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TRADITIONAL MEDICINAL USES, PHYTOCHEMICAL PROFILE AND PHARMACOLOGICAL ACTIVITIES OF *NYCTANTHES ARBORTRIS*

Hetal Bhalakiya, Nainesh R. Modi*

Department of Botany, Bioinformatics and Climate Change Impacts Management, University School of Sciences, Gujarat University, Navrangpura, Ahmedabad, Gujarat, India.

ABSTRACT: *Nyctanthes arbortristis* (Oleaceae) is a mythological plant; and they have high medicinal values in Ayurveda. One of the oldest systems is ayurveda that uses plants and their extracts for treatment and management of various diseases. In India it is considered as one of the most useful conventional medicinal plant. It is considered as an important plant that yields not only unique medicinal products but also has industrial importance. It has several medicinal properties such as anti-helminthic and antipyretic, anti-inflammatory and anti-oxidant activities, hepatoprotective, anti-leishmaniasis, anti-viral, antifungal, anti-pyretic, anti-histaminic, anti-malarial, anti-bacterial besides it is used as a laxative, in rheumatism, skin ailments and as a sedative. The present review is focus on the potential phytochemicals and pharmacological activity of plant *N. arbortristis*. Diversity of plant part like seeds, leaves, flowers, bark and fruits have been investigated for their major pharmacological activity and phytochemicals and revealed the presence of flavanoid, glycoside, oleanic acid, essential oils, tannic acid, carotene, fraudulent, lapel, glucose and benzoic acid known for significant hair tonic.

KEYWORDS: *Nyctanthes arbortristis*, Chemical constituents, Pharmacological actions, Bio-prospection.

Corresponding Author: Hetal Bhalakiya* Ph.D.

Department of Botany, Bioinformatics and Climate Change Impacts Management, University School of Sciences, Gujarat University, Navrangpura, Ahmedabad, Gujarat, India.

1. INTRODUCTION

Conventional Medicine is the drug or care for based on traditional uses of plant existence, animals or their products, other natural substance (including some inorganic chemicals), cultural practices,

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and physical manipulations including affliction. As this system of medicine one-time in use almost unmovable generation subsequent to group throughout the ages for the treatment of a range of physical and psychological diseases, it is by tradition called. Most of the period, the type investigate and uses of traditional medicine be for the most fraction influenced by folklore, customs and the cultural habits, social practices, spiritual beliefs and, within many cases, superstitions of the people who set down or use them ^[1]. The earliest talk about of traditional medicine is established in Rigveda, the oldest repository of knowledge in this subcontinent. Later Ayurveda, developed from the Vedic concept of life, became the significant basis of all systems of therapeutic sciences. In course of time it became a part of culture and heritage of the people of the Indian subcontinent. The Greek word of a plant is 'Phyto' and chemicals created by plants are called phytochemicals/fito-chemicals. In plant flora, 25,000 phytochemicals be known to continue living and of them 10,000 are expected to be alkaloids and 4,000 flavonoids concentrated all around. *Nyctanthes arbortristis* is also called the "tree of sorrow", because the flowers lose their brightness throughout daytime; the methodical name arbor-tristis also means "shade tree". The flowers can be used as a resource of yellow dye for clothing. The blossom is the official flourish of the state of West Bengal, India, and for Kanchanaburi province, Thailand. *Nyctanthes arbortristis* (sometimes incorrectly cited as *Nyctanthes arbortristis* or *Nyctanthes arbo-rtristis*) Higher plants have a unique and rich collection of an assortment of biochemicals, so they are generally known as storehouses of chemo-therapeutants. Secondary metabolites are chemically and taxonomically different group of compound with unintelligible functions broadly used in research, agriculture, human therapy.

2. Plant Description

Coral jasmine, commonly known as night jasmine, is an aboriginal small tree, with a gray or greenish, rough and peeling bark. The shrub grows to a height of 10 meters. The simple leaves are opposite, with an entire edging about 6 to 12 cm long and 2 to 6.5 cm wide. The flowers are fragrant with a five-to-eight lobed corolla and orange-red center, often seen in a cluster of two to seven. The petals are snow white with dew drops sitting on them. The fruit is plane, brown and heart-shaped to round capsule, around 2 cm in diameter with two sections, each containing a single seed.

2.1 Growing season and type

This tree grows well in a variety of loamy soils and in soils found in average garden situations, with pH 5.6-7.5. The plant requires conditions varying from full sunlight to partial shade and needs to be watered regularly, but does not require overwatering.

(Source: https://en.wikipedia.org/wiki/Nyctanthes_arbor-tristis)

2.2 Ecological and distribution

In its native habit, *Nyctanthes arbortristis* found on rocky ground in dry hillside and as undergrowth in dry deciduous forests. *Nyctanthes arbortristis* Linn is native to India, distributed widely in sub-Himalayan regions and southward to river 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 the 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 [2,3]

3. Taxonomical classification[2]

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Lamiales

Family: Oleaceae

Genus: *Nyctanthes*

Species: *arbor-tristis*

Binomial name: *Nyctanthes arbor-tristis*

3.1 OVERVIEW OF FAMILY OLEACEAE

Oleaceae is a family containing 24 extant genera and around 600 species of mesophytic shrubs, trees and occasionally twiners. As shrubs, members of this family may be twine climbers, or scramblers.

Table 1.1: Some genera with common names of Oleaceae family [5]

Genera	Common name
Forsythia	
Abeliophyllum	White Forsythia
Chionanthus	Fringetree
Forester	Swamp-privet
Forsythia	Forsythia
Fraxinus	Ash
Jasminum	Jasmine
Ligustrum	Privet
Osmanthus	Osmanthus
Olea	Olive
Failure	Mock-privet
Syringa	Lilac

4. The plant is named in different vernacular languages.

Unani: Harasingaar.

Sanskrit: Parijatha.

Siddha: Pavazha motif.

Hindi: Harsingar.

Ayurvedic: Paarijaata, Shephaali, Shephaalika, Mandaara.

English: Tree of Sorrow, Night Jasmine, Coral Jasmine.

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Punjabi: Harsinghar.

Sanskrit: Parijata, Parijatah, Parijataka, Sephalika.

Thai: Karanikaa.

Filipino: Coral Jasmine.

Indonesian: Srigading (Sundanese, Javanese).

Vietnamese: Iai Tau.

Gujarati: Jayaparvati, Parijatak.

5. Characteristic Features of *Nyctanthes arbor-tristis*

Morphology:

5.1. Leaves

Leaves are opposite, 5 -10 of 2.5 – 6.3 cm, ovate, acute or acuminate, entire or with a few large, distant teeth, short bulbous hairs rounded or slightcuneate; main nerves few, conspicuous beneath; petiole 6cm long, hairy [4]. Leaves are simple, petiolate and stipulate The lamina is ovate with acute or acuminate apex, the margin entire or serrate, somewhat undulated, particularly near the base, the upper surface is dark green with dotted glands, and the lower surface is pale green and softly pubescent. *Nyctanthes arbor-tristis* venation is unicostate, reticulate with an average of 12 lateral veins leaving the midrib. The petioles are about 5– 7.7–10 mm long with adaxial concavity

5.2 Flowers

Flowers of *Nyctanthes arbor-tristis* are small with delightfully fragrant, sessile in pedunculate bracteates fascicles of 3 -5, peduncles 4- angled, slender, hairy, auxiliary and solitary and in terminal short dichotomous chymes, bracts broadly ovate or sub orbicular, 6- 10 mm long, acuminate, hairy on both sides; Calyx 6-8 mm long, narrowly campanulate, hairy outside, glabrous inside, truncate or obscurely toothed or lobed, ciliated. Corolla glabrous rather more than 13 mm long; tube 6-8 mm long, orange color, about equaling the limb; lobes white, unequally obcordate, Cincaste[5].

5.3 Fruits

Fruits of *Nyctanthes arbor-tristis* are a capsule of 1-2 cm diameter, long and broad, obcordate orbicular, compressed, 2-celled, separating into 2 flat 1- seeded carpels, reticularly veined, glabrous [6]. The macroscopic character of the fruit: The fruit is flat, brown and heart cordite-shaped to rounded-capsule, around 2 cm in diameter with two celled opening transversely from the apex, each containing a single seed. Microscopically fruit shows typical character of the fruit. In the epicarp epidermal cells are compactly arranged, polygonal cells with slightly anticlinal walls covered by a thin cuticle followed by 1, 3 layers of collenchymas, Spongy parenchymatous tissue, sclerenchymatous fibers and oil gland [3].

5.4 Seed

The seed is compressed and is 1 per cell [4] Seeds is exalbuminous, testa thick; the outer layer of large transparent cells and heavily vascularised [5]. phytosterols, phenolic compounds, tannins,

flavonoids, cardiac glycosides, saponins and alkaloids all are found in seeds of *N. arbortristis* [7].

5.5 Bark

Bark of *N. arbortristis* plant is dark gray or brown in color and rough and firm. Bark surface is dippled due to scaling off of circular barks and patchy due to gray brown color regions. Scaling off the bark by circular flakes. The inner bark is creamy white, soft and collapsed and non-collapsed phloem zone distinctly visible[5].

6. Traditional Uses

6.1 Traditional Uses flowers

The flowers are gathered for religious offerings and to make garlands. The orange heart is used for dyeing silk and cotton, a practice that started with Buddhist monks whose orange robes were given their color of this flower. The Parijata is regarded in Hindu folklore as one of the five wish-granting trees of Devaloka. Different parts of *Nyctanthes arbortristis* Linn are known to possess various ailments by tribal people of the Indian subcontinent with its use in Ayurveda, Sidha and Unani systems of medicines. Flowers The flowers are used as stomachic, carminative, astringent for bowel, antibilious, expectorant, hair tonic and in the treatment of piles and various skin diseases and in the management of ophthalmic purposes. The bright orange corolla tubes of the flowers contain a colouring substance nyctanthin, which is identical with α -Crocetin from Saffron. The corolla tubes were formerly used for dyeing silk, sometimes together with Safflower or turmeric. The flowers of *Nyctanthes arbortristis* are used in India, Indonesia (Java) and Malaysia to provoke menstruation. The hot combination of flowers is used by some elderly Sri Lankan Buddhist monks as a sedative. The inflorescence is used to treat scabies and other skin diseases. The flower helps in clearing out mouth ulcers [8]. Oral administration of the decoction of flowers ward off wind in the stomach, stimulate gastric secretions and improve expectoration from the lungs[8] The decoction is also used in the treatment of gout [10]. The flower juice is used as a hair tonic in preventing graying of hair and baldness[11].

6.2 Traditional Uses of leaves

The bitter leaves are used as a colleague, laxative, diaphoretic and diuretic. The leaf juice is used to expel roundworms and threadworms in children, to treat loss of appetite, piles, liver disorders, biliary disorders, chronic fever, malarial fever, obstinate sciatica and rheumatism. A decoction of the leaves is broadly used in Ayurvedic medicine to treat arthritis and malaria. The leaves are also used in fungal skin infection and in a dry cough. The young leaves are used as female tonic and in alleviating gynecological problems [12]. Leaves of *Nyctanthes arbortristis* Linn is used extensively in Ayurvedic medicine for the treatment of various diseases such as sciatica, chronic fever, rheumatism, and internal worm infections, and as a laxative, diaphoretic and diuretic. Leaves are used in cough reduction. Leaf juice is mixed with honey and given thrice daily for the treatment of cough. Paste of leaves is given with honey for the treatment of fever, high blood pressure and

diabetes. The juice of the leaves is used as digestives, antidote to reptile venoms, mild bitter tonic, laxative, diaphoretic and diuretic. Leaves are also used in the enlargement of the spleen. The leaf juice is used to treat loss of appetite, piles, liver disorders, biliary disorders, intestinal worms, chronic fever, obstinate sciatica, rheumatism and fever with rigors. The extracted juice of leaves acts as a cholagogue, laxative and mild bitter tonic. It is given with little sugar to children as a remedy for intestinal ailments [13].

Here is the Ayurvedic remedies supply indicative relief and prevent from complications of Nipah virus.

- Take 6–7 leaves, put in 200 ml of water and boil it and make into 100 ml decoction, at the end add pepper powder and 3 drops of lemon.
- Drink the Kashaya 3–4 times a day [14].

6.3 Traditional Uses of Stems

Traditionally the powdered stem bark is given in rheumatic joint pain, in treatment of malaria and also used as an expectorant. The bark is used for the treatment of snakebite and bronchitis. The stem bark pounded with *Zingiber officinale* and *Piper longum* is boiled in water and the resultant liquid is taken for two days for the treatment of malaria. The resulting paste on mixing with Arjuna bark is rubbed on the body to treat internal injury and for joint broken bones [13]. the bark is used for treatment of bronchitis and snakebite. Its roots are traditionally used as anthelmintics [15,16].

6.4 Traditional Uses of Seeds

The seed powder is used for scurvy, in alopecia and as anthelmintic. It is antibilious and an expectorant, and is also useful in bilious fevers. The powdered seeds are used to cure scurfy affections of scalp, piles and skin diseases [13].

7. Chemical constituents of *Nyctanthes arbortristis* Linn

7.1 Phyto-constituents from leaves

Leaves contain D-mannitol, β -sitosterole, Flavanol glycosides, Astragaline, Nicotiflorin, Oleanolic acid, Nyctanthic acid, Tannic acid, Ascorbic acid, Methyl salicylate, resinous substances, Amorphous glycoside, Amorphous resin, Trace of volatile oil, Carotene, Friedeline, Lupeol, Mannitol, Glucose, Fructose, Iridoid glycosides, Benzoic acid. All the important phytoconstituents are being used in Ayurvedic medication and reported for sciatica, arthritis, fevers, and various painful conditions and as a laxative [17].

7.2 Phyto-constituents from flowers

Flowers contain modified diterpenoid nyctanthin, flavonoids, anthocyanins and an essential oil which is related to that of jasmine [18]. Flowers have modified essential oil, Nyctanthin, d-mannitol, Tannin, Glucose, Carotenoid, Glycosides, β monogentiobioside ester of α -crocetin (or crossing-3), β monogentiobioside, β -D monoglucoside ester of α -Christian, β -digentiobioside ester of α -crocetin (or crossing-1). 1, anthocyanins and essential oil which is similar to jasmine¹⁹

Nyctanthin, tannin and glucose, carotenoid, glycosides viz. β -monogentiobioside ester of α -crocetin (or crossing-3), β monogentiobioside - β -D monoglucoside ester of α crocetin, β -digentiobioside ester of α -crocetin (or crossing-1), 4- hydroxy hexahydrobenzofuran-7-one also reported in flowers. The orange tubular calyx of the flower contains carotenoids [19]. It also contain an antiplasmodial cyclohexylethanoid, rengyolone, a new iridoidglucoside 6-O -trans-cinnamoyl-7- O-acetyl-6- β -hydroxyloganin and three known iridoidglucosides, arborside-C, 6- β -hydroxyloganin and nyctanthoside. Rengyolone was first isolated from Forsythia suspense (Oleaceae), an important plant of the crude drug "rengyo". It was also reported that Halleridone from the African medicinal plant Hallerialucida (Scrophulariaceae) and as a cytotoxic constituent from Cornuscontroversa (cornaceae). It was establish that after several months the mix abused-C has changed in the isomeric structure with the benzene group shifted to C-6-OH. This construction is named as isoarborside-C [20].

7.3 Phyto-constituents from seeds

Seeds contain Arbotristoside A&B, Glycerides of linoleic acid, oleic acid, lignoceric acid, stearic acid, palmitic and myristic acids, nyctanthic acid, 3-4 secotriterpene acid, a water soluble polysaccharide tranquil of D-glucose and D mannose. The seed of Nyctanthes arbortristis contains 15% of pale yellow brown oil, nyctanthic acid, nyctoside A, b-sitosterol, arbortristoside A & B, glycerides of linoleic oleic, lignoceric, stearic, palmitic and myristic acids, 3-4 secotriterpene acid and A water soluble polysaccharide composed of Dglucose and D mammals and used as an immunostimulant and hepatoprotective [20].

7.4 Phyto-constituents from stem

Stem contain β -sitosterol, Glycoside-naringenin-4-0- β -glucapyranosyl- α xylopyranoside and Flower oil Flower oil contains p-cymene α -pinene, 1- hexanol methyl heptanone, phenyl acetaldehyde, 1-deconol and anisaldehyde. β -Amyrin, arbortristoside-a, oleanolic acid, nyctoside-a, nyctantic acid and 6- β - hydroxyloganin [20].

75 Phyto-constituents from the Roots

The root part of the plant composed of alkaloids, tannins and glucosides. From the chloroform extract of the root β -Sitosterol and oleanolic acid has been isolated [20].

Table 1.2: Phytoconstituents from *N. arbortristis*

Chemical Class	Phytoconstituents				
	Stem	Flower oil	Flower	Seed	Leaf
Steroids [21,22]	β -sitosterol			β -sitosterol	β -sitosterol, D-mannitol β -sitosterole, Astragaline, Nicotiflorin, Oleanolic

					acid, Nyctanthic acid, Tannic acid, Ascorbic acid Methyl salicylate, Volatile oil Friedeline Label Mannitol Glucose
Alkaloids [24,25]	Nyctanthine				
Glycosides [24,25]	Naringenin-4'- O β - glucopyranosyl α - xylopyranoside		Cardiac glycosideny mphalin	Phenylpropano id Glycoside- nyctoside A	Flavonol Glycosides- astragaline, nicotiflorine
			Iridoid Glycosidesa rbortristosid e C, 6 β hydroxy loganin, 6- Otrans- acetyl-7- Ocinnamoy l- 6 β hydroxyl oganin, nyctanthosi de, isoarborside C	Eroded Glycosidesarbo rtristosides A, B, C, D and E	Eroded Glycosides- arborsides A, B, C, 6 β -hydroxyloganin, Desrhamnosylverbacos ide, 6,7-Di- Obenzoylnycthanoside , 6-O-transcinnamoyl- 6 β -hydroxyloganin, 7- Otrans-cinnamoyl-6 β - hydroxyloganin
Flavonoids [24,25]		Quercetin, Kaemferol, Apigenin, Anthocyanin			Nicotiflorin

Miscellaneous [26]		1-hexanol, methyl heptanone, phenyl acetaldehy de, 1- decanol, anisaldehy de	Rengylone, carotenoids, essential oil, crocetin	Nyctoside A, Glycerides of linoleic, oleic, lignoceric, stearic, palmitic and Myristic acid, polysaccharide composed of D-glucose and Dmannose, a pale yellow brown oil (15%)	Mannitol, Tannic acid, Ascorbic acid, methyl salicylate, traces of volatile oil, an amorphous resin, carotene, glucose, fructose, hexatriacontane, benzoic acid and benzoic ester of loganin
Terpenes [23,24]		α -pinene, pcymene	Diterpene- Nyctanthin	Triterpenes-3, 4- secotriterpene acid, nyctanthic acid	Triterpenes- β -amyrin, oleanolic acid, friedeline, lupeol

Table 3: Phyto-constituents present in various parts of plant [28]

Part Used	Pharmacological Effect
Bark	Antimicrobial
Flower Oil	Perfume
Flowers	Ant-Bilious Antifilarial Anti-Inflammatory Antioxidant Diuretic Dyspepsia Ophthalmic Sedative
Leaves	Anthelmintic Antibacterial L Antifungal

	Anti-Inflammatory Antioxidant Antipyretic Arthritis Asthma Bronchitis Cholecystagogue Constipation Cough Dyspepsia Flatulence Heartburn Hepatoprotective Immunopotencia L Nausea Reptile Venom Rheumatism Ringworm Sciatica
Seeds	Antibacterial Antifungal Alopecia Antileishmanial Hair Tonic Immunomodulatory Piles
Stem	Antioxidant Antipyretic Bronchitis Snakebite

8. Bio-prospection undertaken for *Nyctanthus arbor-tristis*

8.1) Anti Allergy Activity

The bark of the plant has also been checked for anti-histamine activity. Petroleum ether, chloroform, ethylacetate, ethanolaqueous extracts of *Nyctanthus 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 [29] better than other extracts which they proposed, might be due to B-sitosterol. The potential of extracts to inhibit histamine release seems evident from the above work by different groups, with does under acceptable limits. Though the toxicity studies have not been reported in any of this work, but other reports of toxicity in similar extracts indicate a much safer level. The pretreatment of guinea pigs exposed to histamine aerosol with a water soluble portion of the alcoholic extract of *N. arbor-tristis* leaves offered significant protection against the development of asphyxia. Arbortristoside A and arbortristoside C are present in *N. arbortristis* were reported to be anti-allergic [2].

8.2 Anti Anxiety

Hydroalcoholic extracts of *N. arbortristis* (NAT) have anxiolytic potential. Using hydro-alcoholic mixture, dried plant parts of *N. arbortristis* was extracted, concentrated by distilling off the solvent and then evaporated to dryness on the water bath and then stored in an airtight container in a refrigerator till used [31].

8.3 Anti-Inflammatory activity

The aqueous extract of the whole plant, alcoholic extract of stem and seeds and water soluble portion of the alcoholic extract of leaves of *N. arbortristis* were reported to have acute and sub-acute anti-inflammatory activity. The acute anti-inflammatory activity is evaluated in inflammatory models using different phlogistic agents viz. carrageenan, formalin, histamine, 5-hydroxytryptamine and hyaluronidase in the hind paw of rats. In the sub-acute models, *N. arbortristis* was found to check granulation tissue formation considerably in the granuloma pouch and the cotton pellet test. *N. arbortristis* is also found to inhibit the inflammation produced by immunological methods that are Freund's adjuvant arthritis and purified tuberculin reaction [33].

8.4. Hepatoprotective activity

Ethanol leaf extract of *Nyctanthes arbortristis* protects against carbon tetrachloride - induced hepatotoxicity in rat. For this investigation rats were pretreated with extract (1000mg/kg body weight/day, p.o. For 7 days) prior to the administration of a single dose of CCl₄ (1.0ml/kg, s.c.). The samples of blood were collected at 48 h after CCl₄ administration (9 day) from the abdominal aorta under pentobarbitone anesthetized (350mg/kg i.p.). Silymarin (70mg/kg body weight/day, p.o. For 7 days) were used as a reference standard. In this study the leaf extract of *Nyctanthes arbortristis* and silymarin restored all serum and liver parameters which were altered by (CCl₄) from the normal level, also prevent loss of body weight; both candidates are also protected against (CCl₄) induced increase in liver weight and volume. The mechanism involves the blockade of deactivation of (CCl₄) through inhibition of P 450 2E1 activity and or to accelerate the detoxification of (CCl₄). These effects may be mediated by the antioxidant present in the plant. In another investigation, the ethanolic and aqueous extract of the leaf of *Nyctanthes arbortristis* (500mg/kg oral route for 10

days) reversed the rise in serum AST and total bilirubin in (CCl₄) induced hepatotoxicity in animal models [30].

8.5. Antiviral activity

The ethanolic extract, n-butanol fractions and two pure compounds, arbortristoside A and arbortristoside C, isolated from the *Nyctanthes arbortristis* possess pronounced inhibitory activity against encephalomyocarditis virus (EMCV) and Semliki Forest Virus (SFV). The in-vivo ethanolic extract and the n-butanol fraction at daily doses of 125 mg/kg weight protected EMCV infected mice against SFV by 40 and 60% respectively 30, 30. Khatu na, haue me, mosaddik ma. Laboratory evaluation of *Nyctanthes arbortristis* Linn. Flower extract and its isolated compound against common floral vector, *Culex quinquefasciatus* say (dip. With respect to anti-viral activity, only two reports from ethanolic extract, n-butanol fraction and Arbortristoside A and C isolated from the seed of the plant were traced against Encephalomyocarditis virus and Semlinki forest virus both in vitro and in vivo [34]. Further, it has also been mentioned that Arbortristoside B, D and E were not active against these viruses.

9.6 Anti-Aggressive Activity

The fresh juice obtained from the leaves of the plant was found to have antimalarial activity. The 50% ethanolic extract of the seeds, leaves, roots, flowers and stem of the plant is proven to possess antiamoebic and antiallergic properties. Leaf extract of the plant showed antiinflammatory, analgesic, antipyretic and allergenic activities. The leaves, seeds and flowers of the plant were reported to exert immunostimulant activity. The water soluble fraction of the ethanolic extract is proven to possess tranquilizing, antihistamines, purgative effects and depletion of tumor necrosis. The arbortristoside an isolated from the seeds was found to have antitumor activity [35].

8.7 Anti-Filarial activity

The chloroform extract of the flowers and a pure compound isolated from *N. arbortristis* plant exhibit larvicidal activity against *Culex quinquefasciatus*, a common floral vector [36].

8.8 Antibacterial activity

Infectious diseases are the world's leading cause of premature death. Resistance to antimicrobial agents is conferred in a wide variety of pathogens and multiple drug resistance is becoming more common in diverse organisms such as *Staphylococcus aureus*, *Staphylococcus epidermis*, *Salmonella typhi*, *Salmonella paratyphi A*. In a study, it was reported that methanolic extract of leaves of *N. arbortristis* exhibited significant antibacterial activity against *Staphylococcus aureus*, *Staphylococcus epidermis*, *Salmonella typhi*, *Salmonella paratyphi A* with MIC value ranging between 1-8 mg/ml. The zone of inhibition and the Minimum Inhibitory Concentration (MIC) of the extracts were determined and compared with the standard drugs ciprofloxacin and fluconazole. The chloroform extract was found to have both antibacterial and antifungal activities, whereas the petroleum ether and ethanol extracts hold only antibacterial activity [37].

8.9. Antioxidant activity

Plants produce potent antioxidants and the use of *N. arbortristis* leaves as a decoction in Ayurvedic medicine for various ailments [39]. can be linked to the anti-oxidant activity of classes of compounds which aid in scavenging the free radicals mostly responsible for the pathogenesis. An initial report by Sunil Kumar and Muller (1999) evaluated the effect of the methanolic extract from the leaves of *N. arbortristis* on free radical induced lipid peroxidation using bovine brain phospholipid liposomes and found good activity with IC₅₀ values of 20 mg/ml. The aqueous extracts from the leaves of the plant have been first reported to have DPPH radical, hydroxyl radical scavenging activity, lipid peroxidation preventive property [41] however, the total flavanoid and phenolic content was found to be very low which was correlated to be the lowest antioxidant activity in comparison to other leafy vegetables. Thangavelu and Thomas (2010) indicated that ethanolic extracts of the leaves and stem of the plant are a potent source of antioxidants through assays like di-phenyl picryl hydrazyl (DPPH) radical scavenging assay, reducing power ability, hydrogen peroxide scavenging assay and total antioxidant assay. A study of the antioxidant activity of aqueous extract from the flower and its parts indicated that the DPPH radical scavenging activity is in the order of calyx > flower > petal. A further study on the fractioned alcoholic extract of the leaves showed antioxidant activity in the order of butanol (95.22%) > ethyl acetate (84.63%) > petroleum ether (82.04%) at 100 mg/ml as compared to 93.88% of ascorbic acid at 10 mg/ml [41]. A study by on acetone soluble fraction of ethyl acetate extract from leaves showed impressive antioxidant activity through DPPH, hydroxyl and superoxide radicals as well as H₂O₂ scavenging assays [42]. The fractions have been compared with standard antioxidants like α-tocopherol, BHT, and ascorbic acid and found to be comparable. They further proved it through gamma ray induced DNA damage and Fe (II) induced lipid peroxidation of liposomes. Methanolic extracts of the flowers also exhibit high phenolic content and antioxidant activities, interestingly aqueous extracts showed high enzymatic antioxidants [43]. Methanol extract and flavonoid fraction of leaves exhibited DPPH scavenging activity and strong ferric reducing activity with an IC₅₀ value of 63.670.29 and 61.970.15 mg/ml, respectively [44]. Summarizing the antioxidant activity, it may be concluded that leaves, stem and flower extracts containing phenolics and flavanoids are responsible for the antioxidant activity which overall were detected in extracts derived solvents of lower polarity. The report on an aqueous extract (higher polarity) conclusively indicated lower antioxidant activity.

8.10 Anticancer activity

Fruit, leaf and stem methanol extracts of *N. arbortristis* were tested for in vitro anticancer activities. Moderate activity was observed at 30mg/ml cans. With 71% inhibition of dried *N. arbortristis* leaf methanol extract and least inhibitory activity was observed at 10mg/ml cans. With 86% inhibition of breast cancer cell lines free of pathogens. A high degree of against human breast cancer cell lines (MDA-MB 231) was observed with *N. arbortristis* dried fruit methanol and the IC₅₀ values were

calculated to be 9.72mg and 13.8mg. The phytochemicals isolated from *N. arbortristis* dried fruit methanol are glycosides, tannins, phenols and steroids and are predicted to be responsible for this anticancer activity [36].

8.11 Anti-Diabetic activity

The anti-diabetic activity of methanol extract of root of *N. arbortristis* is comparable to that of diabetic control animals. The extract poses safe and strong anti-diabetic activity. The extract was prepared by extracting 50g root powders with 400mL of methanol for 18 hours by hot continuous extraction method. The methanolic extract was filtered and partitioned by using petroleum ether to remove impurities. The solvent was evaporated under pressure and dried in a vacuum. The dried extract of *N. arbortristis* thus obtained was used for the assessment of hypoglycemic activity. It reduces blood glucose levels after seven days at the 500 mg/Kg in rats compare with standard drug. It was found that methanolic extract of *N. arbortristis* roots were more effective in reducing the blood glucose level compared to the standard drug [45].

8.12 Antimalarial activity

Clinical study on 120 patients of malaria. Administration of fresh paste of medium sized 5 leaves of *N. arbortristis* thrice a day for 7-10 days has cured the disease in 92 (76.7%) patients within 7 days. Another 20 patients were cured by 10 days while the remaining 8 patients did not respond to the treatment. The paste was well tolerated and no severe side effects were reported. Screening of methanol and chloroform extract of leaves for mosquito larvicidal activity against 3 major mosquito vectors-aedesaegypti, Culex quinquefasciatus and Anopheles stephensi has found the two extracts to kill larvae of A. Stephens with LC50 values of 244.4 and 747.7 ppm, respectively [46].

8.13 Anti-Parasitic activity

A crude 50% ethanolic extract of the leaves has been reported to exhibit trypanocidal activity at 1000 g/ml concentration. In vivo studies revealed that the extract exerted antitrypanosomal effects at doses of 300 and 1000 mg/Kg, significantly prolonged the survival period of Trypanosoma evansi infected mice. However, it is also reported that as soon as the treatment with the extract is discontinued, the parasitemia increases and results in the death of the experimental animals. *N. arbortristis* extract has also exhibited potent anti-leishmanial activity in Leishmania donovani infected hamsters. The 50% ethanolic extracts of the seeds, leaves, roots, flowers and stem of the *N. arbortristis* have been found to clear Entamoeba histolytica infections in rat cecum. However, the extracts were not active in vitro. The water soluble portions of ethanolic extract of flowers, bark, seeds and leaves of *N. arbortristis* were found to possess anthelmintic activity which is suggested due to inhibition of motility by relaxing and depression responds to contractile action of acetylcholine [46,47,48].

8.15 Anti-Trypanosomal Potential Antitrypanosomal

The potential of a crude 50% ethanol extract of *Nyctanthus arbortristis* leaves were evaluated in

vitro and in vivo. The extract exhibited trypanocidal activity at the highest concentration (1000 µg/ml) tested. In vivo studies revealed that the extract exerted antitrypanosomal effects at doses of 300 and 1000 mg/kg, intraperitoneally and significantly prolonged the survival period of the *Trypanosoma evansi* infected mice. However, as soon as the treatment with the extract was discontinued, the parasitemia increased and resulted in the death of the experimental animals [49].

8.16 Anti-Leishmanial Activity

The anti-leishmanial activity of *N. arbortristis* has been attributed to iridoid glucosides, arbortristosides A, B, and C and 6-b-hydroxyloganin. The arbortristosides A, B, C, and 6- beta-hydroxy-loganin exhibited both in vitro and in vivo anti-leishmanial activity against amastigotes in macrophage cultures and hamster test systems, respectively [50].

8.17 Anti-Histaminic and Anti-Tryptaminergic activity

The aqueous solubility of the alcoholic extract of *N. arbortristis* leaves (4.0 and 8.0g/kg oral) significantly protect against histamine aerosol - induced asphyxia (2% at 300 mm Hg) in guinea pigs. arbortristosid A and arbortristosid C present in *N. arbortristis* was reported to be anti-allergic [51].

8.18 Anti-Cholinesterase activity

The aqueous extract of *N. arbortristis* stimulated the activity of acetylcholine esterase in mice; it antagonizes the inhibition of this enzyme by malathion. The higher effects were seen in the serum than in the brain. The low anti muscarinic activity against acetylcholine induced contractions of isolated rabbit ileum was already reported [52].

8.19 Anti-Nociceptive and Antipyretic activity

The extract exhibited the antipyretic effect against brewer's yeast-induced proxies in rats. When administered orally for six successive days in rats, it produced dose-dependent gastric ulcers. The aqueous soluble fraction of ethanolic extract of the leaves exhibited significant aspirin-like anti-nociceptive activity which was evidenced by inhibition of acetic acid induced writhing in albino mice, but fails to elicit morphine like analgesia which was tested via the rat tail flick and mouse tail-clip method [53].

8.18 Anti-Anemic Activity

A research was performed as a hematological study on the ethanolic extracts of the flowers, barks, seeds and leaves of the plant and noticed the dose dependent rise in hemoglobin content and red blood cells count in rats. The extracts also protect the decline of hemogram profile in anemic rats [54].

8.19 CNS depressant activity

It was reported that the leaves, flowers, seeds and barks (600 mg/kg) of *N. arbortristis* exhibited significant and dose dependent prolongation of onset and duration of sleep and found to cause a decrease in dopamine and increase serotonin level from which it can be resolved that the CNS depressant activity of the ethanol extracts of seeds, leaves and flowers may be due to the decrease

in dopamine and increase in serotonin level [55].

8.20 Essential oils

The essential oil in the fragrant flowers, which is similar to the oil in *N. arbortristis*, is used as a perfume [56].

8.21 Membrane Stabilizing Activity

From a research work of *N. arbortristis* isolated a carotenoid Anglican Ag-NY1 from the orange colored tubular calyx of flowers. The compound exhibited a good membrane stabilizing activity as compared to the corresponding glycoside crossing [57].

8.22 Sedative Activity

The sedative potential of a hot infusion of the flowers was examined in rats. In this test, male rats exhibited a dose dependent conscious sedative activity while female rats remained unaffected. At these doses, muscle strength and cardio *Nyctanthes arbortristis* were not affected, nor was blood glucose levels affected even at the highest dose. However, glucose absorption from the small intestine was significantly reduced. The sedation was attributed, in part, to the antioxidant and membrane stabilizing activity of the extract [58].

8.23 Treatment of Piles, Gout, Dry Cough

The seeds of *N. arbortristis* are used in the treatment of piles. The decoction of *N. arbortristis* flowers are used in the treatment of gout. Leaves are used against dry cough. The aqueous paste of the leaves is used externally in the treatment of skin related troubles specifically in the treatment of ringworm. The young leaves are used as a female tonic. *N. arbortristis* also has hypoglycemic effect, potentiating action of exogenous insulin and streptozotocin- induced diabetic rat model [43].

8.25 Toxicity

N. arbortristis showed the toxic effect of ethanol extract of leaves in rats. The median lethal dose (LD) 16 GM/kg was observed in rats. No mortality was at 2.0 mg/kg, while 75% mortality was seen at a 32 mg/kg dose. An administration of ethanol extract of the leaves (1, 2 and 4 mg/kg/day) orally for 6 consecutive days is produced gastric ulcers in rats. This extract also showed irritant effects as it, dose-dependently, the formation of unformed semi-fluid collagens pasty stools in albino mice because of a purgative effect. When extract installed into the rabbit's eye produced conjunctival congestion with edema, while the person who grounded the dried leaves developed vesicles on both palms [59].

8.24 Other activities

Acetone extract of the seeds exhibit ovicidal effect on the eggs of rice moth, *Corcyra cephalonica*. The inhibition of egg hatching increased with increase in concentration of plant extracts in contact toxicity test. 80.73% ovicidalaction was observed at 100% concentration of the extract. Petroleum ether extract of *N. arbortristis* also exhibits insecticidal activity against *Bagrada cruciferarum*. The ethanolic extract of *N. arbortristis* leaves, seed and roots were screened in humoral and cell-

mediated immune responses against *Candida albicans* and *Salmonella* antigens. The water soluble portion of an ethanol extracts of the leaves exhibits significant aspirin like anti-nociceptive activity but failed to produce morphine like analgesia. It was also found to possess anti-pyretic activity against brewer's yeast induced pyrexia in rats. The extract also produced gastric ulcers following oral administration for six consecutive days in rats. An Ethanolic extract of the whole plant has been reported to initiate hair growth [60,61,62,63,64,65].

2. CONCLUSION

N. arbortristis has tremendous potential pharmacological activities. Pharmacological activities are widely distributed in medicinal plant of and it is revealed as important of herbal and ayurvedic pathway for effective treatment of various diseases. The preliminary experimentations of biomedical studies related to metabolic conditions like inflammation, allergy, diabetes, duress, hepatoprotection or immunomodulation have been helpful in pointing out the correlation between the biological activity and nature of the chemical constituents with toxicity in some instances. Parallel to the above observation, studies related to infectious conditions like malaria, trypanosomiasis, leishmaniasis or through microbial pathogens have shown that the activities are more pronounced in crude extracts rather than pure molecules, with fairly positive toxicological information. Since the bioactivity guided fractionation studies in most of the conditions have diminished efficacy, efforts towards combination therapy involving therapeutic entities prone to resistance development could be one of the future directions. Further, mechanism of action studies would further support the therapeutic claims. A bird's eye view on the reviewed literature indicates a gap in scientific studies that needs attention in terms of corroboration studies as claimed in the traditional system of medicine. Some of the validation studies, like anti-viral, ophthalmic problems, bronchitis, antidote to snake venom besides piles and gynecological studies have not been touched upon. However, some of the studies get indirectly correlated with biological activities like intestinal worms, through anti-helminthic activity, gout through analgesic and anti-inflammatory activity and anxiety and restlessness through CNS modulatory activity.

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CONFLICT OF INTEREST

Authors have no any conflict of interest.

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