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Review Article

# Review on Coral Jasmine (*Nyctanthesarbor-tristis* Linn) and its Therapeutic Activities

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#### ABSTRACT

Nyctanthes arbor tristis Linn is one of the important medicinal plant widely distributed throughout India. Herbal medicine maintained their popularity because of cultural reasons. Nearly 25% of prescribed drugs are derived from plant sources. Nyctanthes arbor tristis linn is type of ornamental plant used for decorative purposes but it has more medicinal values in each part of the plant. It's availability is from sub-Himalayan region to Southward Godavari region. It is derived from two Greek word 'Nykhta'-Night and 'anthos'-flower. It is a type of mythological plant which is having high medicinal values. This also called as Night Flowering Jasmine because flowering of buds will takes place only during night time and start fall from midnight and become dull in the early morning or during sun raise hence it is called as "Tree of Sadness". By extracting various active constituents from different parts of plant body are used for the management various disorder. Because of presence of high content phytochemicals such as Flavanol glycosides, essential oils, tannic acid, lupeol and oleanic acid, this Night flowering jasmine extract is used in various treatment of diseases and reported as Hepatoprotective, Anti-malarial, Antiinflammatory agent, Anti-Cancer and Anti-oxidant activity.At present world's population, 99% of the peoples are seeking towards herbal medicines due to its less side effects, less ADR, less toxicity and also less cost. Hence at present review emphases on history of herbal medicines, botanical description of coral jasmine, morphology, active constituents, biological activities of essential compounds, synonyms, and pharmacological activities.

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#### INTRODUCTION History of Herbal medicine

Study of botony and usage of medicinal plants for management of various ailments called Herbal medicine. Herb is mainly derived from Latin word known as "herba", in French "herbe". At present days, herb considered as any part of plant like root, seed, flower, stem, leaves, fruit, and bark as well as non-woody plant parts. Almost all developing countries depend on use of traditional herbal medicines for the treatment of various disorders. Herbal medicine maintained their popularity because of cultural reasons. Nearly 25% of prescribed drugs are derived from plant sources [1].

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According to WHO, Traditional medicine is "the knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures, used in the maintenance of health and in the prevention, diagnosis, improvement or treatment of physical and mental illness". Different types of tradition systems are such as Ayurveda, Siddha, Unani, Yoga, naturopathy, and homeopathy [2].

Ayurveda is also known as ancient medical system. It is one of the oldest type medical systems based on ancient writing this system is used nowadays. This system is mainly originated from Vedas, documented 5000 years ago currently identified and following in India. It is considered as a holistic system as physical, psychological, spiritual and social facts of human health and disease.

Actually treatment of various diseases with the help of natural sources was originated in *Rigveda* 

and Atharvaveda) in 5000 to 3000 BC. Ayurveda completely is documented CharakSamhita and Sushruta Samhita. According to Ayurveda objects and living bodies in the earth is composed of Panchacha Mahabhootas (Air, Agni, Vayu, Jal, Prithvi). In this system Pitha considered Kapha. Vata. are physiological factors and Satva, Rajas and tamas are considered as psychological factors for diagnosis of various diseseses in living organisms [3].

Unani system of medicine was established during Medieval period which is passed through various country before take place in India. It mainly originated in Greece. Hippocrates and Gellan are founders of Unani system of medicines which is basically belongs to Arabs. The main theme of these system is curing of diseases are mainly by giving positive health and prevention of disassess. At present this system is following in Egypt, Syria, Iraq, India, China, Persia and other Middle East countries.

Siddha system of medicine was established during Dravidian culture and oldest system followed in India. Siddhars are worked in this siddha system for the achievement treatment goal for various disorder by considering various factors such as patient, age, sex, race, environment, mental frame work, living styles. Diagnosis of various diseases in siddha system; mainly done on the basis of pulse rate, colour of the urine, eyes examination, colour of the body and voice.

Yoga is derived from Sanskrit word "yuju" means "to integrate". Maharshi Patanalli are founder of Yoga by means from Yogasuthra. Yoga is mainly composed of 8 elements such are restraint (Yama), observance of austerity (Niyama), physical postures (Asana) and breathing control (Pranayam) for treating of various disorder without giving medical treatment.

Naturopathy mainly deals with the treating of different diseases by means of stimulating inherent power to gain original or normal health.

Homoeopathy, in 1810 A.D. European missionaries brought homoeopathy system of medicine to India. One of the scientist from Hippocrates rule studied some substance can reduce the symptoms in healthy person and he correlate this idea to diseased person to treat various disorders.

### **Epidemiological Survey of Traditional Herbal Medicine Users**

According to National Institutes of Health use of herbal medicines are plant based products used to recover health. Uses of herbal medicines are regarded as a complementary and alternative medicine (CAM) for treating different types of illness. We can see 95% of intake of herbal medicines is form an aging stroke, obesity and respiratory problems.

According to WHO survey, China peoples are using more number of traditional systems of medicines to cure sevear acute respiratory disorders. Tradition system of medicines are using by 80% of American population. WHO estimated Worldwide as US\$ 60 billion marketed herbal products are used by consumers to treat various ailments [4].

For example: Earlier African flower was used to treat various symptoms of HIV infections but at present this flower extract of herbal medicine is used around worldwide especially local traditional medicine to manage HIV infection [4].

Nyctanthesarbortristislinn is type of ornamental plant used for decorative purposes but it has more medicinal values in each part of the plant. This also called as Night Flowering Jasmine because flowering of buds will takes place only during night time and start fall from midnight and become dull in the early morning or during sun raise hence it is called as "Tree of Sadness". Nyctanthes arbor tristis is one of the useful traditional medicinal plants also known as Parijatha belongs to family Oleaceae.

Its availability is from sub-Himalayan region to Southward Godavari region. It is derived from two Greek words 'Nykhta'-Night and 'anthos'-flower. It is a type of mythological plant which is having high medicinal values. Each part of the plant extract is used for treating various ailments as home remedies.

## Botanical Description of *Nyctanthes arbor tristis* Linn

Binomial name: Nyctanthes arbor tristis Linn

Kingdom : Plantae
Order : Lamiales
Family : Oleaceae
Genus : Nyctanthes
Species : N. arbor-tristis
Class : Eudicots
Division : Angiosperm

**Synonyms :** BruschiamacrocarpaBertol, Nyctanthesdentata Blume, Scabritascabra L, NyctanthestristisSalisb.

#### Other Names of Nyctanthes arbor tristis Linn

Bengali : Harsinghar, Sephalika, Seoli,

Sheoli.

**English** : Coral Jasmine, Night Jasmine.

**Filipino** : Coral Jasmine.

**Gujarati**: Jayaparvati, Parijatak.

**Hindi** : Harsinghar, Harsingur, Seoli,

Sheoli, Sihau.

**Indonesian** : Srigading (Sundanese,

Javanese).

**Kannada**: Goli, Harsing, Parijata.

**Konkani**: Pardic, Parizatak, Parzonto,

Parzot.

Lao (Tibetan) : Salikaa.Malay : Seri Gading.

**Malayalam**: Mannapu, Pavizhamalli,

Parijatakom.

Marathi : Kharbadi, Kharassi, Khurasli,

Parijatak.

Oriya : Godokodiko, Gunjoseyoli,

Singaraharo.

**Punjabi**: Harsinghar.

Sanskrit : Parijata, Parijatah, Parijataka,

Sephalika.

Tamil : Manjhapu, Pavala-Malligai,

Pavazha-Malligai.

**Telugu**: Kapilanagadustu, Pagadamalle,

Parijat, Sepali.

Thai : Karanikaa.

**Urdu**: Gulejafari, Harsingar.

Vietnamese : Iai Tau.

#### **Ecology and Distribution**

It mainly grows in rocky ground areas, grows in dry forest. It is widely distributed in South Asia and spreading towards northern regions of Pakisthan and Nepal to South Thailand through North regions of India. In India it mainly grows in outside of Himalayan regions and borders of Jammu and Kashmir it extends upto Godavari of South. Usually flowering of Harsinghar will takes place during June-October. Parijata likes to grow in moderate climate to semi-shade places.It likes to grows in loamy soils of gardens pH of around 5.6-7.5. This plant requires full sunlight to shade with daily watering for growing. But overwatering leads undergrowth.

#### Morphology

Coral Jasmine tree grow upto 10 meter tall like large shrub with quadratriangle shape young branches and bark of this plant looks like flaky grey rough bark. Leaves are about 6-12cm, 2-6.5cm broad with rough, white hairy texture of entire margin. Flowers are arranged like cluster form of about 2-7 at the tip of the branches or in axils of leaves.

Heart of the flower is orange coloured collora of about length 13mm and tube is about 6-8mm long with five to eight lobes with white colour which is highly pleasant fragrant in nature formed like clusters of two to seven with obcordate and cuneate in texture, each of this flower will opens at dusk and becomes dull on dawn.



**Figure 1:** (A) Whole Plant (B) Tree bushes (C) Leaves (D) Fruits & Seeds (E) Flowers (F) Bark (G) Flower buds.

Nowadays orange colour of the corolla is used for manufacturing of dyes [5].

Calyx is about 6-8cm in length inside globrous obscurely lobed, ciliated and outside its look like hairy. Leaves are opposite about 6-12cm long, 2-6.5cm broad with entire margin. Usually fruits of this plant are heart in shape with two sections each section contains only one seed in each. Brown hearted shape of fruits has diameter of about 2cm nearly orbicular, two celled, compressed. Highly vascularised seeds can be seen in transparent cell of heart to flat shaped fruits [5].

Stem and bark of *Nyctanthes arbor tristis* are look like shrubs of about 10cm tall. Barks are rough brown in colour with round scaly structure. But inside of bark soft white colour with collapsed and non-collapsed distinct phloem region can be seen [6].

#### **Chemical Constituents**

Different types of phytochemical constituents are present in different parts of Parijata. These isolated chemical constituents are having

particular action on particular diseases based on the presence of various secondary metabolites such as alkaloids, glycosides, terpenes, steroids, aliphatic compounds and flavonoids. It contains soluble polysaccharides such as D-Mannose and D-Glucose. Iridoid glucosides such Arbortristoside A. В and C, as major phytoconstituents, Minor constituents such as Arbortristoside D and E, and Other constituent is phenyl propanoid glucoside. Compared to all iridoid group secondary metabolites such as Alkaloids and Glycosides are rich in this plant.

Various types of chemical constituents present in different parts of *Nyctanthes arbor tristis* Linn are described in Table 1.

### Pharmacological Activity of Nyctanthes arbor tristis Linn

**1. Anti-Microbial Activity (Gram Positive and Gram Negative Bacteria):** anti-microbial assay of *Nyctanthes arbor tristis* Linn leaves extract was done on the basis of zone of inhibition on cultured microorganism in *In-vitro* condition.

**Table 1:** Chemical constituents and Pharmacological activities of *Nyctanthesarbortristis* Linn

Plant Part	Active Constituents	Pharmacological Activities
Flowers	Nyctanthine, d-mannitol, essential oils, glycosides, carotenoid, tannin, beta-digentiobioside ester of alpha-crocetin and beta-monogentiobiosideeter of alpha-crocetin.	Antioxidant, Antifilarial, Sedative activity, Diuretic, Anti-bilious, Dyspepsia, Ophthalmic,
Leaves	Mannitol, anamorphousresin, glucoside, glucose and essential oil, Vitamin C and carotene, Mannitol, b-amyrin, b-sitosterol, hentriacontane, and benzoic acid, Flavanol glycosides-Astragaline (Kaempferol3-glucoside), Nicotiflorin (kaempferol3-rhamnoglucoside), Triterpenoid (oleanolic acid, nyctanthic acid, friedeline, lupeoltanni cacid, ascorbic acid, methyl salicylate and amorphous glycoside), Iridoid glycosides (arborsides A, B, C), Iridoid glycoside (6,7-di-O-benzonylnyctanthoside (I)and6-O-trans-cinnamoyl-6-b-hydoxyloganin (II) 7-O-trans-cinnamoyl-6-b-hydroxyloganin), Phenylpropanoid glucoside (desrhamnosylverbascoside5), Iridoid glucoside (arborsideD), Calceolarioside A, Polyacetylenes and flavanol glycoside (quercetin-3,30-dimethoxy-7-O-rhamno glucopyranose), Octacosane and10-hydroxyl-30,4-dimethyl-1,10-bi (cyclohex-3-en)-2one, b-sitosterol	Anti-bacterial, Anti- pyretic, Antioxidant, Anti-inflammatory, Antifungal activity, Reptile Venom, Rheumatism, Ringworm, Sciatica, Dyspepsia, Flatulence, Heartburn, Hepatoprotective, Cholecystagogue, Cough,
Seeds	Glycerides of linoleic, oleic, lignoceric, stearic, palmitic and myristic acids,,3,4-seco triterpene acid, vitaminA, parasitosterol, sterol (nycosterol), Tetracycline terpene (nyctanthicacid), Glycerides (trisaturated, disaturated, mono, di and triunsaturated acid, Arbortristoside A and B, 4-O-b-D-mannopyranosyl-D-mannopyranose and O-b-D-glucopyranosyl-(1-4)-O-b-D-mannopyranose Iridoid glycoside (ArbortristosideA) (I), nyctanthic acid, oleanic acid, friedelin, b-sitosterol glucoside and 6 bhydroxyloganin, Arbortristoside D and E, Melanin, Water soluble polysaccharide composed of D-glucose and D mannose, Arbortristoside A andC, Phenylpropanoid glycoside (nyctosideA), Stearic acid, lauric acid, linoleic acid and oleic acid.	Anti-lesihmanial, Antibacterial, Immunomodulatory, activity, Hair Tonic, Alopecia, Piles.
Stem	Glycoside-naringenin-40-0-b-glucapyranosyl-a-xylopyranoside and b-sitosterol	Antioxidant, Antipyretic, Bronchitis, Snakebite
Bark	Glycosides and alkaloids	Antimicrobial
Flower oil	a-pinene, p-cymene, 1 hexanolmethylheptanone, phenylacetaldehyde, 1-deconol and anisaldehyde	As perfume

They performed anti-microbial assay i.e., antibacterial and anti-fungal assay by using two S. aureus and A.niger respectively. They used different extract of *Nyctanthes arbor* tristis Linn for anti-microbial activity (ethanol, chloroform, petroleum ether and acetone). They reported chloroform extract of Nyctanthes arbor tristis leaves shows highest zone of inhibition about 2.5 to 0.6mm (on bacterium species), 0.3mm on fungus species. There was no inhibition zone found on petroleum ether extract. Ethanolic extract of leaves shows highest degree of inhibition on A.niger species of about 1.6mm. Hence they reported chloroform and ethanolic extract of Nyctanthes arbor tristis leaves is having anti-microbial actions [7].

- 2. Diuretic Activity: Diuretic activity was performed by taking soluble portion of ethanolic extract of different parts of Nyctanthes arbor tristis Linn plant on experimental rats' model. Based on the presence of active constituents such as Flavonoids, terpenoids, carbohydrates, sugars and glycosides in the ethanolic extract of *Nyctanthesarbortristis* they performed diuretic activity on rat model. They kept Furosemide as a control group and extract treated animals as test group. After administering standard and test extract, animals are kept in metabolic cage upto 5hr to measure urine output. They found significant increase in the urine output in ethanolic extract of Nyctanthes arbor tristis treated group similar to standard group. Hence, they reported different parts of ethanolic extract of *Nyctanthes arbor tristis* Linn extract is having Diuretic activity [8].
- 3. Analgesic, Anti-Pyretic and Ulcerogenic **Activity:** Usuall**v** Non-steroidal inflammatory drugs are ulcerogenic in nature. Hence they tried ethanolic extract of *Nyctanthes* arbor tristis leaves extract for analgesic, antipyretic activity along with ulcerogenic activity on experimental animal models. For estimating analgesic activity of *Nyctanthes arbor* tristis leaves extract they used two methods for inducing pain on experimental animals. Tail-flick method for rat models and tail-clip method for mouse models and also they used acetic acid induced writhing method in mice models. They administered different doses of Nyctanthes arbor *tristis* extract of each animal before inducing pain and they found significant increase in time of response, hence they reported it is having analgesic activity.

They used brewer's yeast for inducing pyrexia in rats. 2.0ml of this suspension was administered to experimental rats through subcutaneous route for inducing increased temperature and after confirming increased rectal temperature, they administered different extract of *Nyctanthes arbor tristis* extract and they found significant decrease in temperature by knowing this mechanism they concluded ethanolic extract of *Nyctanthes arbor tristis* leaves is having antipyretic activity. They also reported that ethanolic extract of *Nyctanthes arbor tristis* is having ulcerogenic property by increasing dose not in normal dose (1.0g/kg/day) <sup>[9]</sup>.

**4. Immunostimulant Activity:** Different parts of *Nyctanthes arbor-tristis* Linn such as seeds, flowers, and roots are extracted by using 50% ethanol to perform immunostimulant activity on BALB/c albino mice by considering two factors such as cell mediated and humoral mediated immune response. They administered ethanolic extract of NAT at a dose of 25mg/kg/day on 8consecutive days after completion of test drug administering they started to find out various parameters such as Macrophage migration index, delayed type hypersensitivity response and immune response against sheep red blood cells on BALB/c albino mice.

Macrophage migration index test was performed by using extra peritoneal exudate from both drug treated mice and untreated mice, then collected exudated was packed in micro haematocrit capillary tube and kept in a migration chamber containing RPMI-1640 fluid with 10% fetal calf serum and incubated overnight at 37° C. MMI index was calculated and by using MMI index formula. And they also performed immune responses on mice of ethanolic extract of NAT [10].

5. Hepatoprotective Activity: Alcoholic and aqueous extract of NAT flowers showed hepatoprotective significant action in carbontetrachloride induced liver damage in experimental albino wistar Carbontetrachloride is highly toxic in nature it has been reported to cause degeneration hepatic cells and nephrotic cells. Hence in this study they used CCL4 as inducing agent in experimental rats to know whether aqueous and alcoholic extract of NAT flowers are responsible for regeneration of CCL4 induced liver damage. At the end of experimental procedure animals were sacrificed and blood was taken to analyse various biochemical parameters such glutamate oxaloacetate, SGPT, serum bilirubin

and ALP. They found Aqueous and alcoholic extract of NAT flowers showed significant restoring of SGPT, SGOT, ALP and serum bilirubin content in liver. This revealed that extracts of NAT flower is having Hepatoprotective activity [11].

6. Hypolipidemic and Hypoglycaemic Activity: From the believers of Sri-Lankan peoples, boiled extract of NAT flowers was used determine hypoglycaemic and hypolipidemic activity. It has been already reported diabetes one of the causative factor for various cardiovascular disorder. Because diabetes is always try to increase low density lipoproteins which can forms plagues in arteries of heart leads to atherosclerotic condition and other cardiovascular disorder. Hence study was conducted to manage diabetes. Hence they administered different concentrations (250, 500 and 750 mg/kg) of boiled aqueous extract of NAT flowers on albino mice. By analysing fasting blood sugar on overnight fasted albino mice with ad libitum water and glucose tolerance test was made on 10% glucose administered albino mice. 500mg and 750mg treated NAT flower extract showed significant decrease in fasting blood sugar level and showed highly tolerance to glucose. They also performedin-vitro alphaamylase assay and lipid profile test for aqueous extract of NAT flowers [12].

7. Anti-Cancer and Anti-oxidant Activity: Methanolic extract of Different parts of NAT was used to study anti-cancer and antioxidant property. Methanolic extract of NAT fruit, leaf and stem were used to study anticancer property by using MDA-MB 231 Breast Cancer Cell Lines by the method MTT cytotoxicity reduction assay and for antioxidant property was done by method called DPPH scavenging Assay method. 15mcg/ml of NAT fruit treated cell lines showed significant inhibition of cancerous cell growth compared to 30mcg/ml of seed and leaf extract of NAT treated cell lines and also maximum antioxidant activity of fruit extract showed antioxidant property at a dose 1000mcg/ml which was determined by using DPPH free radicle scavenging assay method [13].

**8. Anti-Amnestic Activity:** Regaining of memory impairment was done by administering hydro alcoholic extract of *Nyctanthes arbor tristis* leaf extract on scopolamine induced amnesia in experimental albino wistar rats. They used Elevated plus maze model and Morris water-

maze model for determining learning and memory power of rats. And also they estimated presence of anti-oxidance NAT extracted treated animals and also to control groups and significant anti-amnetic activity [14].

#### **CONCLUSION**

From this review we concluded that Coral jasmine is having various active constituent in every part of plant which possess significant Anti-microbial activity, Diuretic Analgesic, anti-pyretic, ulcerogenic activity, Immunostimulant activity, Hepatoprotective activity, Hypolipidemic-hypoglycaemic activity, Anti-Amnetic Activity, Anti-Cancer and Antioxidant activity. These pharmacological activities are mainly due to the presence of Flavanol glycoside, oleanic acid, essential oils, tannic acid, carotene, friedeline, lupeol, glucose and benzoic acid.

#### **REFERENCES**

- [1] Nhp.gov.in. (2019). Introduction and Importance of Medicinal Plants and Herbs | National Health Portal of India.
- [2] Benzie, I.F. and Wachtel-Galor, S., 2011. Herbal medicine: biomolecular and clinical aspects. CRC press.
- [3] Ayush.gov.in. (2019).
- [4] Tilburt, J.C. and Kaptchuk, T.J., 2008. Herbal medicine research and global health: an ethical analysis. *Bulletin of the World Health Organization*, 86, pp.594-599.
- [5] Meshram, M.M., Rangari, S.B., Kshirsagar, S.B., Gajbhiye, S., Trivedi, M.R. and Sahane, R.S., 2012. Nyctanthes arbor-tristis a herbal panacea. International Journal of pharmaceutical sciences and research, 3(8), p.2432.
- [6] Jain, P.K. and Pandey, A., 2016. The wonder of Ayurvedic medicine-Nyctanthesarbortristis. *Int J Herb Med*, 4(4), pp.9-17.
- [7] Paikara, D., Singh, S. and Pandey, B., 2015. Antimicrobial activity of Nyctanthesarbortristis. Indian Journal of Life Sciences, 5(1), p.29.
- [8] Sasmal, D., Das, S. and Basu, S.P., 2007. Diuretic activity of Nyctanthesarbortristis Linn. *Ancient science of life*, *27*(2), p.19.
- [9] Nhp.gov.in. (2019). Introduction and Importance of Medicinal Plants and Herbs | National Health Portal of India.
- [10] Puri, A., Saxena, R., Saxena, R.P., Saxena, K.C., Srivastava, V. and Tandon, J.S., 1994. Immunostimulant activity of Nyctanthes

- arbor-tristis L. Journal of ethnopharmacology, 42(1), pp.31-37.
- [11] Wagh, A.E., Yeotkar, U.S., Nimbhorker, M.G., Deshmukh, T.A. and Patil, V.R., 2010. Hepatoprotective activity of Nyctanthes arbor-tristis (L.). Oriental Pharmacy and Experimental Medicine, 10(2), pp.111-115.
- [12] Rangika, B.S., Dayananda, P.D. and Peiris, D.C., 2015. Hypoglycemic and hypolipidemic activities of aqueous extract of flowers from Nycantusarbor-tristis L. in male mice. BMC complementary and alternative medicine, 15(1), p.289.
- [13] Kumari, T.S., Madhuri, T.S., Charya, M.S. and Rao, K.S., 2012. Antioxidant and anticancer activities of Nyctanthes arbor-tristis. Int J Pharm PharmSci, 4(4), pp.452-454.
- [14] Antal, S., Ashwlayan, V.D. and Kumar, A., 2017. "Protective effect of nycthanthesarbor-tristis on scopolamine induced amnesia in rats" a behavioural and biochemical approach". International Journal of Pharmaceutical Sciences and Research, 8(3), pp.1346-1355.