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Systemic Review on Anti-Sciatica Plant “Night Jasmine” (*Nyctanthes arbortristis* Linn.)

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ABSTRACT

Keywords

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Ayurveda is one of the oldest systems of medicine that uses plants and their extracts for treatment and managing of various diseased states. *Nyctanthes arbortristis* Linn (Oleaceae) is an important large flowering shrub of tropical and subtropical regions of the world that has been conventionally used to provoke menstruation, for treatment of scabies and other skin infections, as hair tonic, chalogogue, laxative, diaphoretic, diuretic, in treatment of arthritis, malaria, bronchitis and as anthelmintic. *Nyctanthes arbortristis* is one of the most useful conventional plants in India. The various parts of plant like fruits, leaves, seeds, flowers, barks and stem have important phytochemicals and have some medicinal importance for treatment and management of different disease states. Phytochemicals like flavanol glycoside, oleanic acid, essential oils, tannic acid, carotene, fried line, lupeol, glucose, benzoic acid present in various parts of plant which have significant hepatoprotective, antiviral, antifungal, antipyretic, antihistamine, anti-malarial, antibacterial, anti-inflammatory, antioxidant activities. The present review focus on Chemical constituent, ecosystem And distribution, Biological behavior of important compounds, pharmacological action, Medicinal application. This review will be beneficial for future research work and their Potential Development.

Introduction

Nyctanthes arbortristis Linn (Oleaceae) (Fig. 1) is popularly known as ‘Night Jasmine’ (English) or ‘Harsingar’ (Hindi) due to the detail that its flowers emit a very strong and pleasant fragrance during the whole night (Siddiqui *et al.*, 2006; Rout *et al.*, 2007). The flowers start falling after midnight and by the day break, the plant appears dull.

The generic name ‘*Nyctanthes*’ has been coined from two Greek words ‘*Nykhta*’ (Night) and ‘*anther*’ (flower) (Vats *et al.*, 2009; Meshram *et al.*, 2012). The specific

name ‘*arbortristis*’ meaning ‘the sad tree’ is supposedly derived from dull looks of the tree during daytime (Suresh *et al.*, 2010).

Nyctanthes arbortristis Linn is one of the well-known medicinal plants. It is a common wild hardy large shrub or small tree. It is native of India, distributed wild in sub-Himalayan regions and southwards to Godavari, Lalitpur Nepal. *Nyctanthes arbortristis* Linn is commonly known as Night Jasmine or Parijata (Sandhar *et al.*, 2011). Different parts of this plant are used in

Indian systems of medicine for various pharmacological actions and are known to possess various ailments by tribal people of India esp. Orissa and Bihar along with its use in Ayurveda, Sidha and Unani systems of medicines. It is used in several ailments including sciatica, rheumatism, gout and other joint diseases (Sah and Verma, 2012). The flowers are used as stomachic, carminative, astringent to bowel, ant bilious, expectorant, hair tonic and in the treatment of piles and various skin diseases (Khatune *et al.*, 2001) and in the treatment of ophthalmic purposes (Sasmal *et al.*, 2007). Traditionally the powdered stem bark is given in rheumatic joint pain, in treatment of malaria and also used as an expectorant (Rouf, 2003). The leaves of *Nyctanthes arbortristis* Linn are used extensively in Ayurveda medicine for the treatment of various diseases such as sciatica, chronic fever, rheumatism, and internal worm infections, and as a laxative, diaphoretic and diuretic (Tuntiwachwuttiku *et al.*, 2003).

Scientific classification

Kingdom: Plantae
Order: Lamiales
Family: Oleaceae
Genus: *Nyctanthes*
Species: *N. arbortristis*

Climate and soil

Soil

Loamy, pH: 5.6–7.5. The plant requires conditions varying from full sunlight to partial shade and require to be watered regularly, but does not need overwatering.

Cultivation and collection

It is often cultivated in gardens due to its most agreeable and irregular aroma. The shrub can

be propagated by cutting as well as by seeds. The seeds have been found to exhibit a poor germination rate because of phenolics compounds leaching out of the imbibed seeds. These inhibitory phenolics compounds were stored in per carp assisted by the seed coat. The speed of germination is improved by either removing both the treating seeds with a solution of antioxidants like polyvinylpyrrolidone (PVP) or polyvinylpolypyrrolidone (PVPP) prior to germination (Abhishek Kumar Sah and Vinod Kumar Verma, 2012).

Leaves

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 slightcuneate; main nerves few, conspicuous beneath; petiole 6cm long, hairy (Abhishek Kumar Sah and Vinod Kumar Verma, 2012). Leaves are simple, etiolate and stipulate (Bhosale *et al.*, 2009). The lamina is ovate with acute or acuminate apex, the margin entire or serrated, somewhat undulated, particularly near the base, the upper surface dark green with dotted glands, and the lower surface pale green and softly pubescent. NAT 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 ad axial concavity (Biswas and Mukherjee, 2011) (Fig. 2).

Flowers

Flowers of NAT are small, delightfully fragrant, sessile in pedunculate bracteates fascicles of 3 5; peduncles 4- angled, slender, hairy, auxiliary and solitary and in terminal short dichotomous chimes; bracts broadly ovate or sub orbicular, 6- 10 mm long, aciculate, 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 colour, about equaling the limb; lobes white, unequally obcordate, ciliate (Bhosale *et al.*, 2009) (Fig. 3).

Fruits

Fruits of NAT are a capsule of 1-2 cm diameter, long and broad, obcordate orbicular, compressed, 2-celled, separating into 2 flat 1-seeded carpals, reticularly veined, glabrous (Bhosale *et al.*, 2009).

Macroscopic character of fruit: The fruit is flat, brown and heart cordate-shaped to rounded-capsule, around 2 cm in diameter with two celled opening transversely from the apex, each containing a single seed. Microscopically fruit showed typical character of fruit. In the epicarp epidermal cells were compactly arranged, polygonal cells with slightly anticlinal walls covered by a thin cuticle followed by 1,3 layers of collenchymas, Spongyparenchymatous tissue, sclerenchymatous sclerenchymatous fibers and oil gland (Shinde *et al.*, 2014) (Fig. 4).

Seed

The seed is compressed and is 1 per cell (Abhishek Kumar Sah and Vinod Kumar Verma, 2012) Seeds are exalbuminous, test thick; the outer layer of large transparent cells and heavily vascularised (Bhosale *et al.*, 2009) phytosterols, phenolics compounds, tannins, flavonoids, cardiac glycosides, saponins and alkaloids all are found in seeds of *N. arbortristis* (Shibani Basu *et al.*, 2016).

Bark

Bark of *N. arbortristis* plant is dark gray or brown in colour and rough and firm. Bark surface is dip pled due to scaling off of circular barks and patchy due to gray brown

colour regions. Scaling off the bark by circular flakes. Inner bark is creamy white, soft and collapsed and non-collapsed phloem zone distinctly visible (Bhosale *et al.*, 2009) (Fig. 5).

Traditional uses

CNS depressant activity showed in Seeds, leaves and flowers extract of plant (advance). The *Nyctanthes arbortristis* showed activity against Encephalomyocarditis virus (EMCV) and Semliki forest virus (SFV).

Phytochemical and pharmacological and tissue culture study of *Nyctanthes arbortristis*

The leaves of *Nyctanthes arbortristis* L (Oleaceae) are used in Ayurveda medicine for the management of a range of diseases, but reports on its phytochemicals and pharmacological properties are inadequate. Herein, we report purification of an antioxidative polysaccharide (F2) extracted from its leaves by water. The presence of a highly branched polysaccharide (75 kDa) containing esterified phenolics acids was revealed by chemical, chromatographic and spectroscopic analyses. Particularly, ESMS analysis of per acetylated oligomeric fragments derived by Smith degradation provides important structural information on a spectrum of glycerol tagged oligosaccharides. This polysaccharide showed dose dependent free radical scavenging capacity as evidenced by DPPH and Ferric reducing power assay. This pharmacologically active compound (F2) formed a water soluble complex with bovine serum albumin over pH 4.0–7.4. Accordingly, traditional aqueous extraction method provides a molecular entity that induces a pharmacological effect: this could epitomize a smart approach in phototherapeutic management (Ghosh *et al.*, 2015). The cytotoxic compound Altersolanol A, an

anthraquinone derivative was isolated from PM0409092 a fungus of *Nyctanthes arbortristis* (family Oleaceae). It was identified as a *Phomopsis* sp. by DNA amplification and sequencing of the ITS region. The chemical structure of Altersolanol A was elucidated from its physicochemical properties, 2D NMR spectroscopy and other spectroscopic data. The compound has in vitro cytotoxic activity against 34 human cancer cell lines with mean IC₅₀ (IC₇₀) values of 0.005 µg ml⁻¹ (0.024 µg ml⁻¹) respectively. Altersolanol A, a kinase inhibitor, induces cell death by apoptosis through the cleavage by Caspase-3 and -9 and by decreased anti-apoptotic protein expression. There are several previous reports of the anticancer activity of Altersolanol A, but we report here an extensive study using 36 cell lines which gives wider spectrum of results. This study confirms the cytotoxic potential of Altersolanol A isolated from the endophyte *Phomopsis* sp (PM0409092) of the plant *Nyctanthes arbortristis*. The compound exhibits in vitro cytotoxicity against 34 human cancer cell lines with mean IC₅₀ (IC₇₀) value of 0.005 µg ml⁻¹ (0.024 µg ml⁻¹). This is an in-depth report of Altersolanol A against a panel of 34 human cancer cell lines and extends observations from previous studies indicating that Altersolanol A can be used for the development of chemotherapeutics. Altersolanol A, a kinase inhibitor, induces cell death by apoptosis through the cleavage of Caspase-3 and -9 and by decreased anti-apoptotic protein expression (Mishra *et al.*, 2015).

The present communication is a first-time report on the analyses of n-alkane profile of epicuticular wax extracted from the mature leaves of *Nyctanthes arbortristis* L. during a calendar year. The composition of n-alkanes revealed hentriacontane (n-C31), tritriacontane (n-C33), tetratriacontane (n-C35) and nonacosane (n-C29) as the major constituents with tritriacontane (n-C33) being

the dominant constituent. The cumulative percentage of these four odd-numbered alkanes also showed phenological variation being highest during the fruit ripening stage (average value 63.29%) followed by the flowering stage (mean value 60.74%). The values remained moderate on an average of 54.31% for the rest of the year. This study also confirms the xerophytic feature of the plant having higher proportion of longer carbon chain n-alkanes greater than C31 (dominant peaks are of C33 and C35) (Biswas *et al.*, 2014). An efficient tissue culture technology has been designed for mass multiplication of *Nyctanthes arbortristis* L. by preculturing nodal explants in thidiazuron (TDZ)-supplemented liquid Murashige and Skoog (MS) media. Direct inoculation of nodal segments on semi-solid MS medium augmented with various concentrations of TDZ (0.1 to 0.9 µM) produced shoots but with low regeneration response and few shoots per explant. Hence, nodal explants were pretreated with greater concentrations of TDZ (5 to 100 µM) in liquid MS media for different durations (4, 8, 12, and 16 days) with the aim of improving shoot regeneration response from cultured explants. After pretreatment, explants were transferred to agar-solidified hormone-free MS medium. Best response in terms of percent regeneration (94%), number of shoots per explant (20.00 ± 1.15), and greatest shoot length (7.23 ± 0.83 cm) were obtained with nodal segments pretreated in 75 µM TDZ for 8 days. Similarly, root induction was obtained from pulse-treated micro shoots for 24 h with 200 µM indole-3-butyric acid (IBA) followed by their transfer to 1/2 MS medium which produced an average of 5.50 ± 0.92 roots per micro shoot. The rooted plantlets were transplanted to soil with 80% success rate (Jahan *et al.*, 2011).

Rapid differentiation of multiple shoots was observed in 94% of nodal explants of one year old *Nyctanthes arbortristis* L. plants.

Shoot bud induction and multiplication took place on Murashige and Skoog (MS) medium supplemented with two cytokines, i.e. Benzyl adenine (BA) or Kinetin (KN) either alone or in combination with different auxins, indole-3-butyric acid (IBA), indole-3-acetic acid (IAA) or α -naphthalene acetic acid (NAA). Between different media, pH levels and growth regulators tried, the optimum condition for maximum regenerative response was obtained on MS + Kn (2.5 μ M) + NAA (0.5 μ M) media at 5.8 pH, forming cultures with 23.26 ± 0.89 number of shoots and 6.36 ± 0.80 cm shoot length after 8 weeks of culture. Histological sections confirmed the formation of multiple buds from nodal explants. Rooting was achieved *ex vitro* by dipping the basal ends of micro shoots in 200 μ M IBA for 30 min followed by their transplantation in sterile soil *in vivo*. The plantlets with well-developed shoot and root system were successfully established in garden soil and grown outside in a greenhouse with a 80% survival rate (Jahan *et al.*, 2011). A carotenoid aglycone Ag-NY1 was isolated from the orange coloured tubular calyx of flowers of *Nyctanthes arbortristis*. The elucidation of the structure through a detailed spectroscopic study revealed that the carotenoid molecule is Crocetin, which is the major aglycone present in the stigma of *Crocus sativus*. The compound exhibited a good membrane stabilizing activity as compared to the corresponding glycoside crocin (Gadgoli and Shelke, 2010). The decoction of the leaves of *Nyctanthes arbortristis* Linn (Harsingar) is widely used in Ayurveda system of medicine for the treatment of sciatica, arthritis, fevers, and various painful conditions and as laxative. In the present investigation, the water soluble portion of the alcoholic extract of the leaves was screened for some CNS activities (*viz.* hypnotic, tranquilizing, local anesthetic, hypothermic, anticonvulsant), antihistaminic and purgative activities. The extract produced

general depression of spontaneous motor activity, significantly increased pentobarbitone sleeping time though it had no effect on righting reflex. Furthermore higher doses of the extract abolished CAR without affecting motor coordination. Moreover the extract exhibited hypothermic effect and protected guinea pigs from histamine aerosol. These activities are common to major tranquilizers and support the usage of the plant by Ayurveda physicians in aforementioned conditions. In addition significant purgative activity was also exhibited by the extract (Saxena *et al.*, 2002). On the occurrence of sclerosed palisade cells in the leaf of *Nyctanthes arbortristis* L (Ananda Rao, 1947).

Anti-microbial and inflammatory aspects of *Nyctanthes arbortristis*

To investigate the immunomodulatory activity of aqueous extract of *Nyctanthes arbortristis* flowers (NAFE) with particular reference to splenocytes proliferation and induction of cytokines. Antibody titer was determined by tube agglutination and indirect ELISA assay in four groups of mice-control, antigen alone, and NAFE-treated (400 and 800 mg/kg for 21 days) after immunization with *Salmonella* antigen while cellular immunity was studied in three groups of rats (control and NAFE-treated - 400 and 800 mg/kg) following DNCB application. Splenocytes from untreated and NAFE-treated rats were stimulated using concanavalin-A (Con-A) and optical density (OD) and stimulation index were determined. Splenocytes from control rats were also treated *in vitro* with NAFE (50-1600 μ g/ml) and Con-A to determine the effect on splenocytes proliferation. Interleukin-2 (IL-2) and IL-6 levels in splenocytes supernatant from control and NAFE-treated rats and following *in vitro* treatment of splenocytes with NAFE (50-1600 μ g/ml) were determined

using ELISA kits. Marked to a significant increase in antibody titer by both the methods in NAFE-treated mice and a significant increase in skin thickness in rats after challenge with DNCB, respectively suggested humoral and cell-mediated immunostimulant potential of NAFE. Significant increase in OD and stimulation index following *ex vivo* and *in vitro* exposure of splenocytes and sensitization with Con-A and significant elevation in IL-2 and IL-6 levels in splenocytes supernatant was also observed after their *ex vivo* and *in vitro* exposure to NAFE. Humoral and cell-mediated immunostimulant activity of NAFE seems to be mediated through splenocytes proliferation and increased production of cytokines, especially IL-2 and IL-6 (Bharshiv, 2016).

Exploration of anti-Malassezia potential of *Nyctanthes arbortristis* L. and their application to combat the infection caused by Mala s1 a novel allergen. Malassezia commensal yeasts along with multitude of antigens have been found to be associated with various skin disorders including Pityriasis vesicular (PV). Amongst them Mala s1, a 37 kDa protein has been proved to be a major allergen reacting with a large panel of sera. However, there exists no therapeutic alternative to combat such problems in form of plant based natural compounds. The purpose of this study is in the first place, to determine the anti-Malassezia activity of *Nyctanthes arbortristis* L (NAT) ethanolic leaf extract through turbid metric growth curves, disruption of plasma membrane and secondly, it aims to present in silicon validation of its active constituents over Mala s1a novel allergen. The antifungal susceptibility 50 % ethanolic extract of NAT was determined by broth micro dilution method according to CLSI guidelines. Further MICs and IC50 were determined spectrophotometrically using the software SoftMax® Pro-5 (Molecular Devices, USA).

Active constituents mediated disruption of plasma membrane was studied through flowcytometry by permeabilization of fluorescent dye Propidium Iodide (PI). Antioxidant activity of the extract was determined using the DPPH stable radical. Molecular validation of fungal DNA from the extract was observed using PCR amplification. In silicon analysis of its active constituents over Mala s1 was performed using HEX software and visualized through Pymol. The anti-Malassezia potential of NAT leaf extracts reflected moderate MIC 1.05 µg/µl against *M. globes*, while least effective against *M. restrict* with MIC 1.47 µg/µl. A linear correlation coefficient $R(2) = 0.866$ was obtained in case of *M. globes* while minimum was observed in *M. restrict* with $R(2) = 0.732$. The flow cytometric data reveal ~ 75 % cell death when treated with active constituent's β-Sit sterol and Calceolarioside A. The docking confirmations and the interaction energies between Mala s1 and the active constituents (β-Sit sterol and Calceolarioside A) from extracts showed an effective binding which suggests Mala s1 as efficient allergen for site specific tagging this study revealed that *Nyctanthes arbortristis* L (NAT) extracts possess high anti-Malassezia potential which is driven mainly by disruption of plasma membrane. Also in silicon validation and molecular modeling studies establishes Mala s1 as a novel allergen that could be a potential target in disease treatment. Our results would also provide a foundation for the development of new therapeutic approach using NAT extract as lead compound with high antioxidant property as an added trait for skin care (Mishra *et al.*, 2016).

In order to search for new products that display antimalarial and immunomodulatory mechanisms that complement direct antiparasitic activity, a set of *in vitro* and *in vivo* experiments were designed to evaluate

the effect of *Nyctanthes arbortristis* in Plasmodium Bergheim infected mice. Three extracts of *N. arbortristis* leaves from varying concentrations of alcohol and water were considered for their potential to suppress expression of pro-inflammatory mediators from macrophages primed with lip polysaccharide. The ethanolic extract, which lowered the pro-inflammatory mediators [tumor necrosis factor (TNF), 13.52-55.83 %; interleukin-6 (IL-6), 0-17.29 %; and NO, 39.37-81.63 %], was selected to be examined in malaria (*P. Bergheim*) infected mice. Corroborating the in vitro results, it was observed that the extract could normalize the TNF (78 %) and IL-6 (70.35 %) optimally at 1 g/kg, thus retarding the pathological process in infected mice and increasing the mean survival time from 10.6 to 15.6 days. There were no signs of toxicity in the acute oral toxicity test up to 2 g/kg (1)H NMR of the biologically active extract was obtained to ensure the presence of the compound of interest, *i.e.*, iridoid glycoside. The quality and the reproducibility of results were ensured by means of achieving characteristic high-performance liquid chromatography fingerprint of the extract (Agrawal *et al.*, 2013).

Stem bark of *Nyctanthes arbortristis* Linn. was extracted in methanol to evaluate their analgesic and anti-inflammatory activities. The analgesic activity was determined on Wister albino rats by hot plate method, tail flick assay, and tail immersion method using Morphine sulphate as standard drug at a dose of 5 mg/kg of body weight and the results were expressed as mean increase in latency after drug administration \pm SEM. The anti-inflammatory activity was assessed by Carrageenan-induced rat paw edema using diclofenac sodium as standard drug at a dose of 100 mg/kg of body weight and expressed in terms of mean increase in paw volume \pm SEM. Stem bark extract was given at a dose

of 250 mg/kg and 500 mg/kg of body weight. Both standard drugs and extract were administered orally to the animals. Control received distilled water orally. Results showed that *Nyctanthes arbortristis* Linn. Had potent analgesic and anti-inflammatory activities (Kakoti *et al.*, 2013).

Nyctanthes arbortristis Linn (Oleaceae) is a well-known traditional medicinal plant used throughout the India as an herbal remedy for treating various infectious and non-infectious diseases. To evaluate the antioxidative activity of hydro-alcoholic extract of flower in the lymphocytes exposed to oxidative stress induced by H₂O₂. Isolated lymphocytes were treated in vitro with extract or extract+H₂O₂, and the level of reduced glutathione (GSH) as well as the activity of glutathione-S-transferase (GST) and lactate dehydrogenase (LDH) were measured. Treatment of lymphocyte with flower extract (50, 100, and 200 μ g/ ml) significantly increased the level of GSH and decreased the activity of GST. The LDH activity measured in the cell-free medium decreased significantly. Pre-treatment of lymphocyte with flower extract protects the lymphocyte from the H₂O₂ induced oxidative stress by significantly increasing the levels of GSH as compared to the cells treated only with H₂O₂. Pre-treatment also reduced the activity of LDH significantly as compared to the cells treated only with H₂O₂. The LDH activity in cell-free medium is associated with membrane damage, the decreased levels of LDH activity reflects the reduced level of membrane damage due to H₂O₂. The present findings suggest the protective role of the hydro-alcoholic extracts of the flower of *Nyctanthes arbortristis* against membrane damage induced by H₂O₂. The results also suggest that the extract might be rich in phytochemicals with antioxidant/radical scavenging potentials, which might find application in antioxidant therapy (Hussain

and Ramtek, 2012).

Larvicidal activity of crude chloroform, dichloromethane and methanol extracts of the leaves and roots of six Indian plants, *Eagle marvelous* L., *Balanites aegyptica* L., *Caltrops gigantic* L., *Murraya koenigii* L., *Nyctanthes arbortristis* L. and *Plumbago zeylanica* L., were tested against the early fourth instar larvae of *Aedes aegypti* L. and *Anopheles stephensi*. The larval mortality was observed after 24 h of exposure. All extracts showed moderate larvicidal effects. However, the highest larval mortality was found in methanol extracts of *P. zeylanica* roots and *B. aegyptica* roots against *Ae. aegypti* (LC50 169.61 mg/lit, 289.59 mg/lit) and *An. stephensi* (LC50 222.34 mg/lit, 102.29 mg/lit), respectively. The methanol extracts of plants were more effective than the other extracts. This is an ideal eco-friendly approach aid for the control of mosquito species *Ae. Aegypti* and *An. stephensi* (Patil *et al.*, 2010).

Screening of natural products for mosquito larvicidal activity against three major mosquito vectors *Aedes aegypti*, *Culex quinquefasciatus* and *Anopheles stephensi* resulted in the identification of three potential plant extracts viz., *Saraca indica*/Asoka, *Nyctanthes arbortristis* and *Clitoria ternatea* for mosquito larval control. In the case of *S. indica*/Asoka, the petroleum ether extract of the leaves and the chloroform extract of the bark were effective against the larvae of *C. quinquefasciatus* with respective LC(50) values 228.9 and 291.5 ppm. The LC (50) values of chloroform extract of *N. arbortristis* leaves were 303.2, 518.2, and 420.2 ppm against *A. aegypti*, *A. stephensi*, and *C. quinquefasciatus*, respectively. The methanol and chloroform extracts of flowers of *N. arbortristis* showed larvicidal activity against larvae of *A. stephensi* with the respective LC (50) values of 244.4 and 747.7 ppm. Among the methanol extracts of *C. ternatea* leaves,

roots, flowers, and seeds, the seed extract was effective against the larvae of all the three species with LC(50) values 65.2, 154.5, and 54.4 ppm, respectively, for *A. stephensi*, *A. aegypti*, and *C. quinquefasciatus*. Among the three plant species studied for mosquito larvicidal activity, *C. ternatea* was showing the most promising mosquito larvicidal activity. The phytochemical analysis of the promising methanolic extract of the seed extract was positive for carbohydrates, saponins, terpenoids, tannins, and proteins. In conclusion, bioassay-guided fractionation of effective extracts may result in identification of a useful molecule for the control of mosquito vectors (Mathew *et al.*, 2009).

The flowers of *Nyctanthes arbortristis* showed interesting antibacterial activity against some gram-positive and gram-negative microorganisms (chloroform and ethyl acetate extracts) and significant cytotoxic activity (petroleum ether, chloroform and ethyl acetate extracts) (Khatune *et al.*, 2001). *Nyctanthes arbortristis* L (Oleaceae), a plant widely used in the traditional medicinal systems of India, has recently been reported to possess hepatoprotective, antileishmanial, antiviral and antifungal activities. In the present study strong stimulation of antigen specific and non-specific immunity, as evidenced by increases in humoral and delayed type hypersensitivity (DTH) response to sheep red blood cells (SRBC) and in the macrophage migration index (MMI), has been demonstrated in mice fed with 50% ethanolic extract of seeds, flowers and leaves of this plant.

Maximum activity was found in the seeds in which the active principle(s) appear to be mainly associated with lipids. In flowers and leaves, however, the major activity was found in the aqueous fraction of the 50% ethanolic extract. The immunostimulant substance(s)

found in *N. arbortristis* L. are likely to play a role in its antiameobic, antileishmanial, antiviral and certain other activities (Puri *et al.*, 1994).

The leaves of *Nyctanthes arbortristis*, besides being used in the treatment of sciatica and arthritis, are advocated for various kinds of fevers and painful conditions by the Ayurveda physicians. In the present study, the water-soluble portion of an ethanol extract of the leaves was screened for analgesic, antipyretic and ulcerogenic activities.

The extract exhibited significant aspirin-like antinociceptive activity but failed to produce morphine-like analgesia. It was also found to possess antipyretic activity against brewer's yeast-induced pyrexia in rats. The extract also produced gastric ulcers following oral administration for six consecutive days in rats. Results of the present study tend to substantiate the use of this plant in fevers and painful conditions by Ayurveda physicians (Saxena *et al.*, 1987).

Fig.1 Whole plant of *Nyctanthes arbortristis*



Fig.2 NAT leaves showing morphology



Fig.3 Flowers of *Nyctanthes arbortristis*



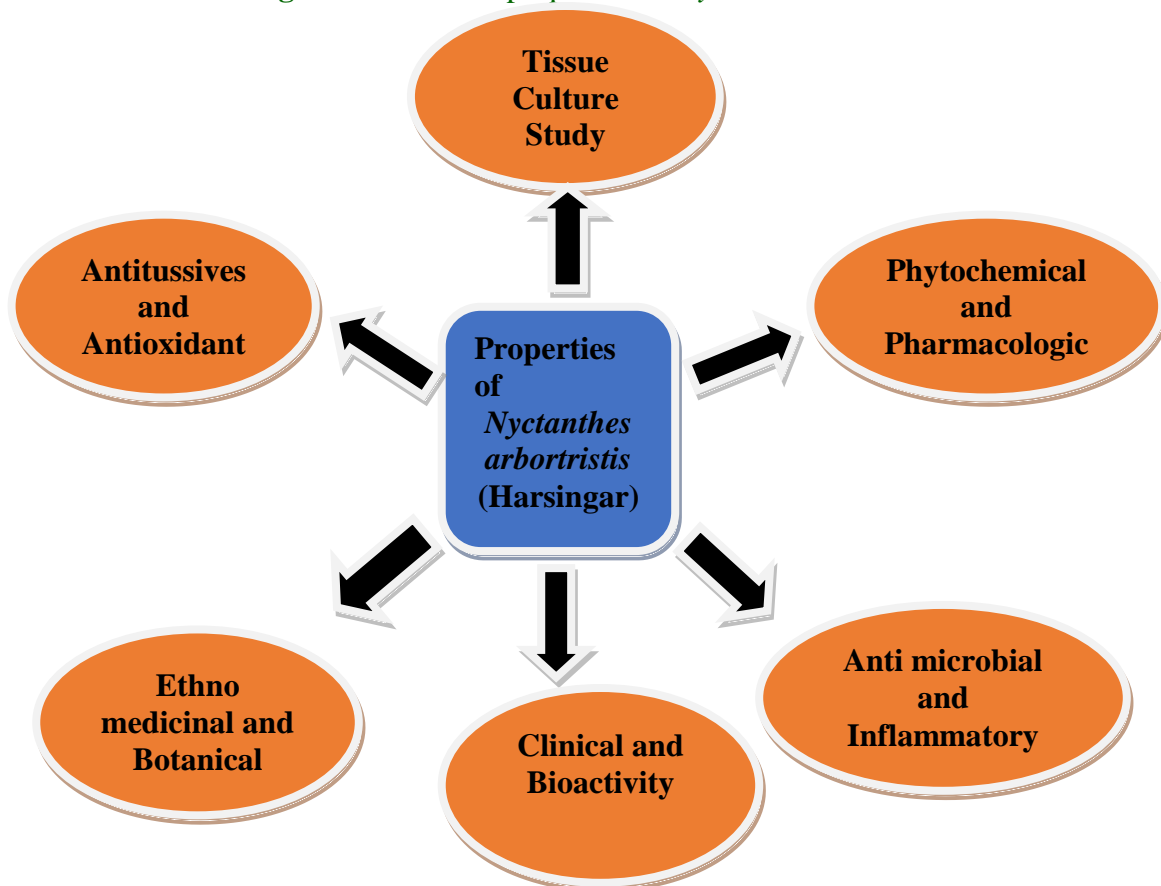
Fig.4 Morphology of *Nyctanthes arbortristis* fruit



Fig.5 Plant having young bark of *Nyctanthes arbortristis*



Fig.6 Flow chart of properties of *Nyctanthes arbortristis*



Nyctanthes arbortristis Linn (Harsingar) is widely used as a decoction in the Ayurveda system of medicine for treatment of sciatica and arthritis, but it has not yet been screened scientifically. In the present study, the water soluble portion of the alcoholic extract of the leaves of *Nyctanthes arbortristis* (NAT) was screened for the presence of anti-inflammatory activity. NAT inhibited the acute inflammatory edema produced by different phlogistic agents, viz. carrageenin, formalin, histamine, 5-hydroxytryptamine and hyaluronidase in the hindpaw of rats. The acute inflammatory swelling in the knee joint of rats induced by turpentine oil was also significantly reduced. In subacute models, NAT was found to check granulation tissue formation significantly in the granuloma pouch and cotton pellet test. Acute and chronic phases of formaldehyde induced Arthritis was significantly inhibited. NAT was also found to inhibit the inflammation produced by immunological methods, viz. Freund's adjuvant arthritis and PPD induced tuberculin reaction. Thus anti-inflammatory activity in leaves of Harsingar supports its use in various inflammatory conditions by the followers of the Ayurveda system of medicine (Saxena *et al.*, 1984).

Clinical and bioactive aspects of *Nyctanthes arbortristis*

An unceasing threat of drug resistance continuously poses demand for new antimalarial drugs. A scientific assessment of traditionally used antimalarial plants through reverse pharmacology is crucial for a fast track drug discovery. An Ayurveda plant *Nyctanthes arbortristis* Linn. - (Parijat) is being used in clinical practice and had shown antimalarial activity, with a parasite clearance in 76.6% of 120 patients, in an earlier clinical study. To further explore antimalarial potential of the plant through additional objective markers. An open-labelled

observational study was conducted at M.A. Podar Hospital - Ayurveda (MAPH-A) after ethics committee approval. Administration of a paste of 5 fresh leaves, thrice a day for a week was a standard practice for management of malaria at MAPH-A. Clinical activity of *N. arbortristis* was evaluated by monitoring pyrexia, parasitemia and morbidity score (MS) in twenty patients. In addition, immune and biochemical markers and organ functions were monitored for objective markers of response. Student's paired-'t' test was applied to assess statistical significance. Ten out of 20 patients showed both fever and parasite clearance, which was confirmed by polymerase chain reaction. Remaining ten patients had persistent but decreasing parasitemia. Four of them needed chloroquine as a fail-safe procedure. Irrespective of the degree of parasitemia all the patients showed decrease in MS. There was also an increase in platelet count and normalization of plasma lactic acid. There was a good clinical tolerability and an improvement in organ function. The inflammatory cytokines showed a reduction; particularly in TNF- α within a day. At the given dosage, *N. arbortristis* showed disease-modifying activity; early clinical recovery with a decline of TNF- α and a gradual parasite clearance. Further studies with a standardized formulation for dose-searching and optimizing the treatment schedule are needed in a larger sample size. The process of trial registration had not begun when the study was conducted in 2000 (Godse *et al.*, 2016). Safety evaluation of a polyherbal formulation containing hydroalcoholic extracts of *Hippophae salicifolia*, *Nyctanthes arbortristis*, *Ocimum tenuiflorum*, and *Reinwardtia indica* in rodents (Kumari *et al.*, 2016).

Boiled aqueous extract of flowers (AEF) from *Nyctanthes arbortristis* L. are used in Sri Lankan traditional Ayurvedic Medicine to manage diabetes mellitus. AEF has widely

been used as a folk medicine for the treatment of various ailments due to its therapeutic activity. However, little is known concerning therapeutic activity of the extract as well as its underline mechanisms and safety. Diabetes is known to increase low-density cholesterol and decrease high-density cholesterol thus triggering coronary diseases. Hence, the primary objective of the present study is to investigate the hypoglycemic and hypolipidemic activities of the AEF. AEF was prepared and male mice (n = 9 group) were gavages either with 250, 500 and 750 mg/kg of AEF or distilled water (DW). Subsequently, fasting and random blood glucose concentrations were determined. To investigate mechanisms of actions of AEF, animals were orally administered with 500 mg/kg or the vehicle (DW) and glucose tolerance was performed before and after glucose challenge. For further studies, in vitro alpha-amylase assay and glucose absorption from the gastrointestinal tract were performed using 500 mg/kg of the extract. Additionally, glycogen content in the liver and skeletal muscles, a complete lipid profile assay, and toxicological and biochemical parameters were conducted after a chronic study. Treatment with AEF did not induce any overt signs of toxicity or hepatotoxicity. Results the present study indicated that AEF possess hypoglycemic and hypolipidemic properties. Therefore, AEF could be used as an alternative medicine in management of diabetes mellitus (Rangika *et al.*, 2015).

Nyctanthes arbortristis (Harshringar, Night Jasmine) has been traditionally used in Ayurveda, Unani and other systems of medicine in India. The juice of its leaves has been used by various tribal populations of India in treatment of fevers resembling malaria. This work reports the antiplasmodial activity guided fractionation of Harshringar leaves extract. Crude ethanolic Harshringar leaves extract and its RPHPLC purified

fractions were studied for antiplasmodial potency against 3D7 (CQ sensitive) and Dd2 (CQ resistant) strains of *P. falciparum* and subsequently subjected to bioassay guided fractionation using reverse phase chromatography to pursue the isolation of active fractions. Harshringar crude leaves extract and some of its RPHPLC purified fractions exhibited promising antiplasmodial potency against 3D7 and Dd2 strains of *P. falciparum*. The present study has provided scientific validity to the traditional use of leaves extract of Harshringar against malaria leading to the conclusion that this plant holds promise with respect to antimalarial phytotherapy. This is the first scientific report of antiplasmodial activity of RPHPLC fractions of Harshringar leaves extract against *P. falciparum* strains (Kumari *et al.*, 2012).

The effect of the water soluble fraction of the ethanol extract of *Nyctanthes arbortristis* (NAT) on tumor necrosis factor-alpha (TNF-alpha) level in plasma of arthritic and soluble protein A (SpA)-treated Balb/c mice has been studied. Oral administration of this fraction in arthritic mice showed a consistent depletion of TNF-alpha from the host plasma. A similar depletion of TNF-alpha in the plasma of SpA-treated mice has been observed. The extract also reduces plasma interferon-gamma level but the plasma IgM and IgG levels are not affected. The implications of these observations are discussed in the light of management of TNF-alpha in clinical disorders (Paul and Saxena, 1997).

Ethno medicinal and botanical study of *Nyctanthes arbortristis*

The global burden of bacterial infections is very high and has been exacerbated by increasing resistance to multiple antibiotics. Antibiotic resistance leads to failed treatment of infections, which can ultimately lead to death. To overcome antibiotic resistance, it is

necessary to identify new antibacterial agents. In this study, a total of 662 plant extracts (diverse parts) from 222 plant species (82 families, 177 genera) were screened for antibacterial activity using the agar cup plate method. The aqueous and methanolic extracts were prepared from diverse plant parts and screened against eight bacterial (two Gram-positive and six Gram-negative) species, most of which are involved in common infections with multiple antibiotic resistance. The methanolic extracts of several plants were shown to have zones of inhibition ≥ 12 mm against both Gram-positive and Gram-negative bacteria. The minimum inhibitory concentration was calculated only

With methanolic extracts of selected plants, those showed zone of inhibition ≥ 12 mm against both Gram-positive and Gram-negative bacteria. Several extracts had minimum inhibitory concentration ≤ 1 mg/mL. Specifically *Adhatoda vasica*, *Ageratum conyzoides*, *Alangium salvifolium*, *Alpena galangal*, *Andrographis paniculata*, *Anogeissus latifolia*, *Annona squamosa*, *A. reticulate*, *Azadirachta indica*, *Buchanania lanzan*, *Cassia fistula*, *Celastrus paniculatus*, *Centella asiatica*, *Clausena excavate*, *Cleome viscosa*, *Cleistanthus collinus*, *Clerodendrum indicum*, *Croton roxburghii*, *Diospyros melanoxylon*, *Eleutherine bulbosa*, *Erycibe paniculata*, *Eryngium foetidum*, *Garcinia cowa*, *Helicteres isora*, *Hemidesmus indicus*, *Holarrhena antidysenterica*, *Lannea coromandelica*, *Millettia extensa*, *Mimusops elengi*, *Nyctanthes arbortristis*, *Oroxylum indicum*, *Paederia foetida*, *Pterospermum acerifolium*, *Punica granatum*, *Semecarpus anacardium*, *Spondias pinnata*, *Terminalia alata* and *Vitex negundo* were shown to have significant antimicrobial activity. The species listed here were shown to have anti-infective activity against both Gram-positive and Gram-negative bacteria. These results may serve as a guide for selecting plant species

that could yield the highest probability of finding promising compounds responsible for the antibacterial activities against a broad spectrum of bacterial species. Further investigation of the phytochemicals from these plants will help to identify the lead compounds for drug discovery (Panda *et al.*, 2016).

To investigate the plants traditionally used for prevention of malaria in Cuttack, Gajapati and Koraput districts of Odisha state, eastern India. An ethnobotanical survey was carried out among 20 traditional healers who were sampled based on recommendations of local elders and local non-government organizations. Data were collected through semi-structured interview. The study revealed the use of 16 traditional plant species belonging to 12 families for prevention of malaria. *Andrographis paniculata*, *Azadirachta indica*, *Nyctanthes arbortristis*, *Ocimum sanctum*, *Piper nigrum*, *Zingiber officinale* were the most commonly reported plants for their malaria prophylactic use by the healers of three districts of Odisha. Most of the remedies were used in decoction form. Findings of this study provide a lead to explore traditional plants for malaria preventive potential through further pre-clinical and clinical studies (Nagendrappa *et al.*, 2013).

Nyctanthes arbortristis (Oleaceae) is a mythological plant; has high medicinal values in Ayurveda. The popular medicinal use of this plant are anti-helminthic and anti-pyretic besides its use as a laxative, in rheumatism, skin ailments and as a sedative. Vitrally, the natives plant it in their home gardens to pass on its medicinal usage to oncoming generations. The present review encompasses an ethnopharmacological evaluation focusing on information on the chemical constituents, pharmacological actions and toxicology in order to reveal the therapeutic potential and

gaps requiring research involvement. The present review is based on searches in Scifinder (®), Pubmed (National Library of Medicine) and books published on the subject during the period 1933 to 2012. *Nyctanthes arbortristis* is most important in local and traditional medicines especially in India for treating intermittent fevers, arthritis and obstinate sciatica. Crude extracts and isolated compounds from the plant were shown to be pharmacologically active against inflammation, malaria, viral infection, leishmaniasis and as an immunostimulant. The major classes of biologically active compounds are the iridoid glucosides including Arbortristoxide A, B and C from the seeds active as anticancer, anti-leishmania, anti-inflammatory, anti-allergic, immunomodulatory and antiviral. Other molecules; calceolarioside A, 4-hydroxyhexahydrobenzofuran-7one and β -sitosterol from leaves have been reported to be active as anti-leishmanial, anticancer and anti-inflammatory, respectively. The crude extracts have been found to be safe with an LD50 of 16gm/kg, while the LD50 of arbortristoxide-An isolated from the seeds was found to be 0.5g/kg. Mostly in-vitro or in some cases in-vivo models provide some evidence especially in the treatment of inflammatory conditions like arthritis, fevers related to malaria and protozoan diseases especially leishmaniasis. The only clinical study found, is for treating malaria, but with crude extract only. Further, more detailed safety data pertaining to the acute and sub-acute toxicity, cardio and immunotoxicity also needs to be generated for crude extracts or pure compounds (Agrawal and Pal, 2013).

Anti tussives and antioxidant aspects of *Nyctanthes arbortristis*

The prevalence of cough is reflected in antitussives being one of the most widely used therapies in the world; however no new

class of drugs has been introduced into the market for many years. Water decoction of the leaves of *Nyctanthes arbortristis* L. is used in Indian Ayurvedic system to alleviate a wide range of diseases including cough. Herein, we have isolated a carbohydrate polymer (CP) containing fraction from its leaves by aqueous extraction method. CP is a branched polysaccharide containing, amongst others, 1,3-/1,3,6-linked galactopyranosyl, 1,5-/1,3,5-linked arabinofuranosyl and 1,2-/1,2,4-linked rhamnopyranosyl residues. Oral administration of CP fraction in doses of 25 and 50 mg kg⁻¹ body weight significantly inhibited the number of citric acid-induced cough efforts in guinea pigs in a dose dependent manner. Remarkably, CP did not alter specific airway resistance of animals significantly. Consequently, aqueous extraction method provided a molecular entity, which exhibited the cough suppressive activity: this could symbolize an attractive approach in phytotherapeutic treatment (Ghos *et al.*, 2015).

To investigate the in vitro antioxidant activity and total phenolic content of the methanolic leaf extract of *Nyctanthes arbortristis* L (NA). The sample was tested using five in vitro antioxidant methods (1, 1-diphenyl-2-picryl hydrazine radical scavenging activity (DPPH), hydroxyl radical-scavenging activity (-OH), nitric oxide scavenging activity (NO), superoxide radical-scavenging activity, and total antioxidant activity) to evaluate the in vitro antioxidant potential of NA and the total phenolic content (Folin-Ciocalteu method). The extract showed good free radical scavenging property which was calculated as an IC50 value. IC50 (Half maximal inhibitory concentration) of the methanolic extract was found to be 57.93 $\mu\text{g}\cdot\text{mL}^{-1}$ for DPPH, 98.61 $\mu\text{g}\cdot\text{mL}^{-1}$ for -OH, 91.74 $\mu\text{g}\cdot\text{mL}^{-1}$ for NO, and 196.07 $\mu\text{g}\cdot\text{mL}^{-1}$ for superoxide radical scavenging activity. Total antioxidant capacity of the extract was found to be (1198

± 24.05) mg ascorbic acid for the methanolic extract. Free radical scavenging activity observed in the extracts of NA showed a concentration-dependent reaction. The in vitro scavenging tested for free radicals was reported to be due to high phenolic content in the leaf extract. The leaf extract of NA showed the highest total phenolic content with a value of 78.48 ± 4.2 equivalent mg TAE/g (tannic acid equivalent). *N. arbortristis* leaf extract exhibited potent free radical scavenging activity. The finding suggests that *N. arbortristis* leaves could be a potential source of natural antioxidant (Michael *et al.*, 2013).

Nyctanthes arbortristis (Harsingar) generally used in traditional system of medicine for various ailments are supported by various studies involving its pharmacological and clinical evaluations. The above article accepted and discovered phytochemicals study, antimicrobial, antioxidant, tissue culture, inflammatory, ethno medicine, botanical, clinical, bioactivity and pharmacological activities of plants. *Nyctanthes arbortristis* is single source of metabolites such as alkaloids, phytosterols, phenolics, tannins, flavonoids, glycosides and saponins which is obtained from basic extracts of various parts of plant and show valuable treatment for various diseases. This review conclude that time has come to make good use of centuries old awareness of *Nyctanthes arbortristis* through modern approaches of drug development. This will provide support among scientist in exploring more information about the valuable therapeutic potential of Harsingar plant to establish the ancient Ayurvedic system with authenticity.

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