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Chemistry and Medicinal properties of *Holoptelea Integrifolia*

Harleen Kaur Sandhar, Mohanjit Kaur, Prashant Tiwari, Manoj Salhan, Pardeep Sharma, Sunil Prasher, Bimlesh Kumar*
Lovely School of Pharmaceutical Sciences, Lovely Professional University, Jalandhar-Delhi G.T. Road (NH-1), Phagwara. Punjab (INDIA) 144402

Abstract
Natural products have evolved as a source of bioactive compounds and possess a potential for developing novel therapeutic agents. *Holoptelea integrifolia* is a roadside plant and has been reported in Charaka Samhita and Sushrutha Samhita. Traditional systems also claimed its potential therapeutic applications. This review presents a detailed survey of the literature on chemistry and medicinal properties of *Holoptelea integrifolia*.

*Corresponding author, Mailing address:
*Bimlesh Kumar (Lecturer)
Department of Pharmaceutical Sciences
Lovely Professional University, Ludhiana-Jalandhar G.T. Road
Phagwara (Punjab), 144402, India
*Mob: +919872260354, +919216260354
E.mail: bimlesh.12474@lpu.co.in, bimlesh1@gmail.com

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INTRODUCTION

Nature has blessed mankind with a treasure of medicinal plants. Natural products have always remained a profile source for the discovery of new drugs and are used since Vedic period [1]. *Holoptelea integrifolia* is a medium-sized large glaborous tree about 15-25 m in height with whitish or yellowish grey bark exfoliating in irregular flakes and possesses an offensive smell when cut freshly [2]. It belongs to family Ulmaceae and is having 15 genera and 200 species.

Vernacular Names: Hindi- Chirmil, Chilbil, Chilla, Dhamna, Kandru, Kanju, Karanji, Kumba, Kunjanali,

Kunj; Gujarati- Charel; Marathi-Papara; Sanskrit-Chirbilva; Tamil-Ayi [5]; Malayalam- Aval; Punjabi-Arjan, Kacham, Khulen, Papri; Telugu- Nemali, Nevili, Pedanevili; Uriya- Dharango [3, 4, 5, 6].

Distribution: It is widely distributed all over tropical and temperate regions of Northern hemisphere including Indian Peninsula to Indo China, Burma and Srilanka. It is abundantly found in sub Himalayan hills of Assam, Bihar, Ajmere, Bundelkhand [3, 6].

PHARMACOGNOSTIC STUDIES:

Holoptelia integrifolia is a large spreading glaborous deciduous tree about 15-18 m high having mucilaginous bark and elliptic leaves [6].

Leaf is green in colour with slight aromatic odour. External margin of leaf is rough, with particulate venation acute apex and symmetrical base with curved petiole and broad alternate lamina. Leaf is broad approx 2-3 cm in size [4]. Leaves are 7.5-12.5 by 3.3-6.3 cm in size. These are elliptic, acuminate, glaborous having rounded base [6]. The upper epidermis of leaf consists of small barrel shaped parenchymatous cells. Trichomes are present on both the surfaces of leaf and majority of them are present along the midrib and minimum are found along the lamina. Stomata are present on lower surface and represented by anomocytic type. The vascular bundle is ovoid in shape. Between the upper epidermis and the vascular bundle, 6 to 7 layer of irregular shaped collenchyma cells are present. The vascular bundle is collateral and open endark. There occur few layers of cambium in between the xylem and phloem. The phloem consists of sieve tubes, companion cells and phloem parenchyma. Xylem consists of xylem vessels, tracheids and parenchyma. Xylem is seen on the upper side whereas phloem is seen towards the lower side of the epidermis [4].

Stem is brown in colour having agreeable smell and smooth texture. The transverse section of stem is circular and covered with many unicellular, uniseriate trichomes. The outermost multilayered periderm consists of cork cambium and secondary cortex. The cork layer is interrupted at many places due to the presence of lenticels. The cortex is multilayered and 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 is towards the pith, while, 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. Flowers are sessile, male and bisexual, ciliate, and obtuse. Stamens are biseriate and anthers are slightly curved, hairy, introrse. Ovary is compressed – ovate. Stalk is elongating in fruit which is dry, winged, compressed samara, reticulate. Seeds are flat and exalbuminous [4].

CHEMICAL CONSTITUENTS:

The plant has been reported to possess chemical constituents like terpenoids, sterols, saponins, tannins, proteins, carbohydrates and alkaloids [3], flavonoids. The phytoconstituents isolated from stem bark are holoptelin- A (Fig I) and holoptelin-B (Fig II), 2-aminonaphthoquinone, Friedlin (Fig III), epifredlin (Fig V), $_{\beta}$-sitosterol, $_{\beta}$-D-glucose, $_{\beta}$-amyrin (Fig IV), hederagenin (heart wood), hexacosanol (Fig VI). 1, 4-naphthalenedione has been isolated from leaves of *Holoptelea integrifolia* and is reported to possess antibacterial activity against *Staphylocopccus aureus* [7].

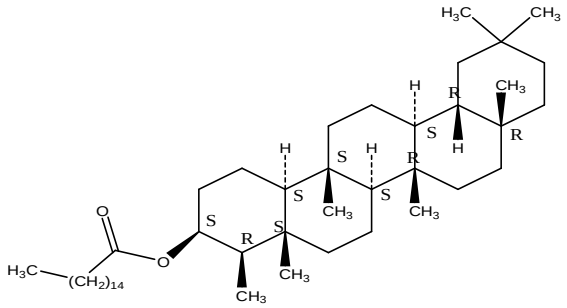

Figure 1: Holptelin-A[8]

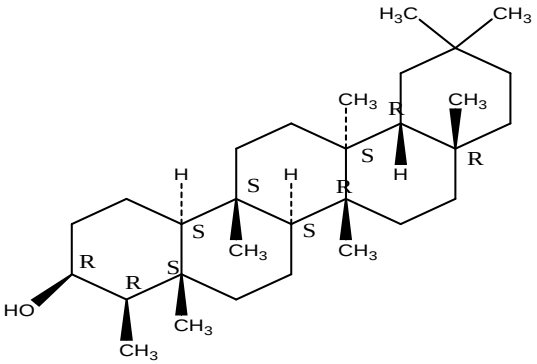

Figure 2: Holoptelin-B [9]

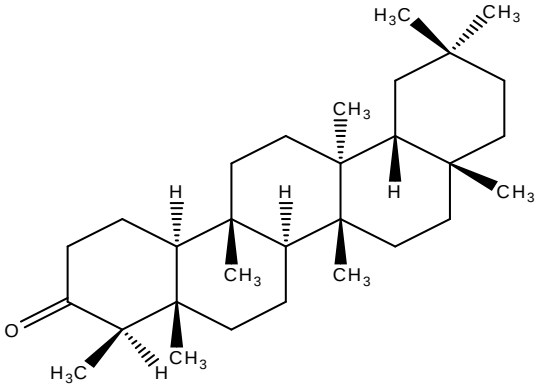

Figure 3: Friedlin[10]

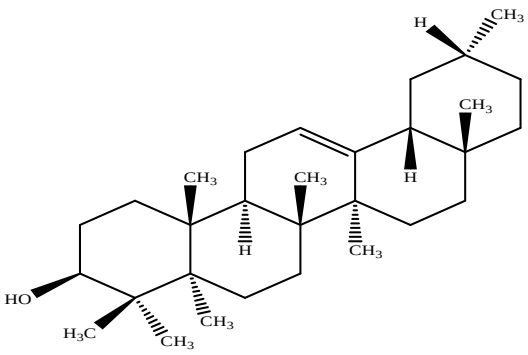

Figure 4: β-amyrin [10]

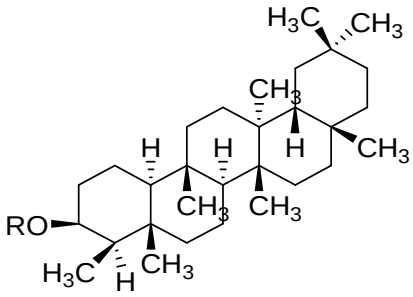

Figure 5: Epifriedlin [10]

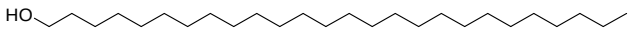

Figure 6: Hexacosanol [11]

ANALYSIS:

Procedure of HPTLC of *Holoptelia integrifolia* fruit as described in Ayurvedic atlas is as follows [12]:

Mobile phase: Toluene: Ethyl acetate: Formic acid (4.0: 5.0:1.0)

Tank saturation: 20 minutes

Sample applied: 10 µl

Solvent front: 80 mm

Drying: For 10 minutes

Detection/ Visualization: At 254 nm, 366 nm & after derivatization

Derivatization: Derivatize the plate with anisaldehyde sulphuric acid reagent and heat the plate at 105° C till the band develop. (Table 1)

Table 1: HPTLC details of sample solution of *Holoptelia integrifolia* fruit

S. No. of Resolved bands	Visualization		After Derivatization Under white light
	UV 254nm	UV 366 nm	
1.	0.61	0.05	0.47
2.	0.68	0.13	0.53
3.	-------	0.62	0.58
4.	-------	0.66	0.65
5.	--------	0.70	0.80
6.	--------	0.79	0.86
7.	--------	0.95	--------

TRADITIONAL USES:

Plant is useful in treatment of obesity, edema, and bronchitis. It has been known to be protease inhibitor. Mucilage and juice obtained from boiled bark has been reported to be useful in rheumatism, intestinal tumour when applied externally. Bark juice is applied to rheumatic swellings [6]. Bark juice is useful as oxytoxic in pregnancy. Paste of seeds and bark stem is externally useful in ringworm, eczema and cutaneous affections. Paste of stem bark is applied externally to treat inflammation of lymph gland and common fever, scabies and ringworm. Paste of bark and leaf is applied externally for treatment of leucoderma [3, 4, 5]. It is used for ornamental purposes in Pakistan [3]. Bark boiled in oil of *Pongamia glabra* and garlic is applied externally for the treatment of eczema [13]. Bark and leaves are astringent, bitter, antihelmintic, and are used for the treatment of diabetes, skin disease, intestinal disorder, leprosy, rheumatism [2] and wound-healing in form of paste [14].It is an important pollen allergent plant of India [5, 15].

PHARMACOLOGICALLY REPORTED ACTIVITIES:

Table 2: Pharmacologically reported activities of *Holoptelea integrifolia*

S.No	Activity	Standard used	Part used	Extract	Dose in mg/kg	Remarks	Reference
1.	Anti-inflammatory	Indomethacin	Leaf	Ethanolic	250, 500	500 mg/kg exhibit maximum activity	10
2.	Antidiabetic	Glibenclamide	Leaf	Methanolic	100, 200	200 mg/kg methanolic extract and pet. Ether extract exhibit maximum activity	5
		Glibenclamide	Leaf	Petroleum ether	100, 200		
3.	Antitumour	DAL (1x 10^6) cells	Leaf	Ethanolic	250, 500	Extract increased life-span of DAL cells	16
4.	Antidiarrheal	Loperamide (3 mg/kg)	Leaf	Ethanolic	250, 500	Dose-dependent action	14
5.	Antioxidant	A- tocopherol	Stem bark	Ethanol	------	Potent antioxidant	17

Table 3: Antimicrobial activity of *Holoptelia integrifolia*

S.No	Microorganism	Standard used	Part used	Extract	Dose in µg/ml	Remarks	Reference
1.	*Klebsiella pneumonia*	Amikacin, Piperacillin	Leaf	Acetone	-----	+++	18
				Methanolic	-----	-	
2.	*Staphylococcus aureus*	Ampicillin, amoxicillin, ceftriaxine, cefotaxime	Leaf	Diethylether	50	+++	7
				Hexane	50	+	
				Acetone	50	+++	
3.	*Bacillus subtilis*	Ampicillin, amoxicillin, ceftriaxine, cefotaxime	Stem bark	Aqueous	50	+++	19
				Benzene	500	+++	
				Chloroform	50	+++	
4.	*Escherichia coli*	Ampicillin, amoxicillin, ceftriaxine, cefotaxime	Stem bark	Pet ether	500	+++	19
				Benzene	100	+++	
				Chloroform	25	+++	
				Methanol	100	+++	
				Aqueous	25	+++	
5.	*Pseudomonas aeruginosa*	Ampicillin, amoxicillin, ceftriaxine, cefotaxime	Stem bark	Pet ether	100	+++	19
				Benzene	500	+++	
				Chloroform	100	+++	

++++ indicates significant activity, + indicates shows activity but not significant, - indicates exhibits no activity, ----- indicates not known

Table 4: Antihelmintic activity of *Holoptelea integrifolia*

S.No	Standard used	Part used	Extract	Dose in mg/ml	Remarks	Reference
1.	Piperazine citrate	Stem	Benzene	20	Benzene and chloroform extract didn't show this activity. Methanolic and aqueous exhibit significant activity in dose-dependent manner	20
			Chloroform	20		
			Methanol	20, 40, 60, 80		
			Aqueous	60, 80		
2.	Piperazine citrate	Bark	Aqueous	10, 25, 50, 100	Ethanolic extract is more potent than aqueous extract	21
			Ethanolic	10, 25, 50, 100		

CONCLUSION:

Holoptelia integrifolia is a deciduous tree belonging to family Ulmaceae. It is rich in phytochemicals including alkaloids, saponins, flavonoids, tannins, fixed oils. It possesses various ethnomedicinal uses. Till now, a very less research has been done on this plant. So a need arises to focus on this plant and its isolated constituents.

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