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THERAPEUTIC AND PHARMACOLOGICAL PERSPECTIVES OF *NYCTANTHES ARBOR-TRISTIS* LINN.: A COMPREHENSIVE REVIEW

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ABSTRACT: The potential phytochemicals and pharmacological actions of the plant *Nyctanthes arbor-tristis* are the main topic of this review. *Nyctanthes arbor-tristis* is an extremely significant traditional plant in India, sometimes called parijata or harsinghar. Ayurveda, Siddha, and Unani medicine have all been used to treat various infectious and non-infectious illnesses. Various medicinal properties, including anti-arthritic, antispasmodic, antibacterial, anti-inflammatory, immunostimulant, anti-diabetic, hepatoprotective, antioxidant, antimicrobial, anthelmintic, antileishmanial, antipyretic, antiallergic, antiviral, and CNS depressant, are known to occur in all parts of the plants. These plant pharmacological activities are attributed to flavonoids, tannins, saponins, glycosides, alkaloids, steroids, and phenolic compounds, which have been identified in the plant through phytochemical studies. The article reviews aim to highlight the need for research and their prospective development while gathering and documenting information on various pharmacological aspects of *Nyctanthes arbor-tristis*.

INTRODUCTION: Today's pharmaceutical industry uses a variety of chemicals to effectively treat illnesses. Because of its possible adverse effects, researchers concentrated on effectively treating diseases with herbal remedies. Since Indian customs, herbs have been the primary component of medical care, and they are currently the most commonly used medicine worldwide. Herbal remedies hold promise for extremely effective new bioactive compounds in addition to traditional and ethnic medicine ¹.

Numerous plants were investigated as potential sources of bioactive compounds with potential medical applications. Out of the 4,22,000 flowering plants in the globe, over 50,000 are said to have pharmacological and therapeutic use ². A significant medicinal herb that has been utilized for a variety of reasons throughout history is *Nyctanthes arbor-tristis* L., which is a member of the Oleaceae family.

The generic name "Nyctanthes" comes from the Greek words "Nykhta," which means "night," and "anthos," which means "flower." The specific name "arbortristis" means "the sad tree" because of the tree's drab appearance during the day. In Ayurvedic, Siddha-Ayurvedic, and Yunani medicine, *Nyctanthes arbor-tristis* is used as an expectorant, digestive aid, laxative, diuretic, and anti-venom.

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Also known as Night Jasmine, Parijata, and Harshingar^{1, 3, 13}. It is native to India extensively as a decorative plant in Indian gardens. It grows wild across the sub-Himalayan region. The whole plant is used extensively by the native people of Andhra Pradesh's Chittoor area to treat cancer, fever, sciatica, and anorexia; the bark is used as an expectorant; the leaves are used to regulate fever

and diabetes; and the leaves are used as a cholagogue, diaphoretic, and anthelmintic. Numerous plant extracts are used to treat intestinal worms, arthritis^{4, 5, 6}, malaria, laxatives, antitrypanosomes, inflammation, and antioxidant properties^{7, 8, 9}. The leaves' juice is used as a laxative, diuretic, mildly bitter tonic, digestive aid, and antidote against reptile venoms^{10, 11, 12}.

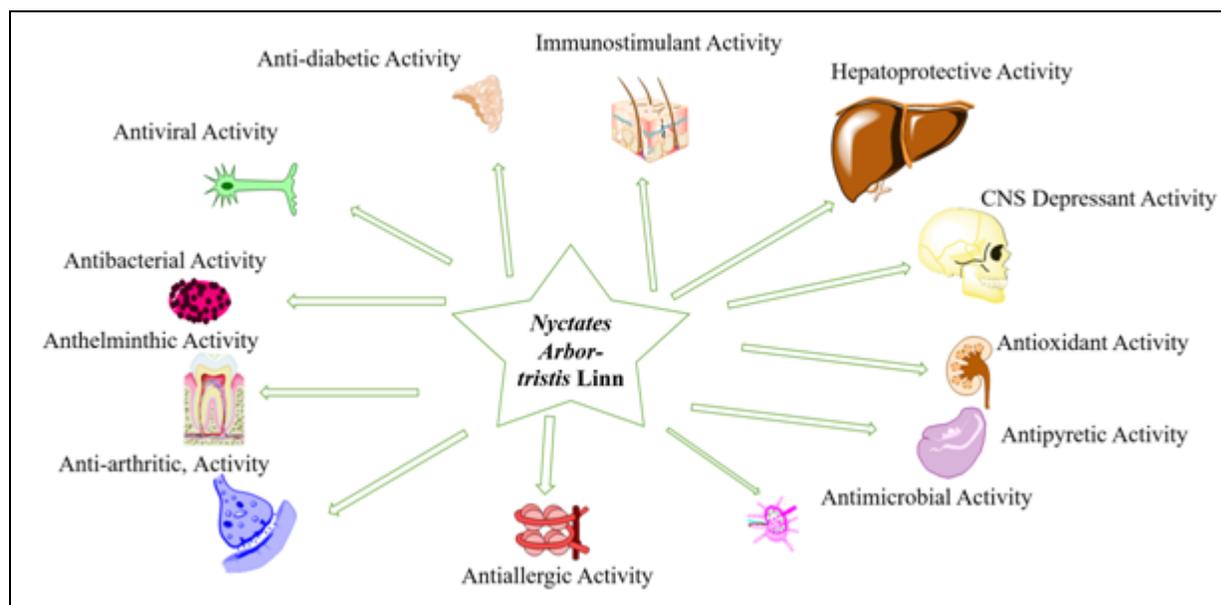


FIG. 1: NYCTANTHES ABBOR-TRISTIS PHARMACOLOGICAL PROPERTIES

Morphological Character: It is a woody shrub with white blossoms that can reach a height of 10 meters. Its aroma is powerful and pleasant all night long, and it can live for 5 to 20 years¹⁴. The plant can be cultivated anywhere from sea level to an elevation of 1500 meters near the equator, as well as in tropical and subtropical climates. It often thrives in reddish-black soil with a pH between 5.6 and 7.5 and favors arid and semi-arid climates^{2, 15}. Flowers are typically found at the tips of branches or in the axile of the leaves in clusters of two to seven, opening at twilight and falling before morning. Flowering typically takes place from July to October. These fragrant, sessile blooms are 6-8 mm long, narrowly campanulate, hairy on the outside, and glabrous on the inside. They feature a ciliated calyx and a tube that is 6-8 mm long, with an orange-red center and 5-8 unequally obovate and cuneate lobed white corollas. The fruits are compressed, flat, spherical, brown capsules that resemble hearts and have two portions, each of which contains a single seed. Cotyledons are flat, radicles are inferior, and seeds are exalbuminous with thick tests and a strongly vascularized outer

layer of big transparent cells. The leaves are simple, hairy, rough, and opposite. They are 6-12 cm long, 2-6.5cm broad, and have a full margin^{16, 17}.

Vernacular Names¹⁸:

English: Night jasmine

Kannada: Parijatha

Telugu: Pagadamalle

Marathi: Parijathak

Gujrati: Jayaparvati

Malayalam: Parijatakam

Sanskrit: Parijatha

Bengali: Sephalika

Hindi: Harsingar

Oriya: Gangasiuli

Taxonomy:

Kingdom: Plantae

Division: Angiosperms

Class: Dicotyledonae

Sub class: Gamopetalae

Series: Bicarpellatae

Order: Gentiales

Family: Oleaceae

Genus: *Nyctanthes*

Species: *Arbor-tristis*

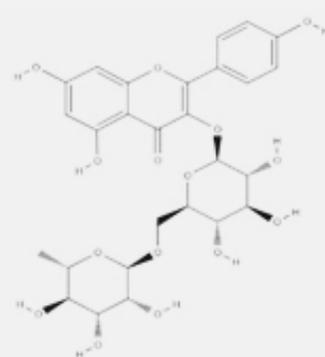
Phytochemicals Present in *Nyctanthes arbortristis*:

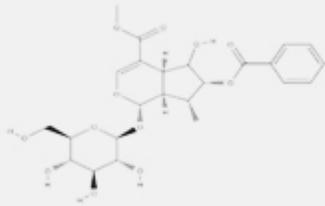
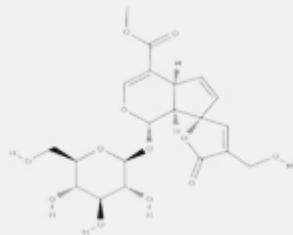
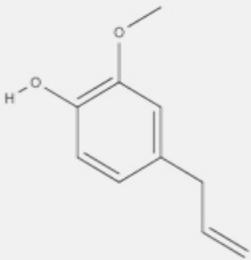
- D-mannitol, β -sitosterole, Astragaline, Nicotiflorin, Oleanolic acid, Nyctanthic acid, tannic acid, ascorbic acid, methyl salicylate, an amorphous glycoside, an amorphous resin, a trace of volatile oil, carotene, friedeline, lupeol, mannitol, glucose, fructose, iridoid glycosides, and benzoic acid derivative of kaempferol and carotene are all present in *Nyctanthes arbor-tristis* leaves^{19, 20, 21}. Every significant phytoconstituent is utilized in ayurveda medicine and has been shown to relieve fevers,

sciatica, arthritis, and other unpleasant ailments in addition to acting as a laxative²².

- Mannitol is widely present in *Nyctanthes arbor-tristis* flowers, which also contain a modified dieterpenoid called nycanthin, flavonoids, anthocyanins, and an essential oil that resembles jasmine²³, d-mannitol, tannin, glucose, carotenoid, and glycosides, such as β -monogentiobioside β -D monoglucoside ester of α -crocetin (or crocin-1), 4-hydroxy hexahydrobenzofuran-7-one, which is also reported in flowers and isolated from chloroform extract. These compounds are being studied for their antifungal, antiviral, and antileishmanial properties²⁴.
- 15% of the seed of *Nyctanthes arbor-tristis* is made up of *nycanthic acid*, *nyctoside A*, *b-sitosterol*, *arbortristoside A & B*, glycerides of linoleic, oleic, lignoceric, stearic, palmitic, and myristic acids, 3-4 secotriterpene acid, and a water-soluble polymer made of D-glucose and D-mannose that is used as an immunostimulant and hepatoprotective²⁵.
- *Nyctanthes arbor-tristis* bark contains alkaloids and glycosides. The glycosides of the iridoid and phenylpropanoid types are found in plant bark. B-sitosterol and glycoside-naringenin-4'-O- β -glucopyranosyl- α -xylopyranoside are found in the stem of *Nyctanthes arbor-tristis*^{26, 27}.

TABLE 1:

S. no.	Phytochemicals	Chemical class	Parts of the plant that constitute the phytochemicals	Structure of phytochemicals
1.	Friedeline	Terpenes	Leaf	
2.	Nicotiflorin	Flavonoid	Leaf	

3.	Lupeol	Terpenes	Leaf	
4.	β -sitosterol	Steroid	Leaf, stem, seed	
5.	Arborside C	Iridoid Glycoside	Flower	
6.	Iridoid		Bark	
7.	Phenylpropanoid		Bark	

Pharmacological properties of *Nyctanthes arbortristis*:

Anti-cancer Activity: In 2001, researchers released the first investigation on the anticancer efficacy of *N. arbortristis*. They found that the flowers' extracts in petroleum ether, chloroform, and ethyl acetate had significant cytotoxic activity. When compared to 5-fluorouracil, a methanolic extract of stem bark demonstrated significant anticancer effectiveness against Dalton's ascetic lymphoma in swiss albino rats. With time and dosage, the ethanolic, methanolic, and aqueous leaf extracts' cytotoxicity against T-cell leukemia cells rises. The extracts significantly decreased normal cell toxicity at all dosages and times²³.

Anti-oxidant Activity: The several leaf extract from *Nyctanthes arbor-tristis* were evaluated in vitro for their ability to scavenge free radicals using

the diphenyl-picryl-hydrazyl (DPPH) test procedure. In this study, DPPH, a persistent free radical, was formed by the antioxidant found in plant extracts reacting with it to produce 1, 1-diphenyl-1, 2-picrylhydrazine, which was detected at 517 nm. The following are some methods in which plant extracts and standards (ascorbic acid and BHT) might scavenge the DPPH radical: Ascorbic acid > Butanol > Ethyl acetate > BHT > Pet ether. At a concentration of 10 mg, the ascorbic acid component was found to be 93.88%, while the BHT, butanol, ethyl acetate, and pet ether components were found to be 97.32%, 95.22%, 84.63%, and 82.04%, respectively²⁸.

Anti-bacterial Activity: The antibacterial activity of ethyl acetate and chloroform extract from flowers, leaves, seeds, and fruit against gram-positive (*Staphylococcus aureus*) and gram-

negative (*E. coli*, *Klebsiella pneumonia*, and *Pseudomonas aeruginosa*) bacteria was examined by K. Priya et al. (2007). 300 µl of both ethyl acetate and chloroform extract substantially inhibited the microorganisms under study. Additionally, Fresh plant fragments were shown to have more antibacterial properties than dried ones. The presence of phytosterols, phenolics, tannins, flavonoids, glycosides, and saponins was demonstrated by phytochemical analysis. It was discovered that tannin and phenolic chemicals were effective against the bacterium.

It has been demonstrated that tannins can form irreversible compounds with proline-rich proteins that prevent the production of cell proteins, in addition to serving as a potent and stable antioxidant, astringent, and in the treatment of diarrhea and dysentery²⁹.

Anti-fungal Activity: The three most common clinical pathogenic fungi *Aspergillus niger*, *Penicillium*, and *Aspergillus flavus* were tested for antifungal activity in various NAT plant sections. Young and old leaves, seeds, stems, bark, and flowers were collected, dried, and then extracted using methanol, chloroform, and distilled water. The antifungal activity of the extract was measured using the well diffusion method in terms of the “zone of inhibition” of fungal growth. The results showed that only the distilled water extract of NAT’s stem and bark had antifungal activity against *A. niger*, while the chloroform extract of the leaves only worked against *A. flavus*. The study found that the most potent antifungal activity against *Aspergillus* and *Penicillium* was exhibited by NAT’s methanolic extract of leaves, stem, and bark¹³.

Anti-inflammatory Activity: Acute inflammatory oedema in rats is significantly reduced by aqueous soluble fractions of ethanolic extract in combination with a variety of phlogistic agents, including formalin, histamine, 5-hydroxytryptamine, carrageenin, and hydronidase. The extract significantly reduced the acute inflammatory swelling that occurred when turpentine oil was applied to rats’ knee joints. The leaf and fruit extracts also exhibit superior anti-inflammatory activity in a mouse model of arthritis induced by immunological techniques, specifically

injections of Freund’s complete adjuvant into the right hind paw’s sub-planter surface over a period of 0–12 days and PPD-induced tuberculin reaction. Rats were given the extract daily for six days after the pouch formed or five days after the peller implantation in subacute models of carrageenin-induced granuloma pouch and cotton pellet granuloma. The extract dramatically reduced the production of granulation tissue in both models^{30, 31, 32}. Carangenan-induced rat paw oedema using diclofenac sodium as a conventional medication is significantly inhibited by the ethanolic extract of the orange tube of the calyx of *Nyctanthes arbor-tristis* and the isolated carotenoid (200 mg/kg, i.p.)³³.

Anti-viral Activity: The *Nyctanthes arbor-tristis* isolated ethanolic extract, n-butanol fraction, and two pure compounds, *arbortristoside A* and *arbortristoside C*, have a strong inhibitory effect against the Semliki Forest Virus (SFV) and the Encephalomyocarditis Virus (EMCV). EMCV-infected mice were protected against SFV by 40% and 60%, respectively, by the *in-vitro* ethanolic extract and the n-butanol fraction, administered daily at doses of 125 mg/kg weight^{34, 35}.

Anti-diabetic: The anti-diabetic effects of NAT root methanol extract are comparable to those observed in diabetic control mice. The extract’s anti-diabetic effects are strong and comparatively risk-free. To create the extract, 50g of root powder was combined with 400 ml of methanol and heated continuously for 18 hours. To get rid of impurities, the methanolic extract was filtered and separated using petroleum ether. The solvent was evaporated using vacuum and pressure. The hypoglycemic effects of the resultant NAT dry extract were tested. Rats’ blood glucose levels are considerably lowered after seven days at 500 mg/kg when compared to the control drug. A methanolic extract of NAT roots was found to lower blood glucose levels more successfully than the gold standard drug³⁶.

Anti-parasitic: A crude ethanolic leaf extract has been shown to have trypanocidal properties at 1000 g/mL. *In-vivo* studies showed that the extract significantly extended the survival period of mice infected with *Trypanosoma evansi* when administered at dosages of 300 and 1000 mg/kg.

But it has also been shown that as soon as the experimental animals quit getting the extract, their parasitemia increases and they pass away. NAT extract demonstrated anti-leishmanial activity in hamsters infected with *Leishmania donovani*. The anti-parasitic effectiveness was confirmed by clinical testing³⁷.

Anti-malarial: 120 people's reactions to malaria treatment. After getting fresh paste made from five medium-sized NAT leaves three times a day for seven to ten days, 92 patients (76.7%) recovered in just seven days. Within a week, twenty more patients were cured, but the final eight showed no improvement at all. There were no reported severe side effects from the paste. With LC₅₀ values of 244.4 and 747.7 ppm, respectively, it was demonstrated that the methanol and chloroform extracts of leaves killed the larvae of *Anopheles stephensi*, *Culex quinquefasciatus*, and *Aedes aegypti*, three important mosquito vectors³⁸.

Immuno-stimulant activity: Both humoral and cell-mediated responses demonstrate the strong immunomodulatory effects of NAT's aqueous leaf extract. Additionally, flowers have demonstrated immuno-stimulant action, which stimulates the immune system mediated by cells. The ethanolic extracts of NAT from seeds and roots showed immunomodulatory action against organized candidiasis in mice. *Arbotristosides* A and C, two iridoid glucosides, were separated from the plant's seeds^{14,16}.

Anti-arthritic Activity: The characteristics of arthritis, an autoimmune disease of the synovial joints that is usually caused by inflammation mediators and viruses, is chronic inflammation that results in pain, inflammation of the synovial joints, pannus formation, cartilage rupture, decreased mobility, and disability. Nonbiologic disease-modifying antirheumatic medications (DMARDs) like methotrexate, NSAIDs (non-steroidal anti-inflammatory drugs) like piroxicam, biological therapies like IL-6, IL-1, and TNF- α inhibitors, and glucocorticoids like methyl prednisolone and triamcinolone are currently used to treat arthritis. The first-line treatment for rheumatoid arthritis is NSAIDs, which significantly reduce joint stiffness, swelling, and pain. However, they come with several negative side effects, such as bleeding,

dyspepsia, stomach ulcers, and an increased risk of cardiovascular issues. Treatment with non-biologic DMARDs may result in reversible alopecia, rash, nausea, loss of appetite, increased rheumatoid nodule formation, mouth ulcer, and neurological issues.

Anti-TNF therapy may cause itching, bruising, bleeding, rash, vomiting, diarrhea, injection site reaction, cellulitis, and respiratory tract infections. Numerous negative consequences are also associated with long-term use of glucocorticoids, such as an elevated risk of osteoporosis, diabetes, peptic ulcers, gastrointestinal bleeding, cataracts, and infections. A growing number of rheumatoid arthritis sufferers are turning to alternative medications due to the negative side effects of the current treatment options. Using a rat model of FCA-induced arthritis, the anti-arthritic properties of methyl, ethyl acetate, and n-hexane extracts of mature NAT leaves were investigated.

The ethyl acetate extract of NAT leaves was the most promising of the extracts, according to the comparison analysis. When compared to the other two extracts, the ethyl acetate extract demonstrated the greatest prevention of paw edema. Compared to the other two and the reference medication, piroxicam, it more dramatically reduced bone degradation, the total leukocyte count, and the infiltration of inflammatory cells in ankle joints. The terpenes and terpenoids were thought to be responsible for the extract's antiarthritic properties. The evaluation of the hepatotoxic and nephrotoxic effects of NAT extracts revealed that there were no such effects in the group of animals given the extracts, indicating that they were safe³⁹.

Hepatoprotective Activity: Carbon tetrachloride (CCl₄)-induced hepatotoxicity in Swiss albino mice was used to test the hepatoprotective effects of petroleum ether and methanol extract of NAT bark. Mice were given CCl₄ injections to cause hepatic toxicity, and the amount of serum glutamate pyruvic transaminase (SGPT), glutamate oxidaloacetic transaminase (SGOT), alkaline phosphate (ALP), direct bilirubin (DB), and total bilirubin (TB) was measured to assess liver function. Silymarin served as the study's standard medication. When Silymarin and both extracts (100 mg/kg and 200 mg/kg) were administered, the

serum marker enzymes (SGPT, SGOT, ALP, DB, and TB) were markedly reduced. It was discovered that the 200 mg/kg methanol extract dose was more efficacious than the 100 mg/kg methanol and the 100 mg/kg and 200 mg/kg petroleum ether extract of NAT. Alkaloids, cardiac glycosides, tannins, saponins, terpenoid, phlobatannins, fixed oils, lipids, and flavonoids were found in the petroleum ether and methanol extract of NAT according to phytochemical study, which may be the cause of the activity⁴⁰.

CNS Depressant Action: Given that NAT (600 mg/kg) in the leaves, flowers, seeds, and barks was found to significantly and dose-dependently prolong the onset and duration of sleep, as well as cause a decrease in dopamine and an increase in serotonin levels, the CNS depressant activity of the ethanol extract of seeds, leaves, and flowers is probably due to a decrease in dopamine⁴¹.

Anti-allergy Activity: Before being exposed to histamine aerosol, guinea pigs were pretreated with a water-soluble part of an alcoholic extract of NA leaves to prevent asphyxia. In NA, *arboristosides* A and C have been demonstrated to have anti-allergic properties⁴².

Wound Healing Activity: In 2011, Matadeen *et al.* examined the wound healing effectiveness of NAT on Wistar albino rats. For 16 days, the rats received treatment with 2% w/w NAT methanolic extract. It was discovered that it took roughly 16 days for both incision and excision wounds to fully epithelize and heal. It was determined that NAT extract at a dose of 300 mg/kg might be regarded as an effective treatment for both kinds of wounds⁴³.

Method of Propagation: Its unique and delightful scent makes it a popular garden plant. The phenolic substances that leak out of the ingested seed slow down the rate at which seeds germinate, yet both cuttings and seeds can be used to proliferate the bushes⁴⁴. Because of low seed laying, poor seed germination from inhibitory compounds, and insect attack throughout the ripening stage, NAT is very difficult to propagate from seed. Natural factors cause many early seedlings to die^{45, 46}. The pericarp of the seed coat contains the inhibiting phenolic chemicals. According to a study, the germination rate can be increased by either

removing both covers or treating seeds with an antioxidant solution such as polyvinylpyrrolidone (PVP) and polyvinylpolypyrrolidone (PVPP) before germination⁴⁴. The plant is drastically declining as a result of overexploitation, environmental degradation, and the unresolved issue of poor germination and seed viability⁴⁷. Therefore, research on large-scale plant production is required for economic, ornamental, and conservation interests⁴⁶.

Propagating these plants using alternate methods, such as tissue culture techniques, is necessary to prevent the extinction of this species⁴⁷. By employing excised cotyledons, hypocotyls, roots, leaves, and bases of internodes that may easily generate callus in the culture, plantlets of NAT can be grown *in-vitro*. In contrast, calli from cotyledons, hypocotyls, and roots grew more quickly than those from leaves and intermodal bases when cultivated in murashige and skoog's (MS) media containing 2,4-dichlorophenoxyacetic acid (2,4D), naphthalene acetic acid (NAA), and coconut milk⁴⁴.

CONCLUSION: Many synthetic chemicals are used extensively to treat a variety of illnesses, yet they also have negative side effects. Owing to these adverse medication reactions, researchers are looking into a number of alternatives, including the same plants. *Nyctanthes arbor-tristis* (NAT) is one such plant. The aforementioned study, which was referenced in the article on the phytochemical and promising pharmacological activities found in *Nyctanthes arbor-tristis*, a medicinal plant, demonstrated the significance of herbal and ayurvedic pathways for the efficient treatment of a variety of illnesses due to their enormous potential pharmacological activities.

The researchers are interested in the broad-spectrum medical application of NAT. The plant's numerous medicinal benefits, including its anti-arthritic, antispasmodic, antibacterial, anti-inflammatory, immunostimulant, antidiabetic, hepatoprotective, antioxidant, antimicrobial, anthelmintic, anti-leishmanial, antipyretic, anti-allergic, antiviral, and central nervous system depressant properties, demonstrate its immense worth. When considering NAT for the treatment of different disorders, it can offer a cost-effective and

efficient substitute for chemical medications that have no negative side effects. It is important to think about, investigate, and clarify the various elements of NAT plants that are used in Ayurvedic, Siddha, and Unani medicine. To increase output, select for desired plant features, and investigate species diversity in germplasm, tissue culture, recombinant DNA technologies, and molecular marker-based approaches can be used.

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CONFLICTS OF INTEREST: Nil

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