with standard drug, Ampicillin\(^{(21)}\). The diethyl ether extract of leaves has shown maximum activity against \(\beta\)-lactam resistant strains of *Staphylococcus aureus* and an active principle responsible for the activity was found. This anti-bacterial principle (1, 4-naphthalenedione) which was comparable with reference drug\(^{(15)}\). The results showed that constituents of bark could be a potent anthelmintic agent for next generation.
that it acts as inhibitor to $\beta$-lactamase. Isolated compound showed synergistic effect with amoxicillin by inhibiting enzymatic activity of $\beta$-lactamase. Modeling and molecular studies indicated that compound can fit into active site of $\beta$-lactamase. The result suggests that this compound can serve as potential lead compound for development of effective $\beta$-lactamase inhibitor.

6.4. Antidiarrhoeal effect

The ethanolic extract of leaves of H. integrifolia was studied for its antidiarrhoeal properties in experimental diarrhoea, induced by Castor oil and Magnesium sulphate in mice. At the doses of 250 and 500 mg/kg per oral, the ethanolic extract showed significant and dose-dependent antidiarrhoeal activity. The extracts also significantly reduced the intestinal transit in charcoal meal test when compared to Atropine sulphate (5 mg/kg). The results showed that the ethanolic extract of leaves of Indian Elm have a significant antidiarrhoeal activity and supports its traditional uses in herbal medicine.

6.5. Antitumor activity

The root of Indian Elm is being used as an important constituent for traditionally used herbal formulations for curing tumors. The antitumor activity of ethanolic extract of leaves of H. integrifolia was evaluated against Dalton’s ascetic lymphoma (DAL) in Swiss albino mice. The evaluated parameters were tumor volume, tumor cell count, viable tumor cell count mean survival time and increase in life span to access antitumor activity. The extract given in concentrations of 250 & 500 mg/kg showed increase in life span of DAL treated mice and restored hematological parameters as compared with DAL bearing mice in dose dependent manner. The extract restored the mean survival time and decreased tumor volume count in treated mice. It suggests that leaves of Indian Elm possess potent anticancer activity and increases life span.

6.6. Adaptogenic effect

The adaptogenic activities of ethanolic extracts of H. integrifolia were studied using forced swimming endurance test and chronic cold restraint stress models. It was concluded that both 250mg/kg and 500mg/kg doses of ethanolic extract of stem bark showed dose dependent adaptogenic activity. This activity was compared with and found closer to the activity of 100mg/kg of Withania somnifera. These effects may be due to the presence of tannins, saponins, alkaloids, phenolics, flavanoids in the extract of Indian Elm bark as flavanoids, tannins and phenolics are mainly responsible for the adaptogenic activity.

6.7. Anti-diabetic effect

Methanol and petroleum ether extracts of leaves of H. integrifolia shows significant anti-diabetic effect. Diabetes was
induced by Alloxan and standard drug used for comparison with extracts was Glibenclamide. Petroleum ether extracts at the concentrations, 100 & 200 mg/kg whereas methanolic extract at concentration of 200 mg/kg showed significantly positive anti-diabetic activity[27].

6.8. Antioxidant activity

Ethanolic crude extract of stem bark of H. integrifolia traditionally used in Indian system of medicine was screened for its antioxidant activity using α-tocopherol as standard antioxidant. The free radical scavenging potential of the extract was evaluated by two different antioxidant methods; ferric thiocyanate method and thiobarbituric acid method. The ethanol extract was found to exhibit good antioxidant property, which is comparable to standard vitamin E, at a specific concentration[28,29].

6.9. Wound healing potentials

The Methanolic extracts of both stem bark and leaves of H. integrifolia were found to possess wound healing potentials. In excision wound model, more than 90% wound healing was recorded in treated groups by 14 days of post surgery, whereas 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 confirmed wound-healing activity of Indian Elm[29].

7. Medicinal use of various parts of Holoptelea integrifolia

The decoction of the bark of this tree is externally used in rheumatism[30]. Oral application of the bark is used to treat intestinal tumors[31]. Dried bark is useful as an oxytocic in pregnant ladies[32]. Decoction of the leaves is orally given to regulate fat metabolism. Leaves along with garlic are externally used to treat ringworm eczema and cutaneous diseases[33]. Paste of the stem bark is externally applied to treat the inflammation of lymph glands. Stem bark paste is externally

Figure 1. Chemical constituents of H. integrifolia.
applied on the forehead of the patient suffering from common fever[34]. Moreover, paste of the stem bark is externally applied in cases of ringworm and scabies. Stem bark acts as an anti-inflammatory agent specifically for eyes[35]. In Nepal, bark is externally used to relieve rheumatic swellings. Bark and leaf paste of plant are applied externally on the white patches[36]. Bark & leaves are bitter, astrigent, acrid, anti-inflammatory, digestive, carminative, laxative, deparutive, and urinary astringent. Useful parts are leaves that act as antioxidant, antidiarrhoeal, antimicrobial and anti-inflammatory agent and grinded leaves are used for alopecia and wounds. It pacifies vitiated kapha, hemorrhoids, skin diseases, dyspepsia, fever, postnatal cares, flatulence, colic and vomiting[37].

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.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgements

The authors are thankful to UGC, New Delhi, India for financially supporting the study [F.No. 39–955/2010].

References


[34] Singh VK and Ali ZA. Folk medicine in primary health care, common plants used for the treatment of fever in India. Fisetopia 1994; 65: 68–74.


