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Phytoconstituents and therapeutic potential of *Nyctanthes arbortristis* Linn.

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ABSTRACT

Nyctanthes arbortristis Linn. is one of the well known medicinal plant. It is a common wild hardy large shrub or small tree. It is a native of India, distributed wild in sub-Himalayan regions and southwards to Godavari. Different parts of this plant are used in Indian systems of medicine for various pharmacological actions. The rural people of Orissa use *Nyctanthes arbortristis* L. to cure various ailments. It's claimed traditional uses have been proved on scientific basis using in-vitro and in-vivo experiments. The present study will give comprehensive information on the chemical constituents and mainly pharmacological activities of this plant.

KEYWORDS: *Nyctanthes arbortristis* L., Pharmacology, Phytochemistry, Review.

INTRODUCTION

Since his existence on planet, man has been dependent on nature for curing various body diseases. From ancient civilization various parts of different plants were used to eliminate pain, control suffering and counteract disease. Most of the drugs used in primitive medicine were obtained from plants and are the earliest and principal natural source of medicines. The plants used as drugs are fairly innocuous and relatively free from toxic effects or were so toxic that lethal effects were well known. The nature has provided the storehouse of remedies to cure all ailments of mankind. There is no doubt that plants are a reservoir of potentially useful chemical compounds which serve as drugs, are provided newer leads and clues for modern drug design by synthesis (1-3).

Of large number of plant species reported on the ethnobotany interest, *Nyctanthes arbortristis* Linn. belonging to family Oleaceae is a well known medicinal plant. This review is to give comprehensive information on the chemical constituents and medicinal importance of *N. arbortristis*.

N. arbortristis is commonly known as Harsinghar or Night Jasmine. *Nyctanthes* means 'night flowering' and *arbortristis* means 'the sad tree' as it loses its brightness during daytime. The plant is known by the following names in the languages mentioned against.

Sanskrit	: Parijatha	Bengali	: Sephalika
English	: Night Jasmine	Hindi	: Harsinghar
Malayalam	: Parijatakam	Marathi	: Parijathak
Gujarathi	: Jayaparvati	Telugu	: Pagadamalle
Oriya	: Gangasiuli	Kannada	: Parijatha.

N. arbortristis is a native of India, flourishing wild in sub-Himalayan regions ranges from the chenabs to Nepal, Assam,

Burma, Bengal, Central India like Chhatanagpur, Rajasthan, Madhya Pradesh and southwards to Godavari. It is cultivated in many parts of India. It is also planted in Indian gardens for ornamental purposes due to its highly fragrant flowers. Its flowers open at the evening and drops at sunrise. In its natural habitat, it grows gregariously and covers dry deep hillsides and rocky gardens (2-6).

TAXONOMICAL CLASSIFICATION:

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Lamiales
Family: Oleaceae
Genus: *Nyctanthes*
Species: *Arbortristis*

BOTANICAL DESCRIPTION

N. arbortristis is a shrub or small tree up to 10m heights with gray or greenish rough bark with stiff whitish hairs; young branches sharply quadrangular. Leaves are opposite, 5 -10 by 2.5 - 6.3 cm, ovate, acute or acuminate, entire or with a few large distant teeth, short bulbous hairs rounded or slightly cuneate; main nerves few, conspicuous beneath; petiol 6cm long, hairy. Flowers are small, delightfully fragrant, sessile in pedunculate bracteate fascicles of 3-5; peduncles 4-angled, slender, hairy, auxiliary and solitary and in terminal short trichotomous cymes; bracts broadly ovate or suborbicular, 6-10 mm long, apiculate, hairy on both sides; Calyx 6-8 mm long, narrowly campanulate, hairy outside, glabrous inside, truncate or obscurely toothed or lobed, ciliated. Corolla globous rather more than 13 mm long; tube 6-8 mm long, orange colored, about equaling the limb; lobes white, unequally obcordate, cuneate. Fruits are a capsule of 1-2 cm diameter, long and broad, obcordate or nearly orbicular, compressed, 2-celled, separating into 2 flat 1-seeded carpels,

reticularly veined, glabrous. Seeds are exalbuminous, testa thick; the outer layer of large transparent cells and heavily vascularised (2-6).

ETHNOPHARMACOLOGY

Different parts of *N. arbortristis* are known to possess various ailments by rural mainly tribal people of India (Orissa and Bihar) along with its use in Ayurveda, Sidha and Unani systems of medicines. They have also been investigated for various pharmacological actions. Juice of the leaves is used as digestives (3), antidote to reptile venoms (4), mild bitter tonic, laxative, diaphoretic and diuretic (2, 4, 6). Leaves are also used in the enlargement of spleen (5). Leaf decoction (one teaspoonful twice a day) is given with honey to cure fever, malaria and blood dysentery by the folk people of Balasore, Orissa (7). The tribal people of Orissa use the juice of three to seven leaves as blood purifier to prevent skin infections (7). Two ounces of its infusion is useful in fever and rheumatism (3-7). A decoction of the leaves is a specific for obstinate sciatica (3-7) and so given one teaspoonful twice a day for three days to treat body ache in Dhenkanal District of Orissa (7). Upper surface of leaf is used to scratch eczematous patches by the tribal people of Orissa (7). Six or seven of the young leaves are rubbed with water and a little fresh ginger and administered in obstinate fever of the intermittent type by the tribal people of Bihar (4-7). Leaves are given with honey or sugar mixed with common salt for anthelmintic activity mainly in intestinal worms like round and tape worms mainly in children by the tribal people of Balasore, Orissa (4-8). One teaspoonful of leaf decoction with honey is given at bed time as antibilious and expectorant to cure cough by the folk people of Orissa (6-7). The extracted leaf juice is acrid and bitter and useful as colagogue and laxative (4-7). The leaves are also used in menorrhoea and ulcer (8). The powdered seeds are used to cure scurfy affections of scalp (4, 6-7) and in piles and skin diseases (5). Traditionally the powdered stem bark is given in rheumatic joint pain, its oil is used for pain in the eye and with Arjuna bark it is rubbed on the body in internal injury (5). The bark of the plant is expectorant (6). About 5 grains of the barks are eaten with betel nut and leaf to promote the expectoration of thick phlegm (4-7). Bark and flower decoction are usually given in malarial fever (7). Stem bark with *Zingiber officinale* and *Piper longum* pounded together and boiled in water. The resultant liquid is taken for two days to treat Malaria by the tribal people of Orissa (7). The resulting paste on mixing with the bark with that of Arjuna is rubbed on the body in case of internal injury. It is also used to joint broken bones (7). Its flowers are bitter, astringent, carminative, stomachic and used in ophthalmic purposes (2, 4). The flower juice is used as a tonic to the hair in preventing greying of hairs and baldness (7). Decoction of its roots is used in enlargement of spleen (5). Its roots are traditionally used as anthelmintics (7) and barks as antidyseric and anti diarrhoeals (8). The corolla tubes are formerly used to dyeing silk (6). The woods form a batten base for tile or grass thatch of the roofs. Young branches are used for making baskets. The bark of the tree may be used as

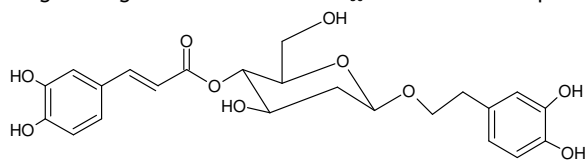
a tanning material and leaves for polishing wood and ivory (6).

PHYTOCHEMISTRY

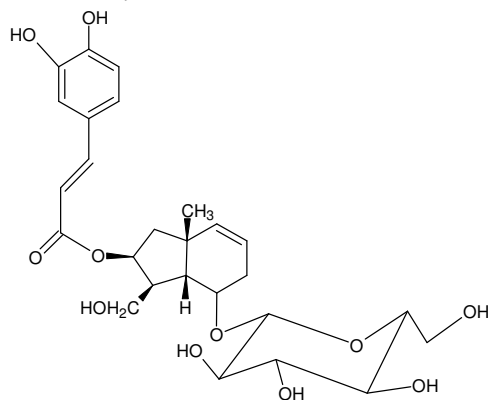
Leaves of *N. arbortristis* contain an alkaloidal principle named nyctanthine, they also contain mannitol, astringent principles, resinous substances, ascorbic acid, alkaloids (nyctanthin), coloring matters, sugar and traces of an oily substance, tannic acid, methyl salicylate, carotene, an amorphous resin and trace of volatile oil. Seed kernels yield 12-16% of the pale yellow brown fixed oil, which consists of contain fixed oil containing glucosides of linoleic, oleic, lignoceric, stearic, palmitic acid and β -sitosterol (4-9). On keeping the oil several weeks at 0°, a tetracyclic triterpenoid acid named nyctanthic acid is deposited (6). Flowers contain essential oils, coloring matter (nyctanthin), mannitol, tannin and glucose. Its roots are composed of alkaloids, tannins and glucosides (4-8). The bark contains a glycoside and two alkaloids, one soluble in water and the other in chloroform. The glycoside increase the amplitude of the frog's heart in small doses, but in large doses diastolic period is decreased till the heart stops with A-V block, it also depresses the CNS. The water soluble alkaloid stimulates the ciliary motility of oesophagus; the chloroform soluble alkaloid has no such action (6).

The plant is mainly investigated for flavonoids and iridoid glucosides. Desrhamnosylverbascoside was reported to be present in the leaves (9). New benzoic esters of loganin and 6 β -hydroxy loganin (10) were found to be present in its leaves. A minor glucoside Arborside D was found out in the leaves of *N. arbortristis* and assigned as 10-benzoyl nyctanthoside (11). From the leaves of *N. arbortristis*, two iridoid glycosides, 6,7-di-O-benzoyl nyctanthoside and 6-O-trans-cinnamoyl-6 β -hydroxyloganin have been isolated along with the previously reported iridoid, 7-O-trans-cinnamoyl-6 β -hydroxyloganin (12). Iridoid glucosides along with nyctanthic acid, oleanolic acid, friedelin, β -sitosterol glucoside, 6 β -hydroxy loganin and arbortristoside- A (13), B (14, 15), C (14, 16) have been proved to be present in its seeds. Prophylactic treatment with the ethanol extracts of the leaves, seeds and roots of *N. arbortristis* provided significant protection to swiss mice against *Candidia albicans* systemic infection. The protective effect of these extracts may possibly due to the strong stimulatory activity of arbortristoside-A and C elicited by significant increase in humoral and delayed type hypersensitivity response to sheep red blood cells and macrophage migration index in mouse (14). Arbortristoside-A and C showed significant inhibition of passive cutaneous anaphylaxis in a dose dependent manner which proved to be due to its mast cell stabilizing activity (16). Arbortristoside-A, B and C and 6 β -hydroxyloganin isolated from the seeds showed antileishmanial activity both in-vitro (against amastigotes and macrophage cultures) and in-vivo (in hamsters) test systems (17). Phytochemical examination of the stem of *N. arbortristis* resulted in the isolation and identification of β -sitosterol a new glycoside naringenin-4'-O- β -glucopyranosyl- α -xylopyranoside (17). A phenyl propanoid glycoside, nyctoside-A (18), water soluble glucomannan (19) was found in its seeds. After extracting the polysaccharides

from its seeds and then acid hydrolysis of fully methylated polysaccharides gave 2,3,4,6-tetra and 2,3,6-tri-O-methyl-D-glucose along with 2,3,6-tri and 2,3,-di-O-methyl- D-mannose. Two iridoids having trans-cinnamoyl and benzoyl ester groups respectively at C-7 in stead of p-methoxy cinnamoyl ester groups in arbortristoside A were found from the seeds of this plant (21). Its flowers have been investigated for anthrocyanin (22). The chloroform extract and the isolated compound (NCS-2) from its flowers were found to have larvicidal activity against common filarial vector, *Culex quinquefasciatus*. The results were also showed that the late instar larvae were more resistant to the extracts than the early instars (23). The potential cytotoxic effect of a new benzofuran derivative, 4-hydroxy hexahydrobenzofuran-7-one isolated from its flowers was evaluated on Ehrlich Ascite Cacinoma cells in swiss albino mice. The compound inhibited the cell growth by 43.27% only and found to have no significant cytotoxic effect on mice. A new benzofuran (3-3a-,7, 7a-tetrahydro 3a-hydroxy-6 (2H) benzofuran) has been reported to be present in its flowers and found to have significant antibacterial activity against both gram positive and gram negative bacteria. The LD₅₀ value of the compound

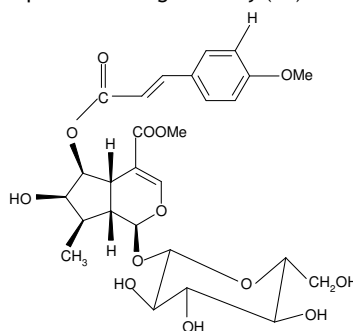


Desrhamnosylverbascoside

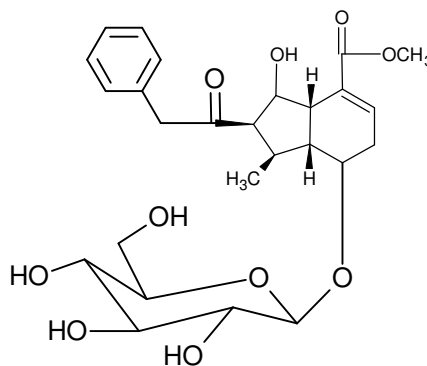


Arbortristoside B

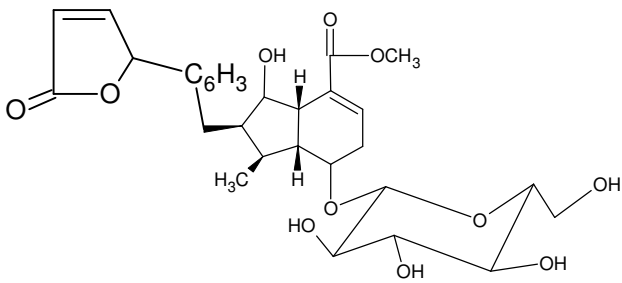
was found to be 8.73 mg/kg in brine shrimp lethality bioassay (24). The ethanol extract from the flowers of this plant was fractionated to isolate an antiplasmodial cyclohexylethanoid, rengyolone; a new iridoid glucoside, 6-o-trans-cinnamoyl-7-o-acetyl-6 β - hydroxyloganin; and three known iridoid glucosides, arborside C, 6 β - hydroxyloganin and nyctanthoside. Rengyolone and its acetate derivative exhibited antiplasmodial activity against *Plasmodium falciparum* (26). Except these 6 β - hydroxyloganin, nyctanthoside, arborside-C and Isoarborside-C were also identified in the flowers of *N. arbortristis* (29). The ethanolic extracts, various fractions and two pure compounds (arbortristoside A and C) isolated from *N. arbortristis* were tested against Encephalomyocarditis virus (EMCV) and Semliki Forest virus (SFV). Pronounced in-vitro antiviral activity was observed with the ethanolic and n-butanol fractions as well as with arbortristoside A and C. The ethanolic extracts and n-butanol fraction protected EMCV and SFV infected mice a daily dose of 125 mg/kg body weight (31). The ethanolic extracts and the isolated carotinoid from the extract of *N. arbortristis* inhibited carrageenan induced rat paw edema significantly (36).



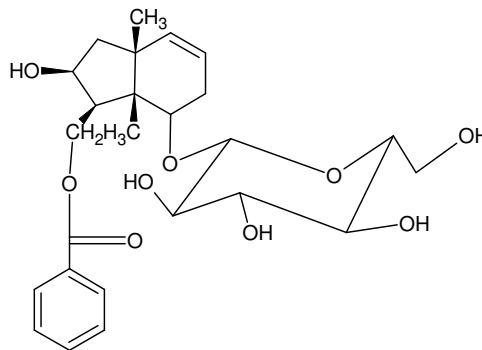
Arbortristoside -A



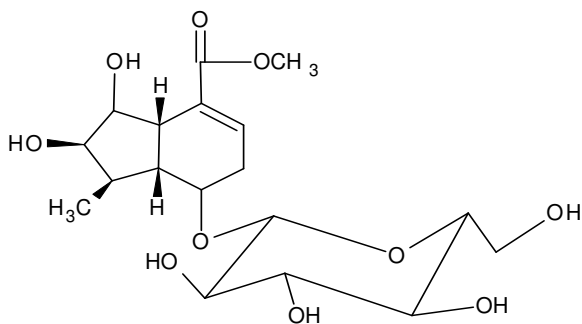
Arbortristoside C



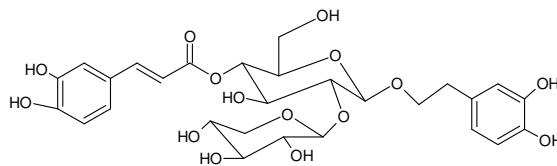
Arborside C



Arborside D



6B- hydroxyloganin



Nyctoside A

PHARMACOLOGICAL ACTIONS

The claimed traditional medicinal uses have been proved on scientific basis using in-vitro and in-vivo experiments. The ethanolic, aqueous and hydroalcoholic extracts of the leaves were established for antibacterial activity against both antibiotic resistant and nonresistant strains of *Staphylococcus aureus* (26). The water soluble portion of the alcoholic extract of the leaves was found to have antihistaminic activity by Saxena *et al* (27-28). The water soluble portion of the ethanolic extract of the leaves was investigated for some CNS activities (viz. hypnotic, tranquillizing, local anesthetics). The extract produced general depression of spontaneous motor activity and significantly increased pentobarbitone induced sleeping time (27-12). Moreover the extract exhibited hypothermia effect and significant purgative activity. Ratnasooriya *et al.*, have taken an attempt to establish the sedative effect of hot flower infusion of *Nyctanthes arbortristis* on rats. The results showed sedation in rats, which was due to antioxidant and membrane stabilizing effect (30). Deshmukh and Juvekar screened anxiolytic, antistress and nootropic activity of the methanolic extract of the leaves. The results of this study showed that the treatment with the extract ameliorated the stress induced variations in the biochemical levels of corticosterone, glucose, triglycerides, dopamine, 5-HT and norepinephrine. From which it was concluded that a significant anxiolytic, antistress and nootropic activity with utility in oxidative cognitive impairment due to its antioxidant potential (31). Fresh juice of the leaves is proved to have antimalarial activity by Badam *et al.* and Aminudin *et al.* (32-33). Anti-inflammatory activity of the alcoholic extracts of the leaves, flowers, stem and

fruits were studied on carrageenan induced rat paw edema model. All the extracts showed significant anti-inflammatory activity (34-37). The water insoluble fraction of its leaves inhibited the acute inflammatory edema produced by different phlogistic agents viz. carrageenan, formaline, histamine, 5-HT and hyaluronidase. It also inhibited the inflammatory swelling in the knee joint of rats induced by turpentine oil. In subacute models, it was found to check granulation tissue formation significantly in the granuloma pouch and cotton pellet test. Acute and chronic phases of formaldehyde induced arthritis were significantly inhibited. It was also found to inhibit the inflammation produced by immunological methods (37). Saxena *et al.*, investigated the analgesic, antipyretic and ulcerogenic activity of *N. arbortristis* leaf extract and observed to have significant analgesic and antipyretic activity. It was also found to produce gastric ulcers following oral administration for six consecutive days in rats (38). Gyanchandrani *et al.*, reported that arbortristosides from its leaves modulate murine peritoneal macrophages and intracellular killing of *Candidia albicans* (39). Strong stimulation of antigen specific and non specific immunity by increases in humoral and delayed type hypersensitivity response to sheep red blood cells and in macrophase migration index has been demonstrated in mice fed with 50% ethanol extracts of seeds, flowers and leaves of this plant. Maximum activity was found in the seeds in which the active principles appear to be mainly associated with lipids (40). Oral administration of the water soluble portion of the ethanolic extract of its leaves in mice showed consistent depletion of factor- α (TNF- α) in the plasma of soluble protein A treated mice and interferon- γ level without affecting IgM and IgG levels from the host plasma (41). Gupta *et al.*,

screened the alcoholic extract of its seeds, leaves and roots for anti-allergic activity and found to have significant effect (42). Its antifungal activity of the leaves was established against *Alternaria alternata* (43). The antifungal activity of the extracts is evident from their inhibitory effects on mycelial growth of dermatophytes and related keratinophilic fungi (44). The aqueous extracts of the leaves and seeds were proved to have anti-hepatotoxic activity against CCl₄ induced hepatotoxicity (45-46). Hukkeri *et al.*, established that the alcoholic and aqueous extracts showed significant hepatoprotective activity by reducing the levels of SGPT, SGOT and serum bilirubin (total and direct). The results were supported by histopathological studies of liver samples which showed regeneration of hepatocytes by the extracts (47). An attempt had been made to evaluate the antitrypanosomal activity of 50% ethanol extract of its leaves and found to possess significant activity (48). Methanolic extract of the leaves was reported to possess anti-influenza activity by Rajbhandari *et al* (49). Aqueous extract of the leaves was observed to possess anti-edema activity by Thane *et al* (50). Alcoholic extract of the leaves was reported to prevent the accumulation of Tumor necrosis factor- α in bronchoalveolar lavage fluid. The extract was also effective against silica induced early fibrinogenesis reaction like congestion, edema and infiltration of nuclear cells in the intestinal alveolar spaces and thickening of alveolar septa in mouse lungs. This was concluded that the leaf extract of *N. arbortristis* helps in bypassing silica induced fibrinogenesis of lungs of mice (51). The 50% ethanolic extracts of the leaves, seeds, flowers and stem of *N. arbortristis* showed promising effect in clearing *Entamoeba histolytica* infections in the caecum of rats (52). The methanol extract of *N. arbortristis* stem bark was evaluated for antispermatic activity in male albino rats. The treatment resulted in impairment of testicular function and affects on the spermatogenesis with the changes in structural activity of Sertoli cell and Leydig cell in rats (53). Osteoinductive property of the aqueous suspension of the Parijata roots was reported by Kumar *et al* (54). The ethanolic extracts, different fractions and the pure compound from *N. arbortristis* L were tested against Encephalomyocarditis virus and Semliki Forest virus. The results showed pronounced in vitro virus inhibitory activity with ethanolic extract and n-butanol fraction as well as pure compounds, arbortristiside-A and arbortristiside-C. Ethanolic extracts and n-butanol fraction protected viral infected mice at a daily dose of 15 mg/kg body weight (55). The acetone-soluble fraction of its ethyl acetate extract showed impressive antioxidant activity as revealed by several *in vitro* experiments, e.g., DPPH, hydroxyl and superoxide radicals, as well as H₂O₂ scavenging assays. Moreover, its preventive capacity against Fe (II)-induced lipid peroxidation of liposomes and γ -ray-induced DNA damage also confirmed this. The strong reducing power and high phenolics and flavonoids contents could be responsible for the antioxidant activity (56).

CONCLUSION

The plant *N. arbortristis* is one of the most important sources of medicinally important phytochemicals widely

experimented by scientists. So far most of the scientific works have been conducted on the leaves and seeds of *N. arbortristis* plant although there are reports about using bark powder and root extract in folk medicine. From these studies it reveals that the main active constituents in those plant parts are 6 β -hydroxyloganin, propanoid lucosides (nyctoside-A), iridoid glucosides (arbortristiside-A, B and C) along with other glucosides like arbortristiside-C, arbortristiside-D and isoarbortristiside-C. The main initiation to such a huge number of investigations on this plant came from Ethnopharmacology where a number of uses of all the parts of this plant have been cited. So far major uses have been found on the extracts of leaves of *N. arbortristis* which include from bitter tonic to digestive, laxative, diaphoretic, diuretic, in spleen enlargement, to cure malarial fever, blood dysentery, blood purifier, obstinate sciatica, body ache, anthelmintic, expectorant, menorrhoea, ulcer even as antidote to reptile venom. Powdered seeds have been in use to cure scurfy affection of scalp and in piles and skin diseases. Powdered stem bark are used traditionally in rheumatic joint pain and internal injury. The bark is also used as expectorant along with other adjuvants. The flowers as such are bitter, astringent, carminative, stomachic and so used in some of the ophthalmic purposes. The juice of the flowers is used to prevent graying of hairs and baldness.

The reason for the recent scientific work on the leaves of this native plant may be due to presence of number varied chemical constituents right from alkaloids to resinous substances, sugars, ascorbic acid, traces of oily substances, coloring matter, tannic acid, methyl salicylate, carotene and traces of volatile oil. Seed kernels are reported to yield 16% of the pale yellow fixed oil which is glucosides of linoleic, oleic, lignoseric, stearic, palmitic acids along with β -sitosterol. The flowers contain essential oils, coloring matter (nyctanthin), mannitol, tannins and glucosides, while the barks contain alkaloids and glucosides mainly.

The major pharmacological works worth mentioning on the various chemicals like iridoid glucosides and alkaloids.

Pharmacological properties of the plant parts have been studied from different perspectives like amoebicidal, antifungal, anthelmintic, antitrypanosomal to antidepressant, antiviral, immunomodulatory to antidepressant, tranquilizing, antiedematous and anti-inflammatory. Of all these activities, by far the most potent one may be the anti-inflammatory activity of the leaf extracts. Thus it is worthwhile to reveal the mechanism of action of the phytochemicals present in the leaves in order to disclose it as a potent medicinal agent.

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