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A Review on the Anti-Inflammatory and Analgesic Activity of the Plant-Nycthanthes Arbor-Tristis Linn

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ARTICLE INFO	A B S T R A C T
Article history: Received 20 August 2024 Revised 02 September 2024 Accepted 07 September 2024 Published 16 September 2024	The mythological plant Nyctanthes arbor-tristis (Oleaceae) plant has significant medicinal prop- erties according to Ayurveda. The traditional medical system uses the leaves of Nyctanthes ar- bor-trisitis Linn. to treat rheumatism, sciatica, and other inflammation-related conditions. The different parts i.e., leaves, bark, etc. Nyctanthes arbor-tristis linn were extracted for analgesic and anti-inflammatory evaluation. The extract was then tested on several in-vitro and in-vivo evalua- tion parameters to ensure that it had an efficient therapeutic effect. This formulation should result
Keywords: Nyctanthes arbor-tristis, Analgesic and Anti-inflammatory, Traditional medicine	in a herbal remedy with great efficacy, low cost, and minimal adverse effects. The effectiveness of plant-based medications used in traditional medicine has drawn a lot of interest due to their low cost and little adverse effects.
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Introduction

Nyctanthes arbor-tristis Linn. (NAT) is a small divine ornamental tree used to pray the God according to Indian mythology known across the country for its fragrant white flowers [1,2]. NAT is commonly known as night flowering Jasmine [3,4] or Parijata [5].

Nyctanthes arbortristis Linn. (Division: Magnoliophyta; Class: Magnoliopsida; Order: Lamiales; Family: Oleaceae), commonly known as Harsinger or Night jasmine, is a well-documented plant. It is a native of India, distributed wild in sub-Himalayan region and also found in Indian garden as ornamental plant. The indigenous people of Chittoor district Andhra Pradesh (India) widely use the whole plant for treatment of cancer, root for fever, sciatica, anorexia; bark as expectorant, Leaf for control fever, diabetes and as cholagogue, diaphoretic and anthelmintic. Various extracts of the plant is used to treat arthritis, [6-8] malaria, intestinal worms tonic, laxative, anti-trypanosomal, anti-inflammatory and antioxidant activity [9-11]. Juice of the leaves is used as digestives, antidote to reptile venoms, mild bitter tonic, laxative, diaphoretic and diuretic [12-14].

Taxonomical Classification

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Lamiales

Family: Oleaceae

Genus: Nyctanthes

Species: arbor-tristis

Binomial name: Nyctanthes arbor-tristis [15]

Distribution of the plant:

Nyctanthes arbor-tristis Linn is native to India, distributed widely in sub-Himalayan regions and southward to Godavari. It is also widely distributed in Bangladesh, Indo-Pak subcontinent and South-East Asia, tropical and sub-tropical South East Asia. It grows in Indo-Malayan region and distributed across Terai tracts as well as Burma and Ceylon. It tolerates moderate shade and is often found as undergrowth in dry deciduous forests. It is also found in Thailand [15,16].

Description of plant:

NAT is a large shrub with flaky grey bark [17] and height up to 10 m tall, stiff whitish hair, young branches [18] and rough leaves [19]. It has fragrant flowers with five to eight lobes which are white in colour, and corolla is orange coloured centrically they are produced in clusters of two to seven together, with individual flowers opening at dusk and finishing at dawn [17]. Calyx is 6-8 mm long, narrowly campanulate, hairy outside, glabrous inside truncate or obscurely toothed or lobed, ciliated. Corolla is glabrous and more than 13 mm long; tube is 6-8 mm long, orange coloured, about equalling the limbs; lobes are white and unequally obcordate and cuneate [18]. The leaves are opposite, simple, 6–12 cm long and 2–6.5 cm broad, with an entire margin. The fruit is a flat brown heart-shaped to round capsule 2 cm diameter, with two sections each containing a single seed [17]. These are long and broad, obcordate or nearly orbicular, compressed, 2-celled. Seeds are exalbuminous, testae are thick, and outer layer of large transparent cells is heavily vascularised [18].

Significance of plant in mythology:

The orange heart is used for dyeing silk and cotton, this practice was started with Buddhist monks whose orange robes were given their colour by this flower. The Parijata is regarded in Hindu mythology as one of the five wish granting trees of Devaloka [20].

Plant part used: Fl—flower Fr—Fruit Lf—Leaf Sd—Seed.

Extract: Ews—Water soluble portion of ethanol extract Pe—Petroleum ether Et—Ethanol.

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Chemical Compound	Plant Part	References
D-mannitol	Leaves	21,22,23
β-sitosterole	Leaves	21,22,23
Astragaline	Leaves	21,22,23
Nicotiflorin	Leaves	21,22,23
Oleanolic acid	Leaves	21,22,23
Nyctanthic acid	Leaves	21,22,23
Tannic acid	Leaves	21,22,23
Ascorbic acid	Leaves	21,22,23
Methyl salicylate	Leaves	21,22,23
Volatile oil	Leaves	21,22,23
Friedeline	Leaves	21,22,23
Lupeol	Leaves	21,22,23
Mannitol	Leaves	21,22,23
Glucose	Leaves	21,22,23
Diterpenoid nycanthin	Flower	24
Flavonoids	Flower	24
Anthocyanins	Flower	24
Essential oil	Flower	24
β-monogentiobioside	Flower	24
β-digentiobioside	Flower	24
Arbortristoside A & B	Seed	24
Glycerides	Seed	24
Lignoceric acid	Seed	24
Stearic acid	Seed	24
Palmitic acid	Seed	24
Myristic acids	Seed	24
3-4 secotriterpene acid	Seed	24
D-glucose	Seed	21,24
D mannose	Seed	21,24
Iridoid	Bark	25,26
Phenylpropanoid	Bark	25, 26

 Table 1: Chemicals present in different parts of Nyctanthes arbor-tristis linn.

Activity	Plant part used	Extract	Reference
Pain and Inflammation		E-ws/Pe	
			Saxena et al. (1984 1987)
	Lf		Paul and Saxena (1997) Paul
	Fl/Lf and Fr		et al. (2002)/Nirmal et al.
			(2012a 2012b)
		Et/Ews	Omkar et al. (2006)/
	Lf Sd and Fr		Rathore et al. (2007)
			Das et al. (2006)
		Ews	

Table 2: Analgesic and Anti-inflammatory activity of the extracts derived from different parts of Nyctanthes arbor-tristis [27]

Plant part used: Fl—flower Fr—Fruit Lf—Leaf Sd—Seed.

Extract: Ews—Water soluble portion of ethanol extract Pe—Petroleum ether Et—Ethanol.

Materials and Methods:

Extract Preparation: The present study was conducted with leaves of N. arbor tristis growing on the premises of L.L.R.M. Medical College Meerut. Green foliage was collected in the months of February and July. The leaves were allowed to dry in shade and powdered. A 95% ethanol extraction was done by maceration for 10 days with agitation twice daily (Riebling and Walker 1975). The extract was filtered and the solvent evaporated using a water bath. The residue was then mixed with a sufficient amount of distilled water shaken allowed to stand for half an hour and filtered. This procedure was repeated thrice to recover the maximum possible amount of the water-soluble portion. The filtrate was dried on a water bath and then at room temperature until completely solidified. The final yield was 5.16% relative to dried starting material. This extract (NAT) was subjected to screening for analgesic and antipyretic activities and ulcerogenic potential [8].

Laboratory animals: Studies were conducted in albino rats and mice (random bred) of either sex weighing 100-150 g and 20-30 g respectively fed on commercial diet (Gold Mohur Lipton India Ltd.). The animals were divided in groups of six each. A saline-fed group served as control for each experiment. The watery solution of the extract was administered orally (10 ml/kg) in different doses ranging from 0.5 to 8.0 g/kg [8].

Pharmacological Activities

Analgesic activity: Methods were selected for screening both morphine-like as well as aspirin-like analgesic activities. For morphinelike analgesia the rat tail-flick method and the mouse tail-clip method (Bianchi and Franceschini 1954) were employed. The tail-flick method involves the use of an analgesignmeter containing a heated nichrome wire for producing pain in the rat's tail. For the tail-clip method only those mice responding within 15 s to clip pressure at the base of the tail were selected for testing. The analgesic effect was measured by determining the reaction time before and at 15, 30, 60 and 90 mins following administration of the drug in both experiments. To test for aspirin-like analgesia a writhing syndrome was produced by i.p. injection of 0.1 mU10.0 g of 0.7% acetic acid in albino mice (Kita et al. 1979). Only those mice exhibiting writhing movements within 10 min of acetic acid challenge were selected and reused for testing after a gap of one week. Drugs were administered 1 h before the challenge. The number of writhing motions were observed for a 15-min period starting 15 min after injection of the acetic acid [8].

Anti-inflammatory activity: Aqueous soluble fractions of ethanolic extract significantly possess anti-inflammatory activity against acute inflammatory oedema in rats using different phlogistic agents like carrageenan formalin histamine 5-hyroxytrypatamine and hyaluronidase. The extract significantly reduced acute inflammatory swelling in knee joint of rats in turpentine oil-induced inflammation. The leaf and fruit extracts also possess better anti-inflammatory activity in arthritis - induced mouse model which was elicited by immunological methods namely injections of Freund's complete adjuvant into the sub-planter surface of the right hind paw on 0 to 12 days and PPD-induced tuberculin reaction. In subacute models of carrageenin-induced granuloma pouch and cotton pellet granuloma rats were fed daily with the extract for 6 days from the day of pouch formation or for 5 days from the day of peller implantation. Granulation tissue formations in both models were significantly inhibited by extract [21-28]. The ethanoic extract of the orange tubular of calyx of Nyctanthes arbortristis and the isolated carotenoid (200 mg/kg i.p.) possess significant inhibition of carrageenan-induced rat paw oedema using diclofenac sodium as a standard drug [11].

Analgesic and anti-inflammatory activity: The leaves of the plant have been used by avuryedic physicians for arthritis and obstinate sciatica. The juices of its leaves in different forms have been advocated for acute and chronic as well as intermittent fevers (Chopra et al. 1958). Interestingly Saxena et al. (1984) reported the presence of anti-inflammatory activity in water soluble portion of an ethanol (absolute) extract of the exhibited antipyretic activity but pronounced gastric ulcer's following oral administration for six consecutive days in rats at doses ranging from 0.5 to 8.0 gm/kg (Saxena et al. 1987). Studies on the ethanol (absolute) extract of the orange tubular calyx and its isolated carotenoid indicated significant anti-inflammatory activity at 200 mg/kg in carrageenan induced rat soluble protein A (SpA)-treated Balb/c mice without affecting the immunoglobulin (Ig)G and IgM levels suggesting the possibility of its use in the management of TNF-a in clinical disorders. In another study Paul et al. (2002) showed that a pre-treatment of silica exposed mice with leaf extract at 50 mg significantly prevented the accumulation of TNF-alpha in the broncheoalveolar lavage (BAL) fluid of mice. A similar study (Rathore et al. 2007) utilizing 25 mg/kg bd.wt. of the water soluble portion of the ethanolic extract of leaf and fruit to treat Freund's complete adjuvant induced arthritis in mice suggested its role as a modulator of pro- and anti-inflammatory cytokine balance. An acute oral no observable adverse effect level (NOAEL) of 2000 mg/kg was established for the extracts. An iridoid glycoside arbortristoside-A isolated from the ethanolic extract of seeds was found to possess significant (50 and 75 mg/kg) and dose dependent anti-inflammatory and antinociceptive activity which they suggested might be due to inhibitory action of prostaglandins (Das et al. 2008ab). The LD50 of the compound was found to be 500 mg/kg. A recent report on petroleum ether extract of leaves at 50 mg/kg and b-sitosterol isolated from the same extract showed significant analgesic activity in hot plate and acetic acid induced writhing test in mice as compared to standard drug pentazocine at 10 mg/kg and paracetamol at 50 mg/ kg and at the same dose showed significant (Gupta et al. 1993). Further when Arbortristoside A and C isolated from the seed were evaluated at 25 and 50 mg/kg they produced significant inhibition of PCA at 25 and 50 mg/kg and significant protection of mast cell degranulation induced

by compound 48/80 at 10 mg/kg due to its mast cell stabilizing activity when compared with DSCG. Thus both the compounds demonstrated significant anti-PCA and mast cell stabilizing activity in rats when given orally whereas DSCG is poorly absorbed when given orally (Gupta et al. 1995). The bark of the plant has also been checked for anti-histaminic activity. Petroleum ether chloroform ethyl acetate ethanol and aqueous extracts of Nyctanthes arbor-tristis bark were examined of which petroleum ether extract at 50 and 100 mg/kg showed maximum protection against mast cell degranulation by clonidine and resisted contraction (bronchodilation) induced by histamine at 50 and 100 mg/ kg (Nirmal et al. 2012a 2012b) better than other extracts which they proposed might be due to b-sitosterol. The potential of the extracts to inhibit histamine release seems evident from the above work by different groups with doses under acceptable limits. Though the toxicity studies have not been reported in any of these work but other reports of toxicity in similar extracts indicate a much safe level [27].

Conclusion

The study on Nyctanthes arbor-tristis Linn. demonstrates its significant analgesic and anti-inflammatory properties validating its traditional use in Ayurveda. Extracts from various parts of the plant including leaves flowers seeds and bark were tested through in-vitro and in-vivo methods showcasing their effectiveness in treating conditions like rheumatism sciatica and other inflammation-related ailments. The plant's therapeutic potential coupled with its minimal adverse effects and cost-effectiveness highlights its promise as a valuable herbal remedy. These findings support the growing interest in plant-based medications for their efficacy and safety in traditional medicine.

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