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Therapeutic Potential of Nyctanthes Arbor-Tristis on Cancer and Various Diseases

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Abstract: Nyctanmthes arbotristis (N. Arbotristis) is a multipotent traditional Indian medicinal herb widely used in Ayurveda, Siddha, Unani and Homeopathy treatment systems. It has caught the eye of the scientific community for its medicinal in the folklore for ailments like wound healing, malaria, menstruation, bronchitis, chronic fever, rheumatism, obstinate sciatica, stomachic, astringent, liver, biliary and skin disorders. The primary goal of this review is to discuss the potential pharmacological activity of NAT that has been explored till date. The phytochemicals like flavonol glycosides, benzoic acid, friedeline, essential oils, glucose, tannic acid, carotene, oleanic acid, and lupeol were isolated from various parts of NAT including seeds, leaves, flowers, bark, fruits etc. Furthermore, these phytochemicals were reported to have significant medicinal properties significant hair tonic, hepatoprotective, and anti-leishmaniasis, anti-viral, anti-fungal, anti-pyretic, anti-histaminic, anti-malarial, anti-bacterial, anti-inflammatory anti- cancer and anti-oxidant activities.

Key words: Nyctanthes arbor-tristis, Cancer, Phytomedicine, Ethnophamacology, Oleaceae

Introduction:

Plants are the natural synthesizers that play a vital role in meeting the daily needs of the mankind. Nyctanthes arbor-tristis, which is commonly known as Harshingar, coral jasmine, Night Jasmine, and queen of night. The genus name ‘Nyctanthes’ is derived from two Greek words Nykhta(night) and Anthos (flower) and is consequently known as the night flower.(Sharma, Dhiman, Singh, & Sharma, 2021) It is also familiar as “The sad tree” or “The tree of sorrow” since the blossoms bloom only during the night and are shed throughout the day. These flowers are well known for their lovely scent and decorative applications. It is a wonder tree with a plethora of medical benefits.(Baas, 1984)N. arbor-tristis (NAT) belongs to the

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Division-Magnoliophyta; Class-Magnoliopsida; Order-Lamiales; Family-Oleaceae.(Baas, 1984; Ruchita Shrivastava, n.d.) It is a terrestrial, woody perennial plant with a 5–20 year lifespan that grows up to 10 meters tall. Nyctanthes arbor-tristis is found growing in the loamy soils on the rocky terrain in the dry foot hills and as undergrowth in dry deciduous forests in its native habitat(Sharma et al., 2021). It is indigenous to southern Asia, ranging from northern Pakistan and Nepal to northern India and south east Thailand. In India it is mostly found in the outer Himalayas and parts of Jammu and Kashmir, Nepal, to the east of Assam, Bengal, and Tripura, which stretch from the central area to the Godavari in the south(Rani et al., 2012; Sharma et al., 2021). It grows best in arid and semi-arid climatic conditions and thrives in red and black soils with a pH of 5.6–7.5. Tribal people in Tripura use the flowering phenology of night blossoming jasmine to predict weather and rainfall variations, which help them, plan agro forestry activities and disaster prevention. It is a versatile plant with scented flowers that fall off before sunrise. (Manjulatha Khanapur ; Ravi K. Avadhanula; Oruganti H. Setty, 2014a; Omkar, Jeeja, & Chhaya, 2006; Rani et al., 2012; Sharma et al., 2021) Since ancient times, it has been utilized in folk medicine for antibilious, gynecological problems, and hepatoprotective action(Tom & Benny, 2016).

Table 1: Nyctanthes arbor- tristis vernacular names in different languages.

Language	**Name**
English	Night jasmine
Sanskrit	Parijatha
Hindi	Harsingar
Bengali	Sephalika
Guajarati	Parijathak
Oriya	Gangasiuli
Marathi	Pagadamalle
Kannada	Parijatha
Telugu	Jayaparvati
Malayalam	Parijatakam
Tamil	Manjatpu Pavelam
Indonesian	Srigading (Sundanese, Javanese)
Filipino	Coral Jasmine
Thai	Karanikaa
Vietnamese	Iai Tau

Phytoconstituents:

Tribal people in central India use various portions of this plant to treat coughs, hiccups, diarrhea, snakebite, and ulcers. Researchers have also tested NAT for antihistaminic, CNS, antipyretic, amoebicidal, anthelmintic, antidepressant, antioxidant, and anticancer properties. Since antiquity, every part of the tree has been employed as traditional medicine for household cures to treat

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various human illnesses. (Ruchita Shrivastava, n.d.) N. arbortristis contain various phyto chemicals like(Hetal Bhalakiya, 2019)

Steroids: Steroids are one of the key compounds of plant cell membrane. They act as growth hormones and also as insect repellents. In traditional medicine, plant derived steroids have been historically utilized and some remain significant and valuable medication even till today.(mathew Dean, Brian T. Murphy, n.d.; Zeelen, 1995) The compound β-sitosterol is the most commonly occurring in Nyctanthes it has been isolated from stem, seed and leaf extracts. However leaves contain other steroids as well like D-mannitol β-sitosterole, Nyctanthic acid, Astragaline, Nicotiflorin, Tannic acid, Oleanolic acid, Ascorbic acid Methyl salicylate, Volatile oil Friedeline Label Mannitol Glucose(Khatune, Mosaddik, & Haque, 2001).

Terpenoids: Terpenoids are the most diverse group of organic molecules that consist of several isoprene units. They are the major components of the forest aerosols. (*2016 Terpenes from Forests.Pdf*, n.d.) Therpinoids are widely used in the industrial sector as flavors, scents, spices, also in the perfume and cosmetics industry. Many terpinoids have biological functions and are used in medicine. The terpenoids p-cymene and α-pinene Diterpene Nyctanthin were isolated from the NAT flower oil extract while 4- secotriterpene acid, Triterpenes-3, nyctanthic were identified in the seed. The leaves have Lupeol ,Triterpenes ,β-amyrin, oleanolic acid, friedeline, (Arbortrlstls, 1991; Karan, Maity, Pal, Singha, & Jana, 2019).

Flavonoids: Various substances fruits, vegetables, flowers, grains, bark, roots, stems, tea and wine all are rich in flavonoids. They are a collection of natural compounds with varying phenolic structures well known for their health benefits on which a lot of studies are being made. Flavonoids have become essential components in a wide range of pharmacological, therapeutic, cosmetic and nutraceutical applications.(A.N.Panche, A.D. Diwan, 2016) Some of the well distinguished flavonoids like Quercetin, kaemferol, anthocyanins, apigenin in the flower oil extracts while in the flavonoids Nicotiflorin were identified in the stem extracts of NAT(Bansal, Bharati, & Bansal, 2013).

Alkaloids: Alkaloids are a fascinating group of substances having a wide range of unpleasant and beneficial effects on animals and humans. Antibacterial, antimitotic, anti-inflammatory, analgesic, local anesthetic, hypnotic, psychotropic, and anticancer activities are only a few of the physiological effects of alkaloids. (Hassan et al., 2012) Organic chemists, biologists, biochemists, pharmacologists, and pharmacists are nevertheless fascinated by alkaloids derived from plants rather than animals. Morphine, caffeine, strychnine, quinine, ephedrine, atropine, and nicotine are examples of well-known alkaloids. Nyctanthine is the alkaloid derivative of NAT(B.N. Paul, 1997; Hassan et al., 2012; *R 2005, Sedative Effects of Hot Flower Infusion of Nyctanthes Arbo-Tristis. on Rats _ Enhanced Reader.Pdf*, n.d.).

Glycosides: Glycosides involve a wide range of biologically active compounds including hormones, sweeteners, alkaloids, flavonoids, antibiotics and etc. Glycosides are typically

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classified based on two factors the aglycone residue and the biological activity. Flavanol, iridiod, phenylpropanoid, and polyacetylenes are some of the glycosides found in NAT. Numerous glycosidic substances have been identified in the leaves of NAT, including Irridoid Glycosidesarbortristoside C, Astragaline(Kaempferol 3-glucoside) cardiac glycosideny mphalin, nyctanthoside ,6βhydroxy loganin, 6- Otransacetyl-7- Ocinnamoy l6βhydroxyl oganin, and isoarborside C have been isolated from the flower. The glycoside,Naringenin-4'- O-β-glucopyranosylαxylopyranoside is found in the stem, , while Phenylpropanoid Glycosidenyctoside A, C Eroded Glycosidesarbortristoside A, B, C, D and E, were isolated from seed extracts. In addition, Flavonol, Glycosides Astragaline Nicotiflorin, , 7- Otrans-cinnamoyl-6βhydroxyloganin, Desrhamnosylverbacoside, Eroded Glycosidesarborsides A, B, C, 6β-hydroxyloganin, 6,7-DiObenzoylnycthanoside , 6-O-transcinnamoyl6β-hydroxyloganin were isolated from the leaves(Kren & Martinkova, 2012; Louie et al., 2020).

Miscellaneous: Apart from the already discussed phytochemicals, several bioactive phytoconstituents have been identified in NAT, the leaves include D-mannitol, essential oil, and methyl salicylate, whilst seeds contain glycerides of stearic, palmitic, oleic, linoleic, lignoceric, and myristic acids, lauric acid, D-glucose and D-mannose. Flower oil also contains 1-deconol anisaldehyde, according to reports. NAT stems were used to isolate frie-del-1-ene-3-one, 1ahydroxyfriedel-4-(23)-en-3-one, 1-triacontanol, lignoceric acid and pelargonic acid. Sigmasterol and, a newly discovered rangy-olone, n-Tetradecyl-b-D-glucopyranoside. There are other compounds as well namely, 2-phenylethyl b-D-glucopyranoside. A range of biological problems have been claimed to be improved by some of the natural chemicals extracted from this plant species. Some of these chemicals identified and extracted have shown to cure a wide range of biological ailments.(Kumari, Madhuri, Charya, & Rao, 2012; Santhi Latha Pandrangi, Prasanthi Chittineedi, Sphoorthi Shree Chalumuri, Avtar Singh Meena, Juan Alejandro Neir Mosquera, Sungey Naynee Sánchez Llaguno, Ramachandra Reddy Pamuru,Gooty Jaffer Mohiddin, 2022)

Pharmacological importance of Nyctanthes arbor-tristis:

Ayurveda, Siddha, and Unani systems of medicine have recognized NAT to be a potential source of medicines and curatives for various ailments. Much research has been done on the leaves and seeds of N. arbor tristis, proving it to be one of the essential sources of medically significant pharmacological compounds. NAT has been observed with hepatoprotective, antileishmanial, antipyretic, antihistaminic, antimalarial, antibacterial, anti-inflammatory, antioxidant, antiviral, and antifungal properties. It also has a promising future in nanoscience, food and textile industries, cosmetics, and other fields. Additionally, metabolic analysis in recent times has encouraged its wide use in curative pharmacological applications.

Antidiabetic activity: In a study, the ethanol extracts of NAT stem and bark were found to have dose-dependent antidiabetic properties. In serum, the cholesterol and triglyceride levels were higher in diabetic rats, but they were significantly decreased after treatment with NAT stem and

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bark extracts. It was discovered that the stem and bark extracts were more effective due to their hypolipidemic effect. Ethanolic extracts significantly reduced the TBARS in the liver. It was also proven to have antioxidant and antidiabetic properties. Oral administration of different doses(50,100 and 200mg/kg) of NAT leaves and flower chloroform extract for 27 days resulted in a substantial reduction in lipid peroxidation (LPO), SGPT, SGOT, Alk-Phos, cholesterol, and triglyceride levels in streptozotocin (STZ) treated diabetic rats in comparison with diabetic rats. Furthermore, when compared to diabetic control rats, the diabetic rats that have been treated with NAT extracts have shown a substantial increase in superoxide dismutase (SOD) and catalase (CAT) enzymatic antioxidant activity (Chikati, Gulati, Garimella, & Chalumuri, 2021; Pandrangi et al., 2014).

Anti microbial activity: Infectious diseases are the leading cause of premature death worldwide. It has become a significant source of morbidity and mortality in immunocompromised patients in underdeveloped nations with the growing resistance of infectious bacteria towards various synthetic medications. Antimicrobial and multidrug resistance is becoming widespread in species like Staphylococcus aureus, Staphylococcus epidermis, Salmonella typhi, and Salmonella paratyphi A(Gundampati Ravi kumar, Rajasekhar Chikati, Santhi Latha Pandrangi, Manoj Kandapal, Kriti Sonkar, Neeraj Gupta, Chaitanya Mulakayala, Medicherla V. Jagannadham, Chitta Suresh Kumar, Sunita Saxena, 2012; Khatune et al., 2001). According to one study, methanolic extract of NAT leaves displayed potent antibacterial activity against these species with Minimum Inhibitory Concentration (MIC) values ranging from 1-8mg/ml(Chikati et al., 2021). In an in vitro antibacterial study, Staphylococcus aureus, micrococcus luteus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa, Candida albicans, and Aspergillus niger were put to the test using cup plate method. The zone of inhibition and MIC was determined compared to commercially available drugs ciprofloxacin and fluconazole. The chloroform extract has antibacterial and antifungal action, whereas the petroleum ether and ethanol extract only exhibit antibacterial activity(Hanan et al., 2018; Pavan Kumar Rambatla, Santhi Latha Pandrangi, Satyanarayana Rentala, 2021; Santhi Latha Pandrangi, Sarangadhara Appala Raju Bagadi, Navin Kumar Sinha, Manoj Kumar, Rima Dada, Meena Lakhanpal, Abha Soni, Shreshtha Malvai, Sheeba Simon, Chintamani Chintamani, Ravindar Singh Mohil, Dinesh Bhatnagar, 2014).

Anthelmintic activity: The anthelmintic activity of an ethanolic extract of fresh flowers and dried leaves, stem, and bark of NAT was investigated using piperazine citrate as a reference. The anthelmintic action of this extract was investigated by inhibiting the contractile effect of acetylcholine with various dilutions(Ansari Imtiyaz Ahmed, Patil Javesh K., Kamora Kunal Rajeshlal, Mandhan Priyanka Mahesh, Poptani Taruna Harshlal, 2016; Overview, Dyslexia, & Treatment, n.d.; Santhi Latha Padrangi, Prasanthi Chittineedi, Rajasekhar Chikati, Joji Reddy Lingareddy, Meeravali Nagoor, 2022). It was shown that ethanolic extracts of seeds and flowers had more decisive anthelmintic action than bark and leaves but less than piperazine citrate. Furthermore, these extracts enhanced atropine's anthelmintic effect, which might be attributed to the inhibition of motility by relaxing and decreasing responsiveness to acetylcholine contractile action(Hanan et al., 2018).

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Anti-inflammatory activity: According to one study , the water-soluble ethanolic extract of NAT leaves was tested for anti-inflammatory efficacy. NAT inhibited the acute inflammatory edema caused by various phlogistic agents, including carrageenin, formalin, histamine, 5-hydroxytryptamine, and hyaluronidase, in the hind paw of rats. The acute inflammatory edema in the knee joint of rats caused by turpentine oil was also dramatically decreased. Another study demonstrated that in subacute models. NAT reduced granulation tissue formation in the granuloma pouch and cotton pellet tests. The acute and chronic phases of formaldehyde-induced arthritis were dramatically reduced. NAT was also discovered to prevent the inflammation caused by immunological approaches such as Freund's adjuvant arthritis and the PPD-induced tuberculin reaction. Arbortristoside-A was discovered to have potent anti-inflammatory and antinociceptive action that was dose-dependent. It appears that arbortristoside-A suppressed histamine, serotonin, and carrageenan-induced edema, implying its anti-inflammatory activity may be linked to the inhibitory effect of prostaglandin, histamine, and serotonin. The analgesic efficacy of arbortristoside- A may be attributed to suppressing prostaglandin action
(Lakhanpal et al., 2014; Malla, Pandrangi, Kumari, Gavara, & Badana, 2018).

Antioxidant activity: Free radicals are produced as a part of the regular metabolic activity in a live body. Antioxidants and free radical scavengers protect the human body from pathological disorders, including asthma, ischemia, arthritis, anemia, inflammation, neurodegeneration, Parkinson's disease, mongolism, aging, and maybe dementia. The antioxidant activity of NAT was measured using the DPPH test, free radical scavenging activity reducing power assay, and total antioxidant capacity was determined in a study where it was determined that the plant has a high level of antioxidant activity. In traditional medicine, NAT leaf extracts are often employed. Several in-vitro tests, including DPPH, hydroxyl and superoxide radicals, and H2O2 scavenging tests, demonstrated that the acetone soluble component of its ethyl acetate extract has excellent antioxidant activity. Furthermore, its ability to inhibit Fe (II) - induced lipid peroxidation of liposomes and γ-ray-induced DNA damage verified this. The antioxidant activity might be attributed to the strong reducing power and high phenolic and flavonoid content(Manjulatha Khanapur ; Ravi K. Avadhanula; Oruganti H. Setty, 2014b).

Anti-arthritic activity: Arthritis is a joint disorder that, in the longer run, damages the bone and its joint. Cytokines have a crucial role in arthritis. The effectiveness of NAT seed, leaf, and fruit extract in adjuvant-induced arthritis models was studied. The TNF-α, IL-1, and IL-6 levels were lowered in ethanolic leaf and fruit extracts, which have been shown to have anti-arthritic properties(Hanan et al., 2018; Milind M Meshram, Swatee B. Rangari, Shashank B. Kshirsagar, Suraj Gajbhiye, Madhuri R. Trivedi, 2012).

Anti cancer Activity of Nyctanthes: Cancer being the biggest challenge of the modern world, Nat has been further investigated for anticancer properties. In a study against the triple-negative breast cancer cell line, the IC50 values of the methanolic extracts of the dried fruit of NAT were calculated to be 9.72g and 13.8g. It has further identified the bioactive phytochemicals, including glycosides, tannins, phenols, and steroids which are suspected to be responsible for its anticancer

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action(Kumari et al., 2012). In another study, (Manjulatha Khanapur ; Ravi K. Avadhanula; Oruganti H. Setty, 2014a) various solvent extracts of the dried flowers of NAT were examined for the anticancer potential on five different tumor cell lines, including colorectal adenocarcinoma(Colo 205); retinoblastoma (Y79); chronic myelogenous leukemia (K562); breast adenocarcinoma (MCF-7); breast adenocarcinoma (MDAMB-231), and the chemotherapeutic drug, Doxorubicin, as a positive control. Ethanol and ethyl acetate extracts were found to be cytotoxic in a concentration-dependent manner to the tested cell lines, out of which ethanol extract has been proven to be the most potent. Iridoids and carotenoids are the most common chemical constituents in NAT, which have been linked to affecting a variety of biological activities(Ghisalberti, 1998; Lee et al., 1999). In a computational study to analyze the therapeutic Efficacy of NAT flowers in inhibiting proliferation of acute and chronic primary human leukemia cells, with adipocyte differentiation and analysis of interactions between the selected secondary metabolites and survivin protein, the suppression of the amylase enzyme and glucose uptake by yeast cells were used to assess the invitro hypoglycemic efficacy. In the crude and tested fractions of hexane and ethyl acetate extracts, the percentage of glucose absorption and amylase inhibitory activity increased dose-dependently(Chikati et al., 2021, 2018; Lakhanpal et al., 2016, 2014; Malla et al., 2018; Saumya Nishanga Heendeniya, Lakshika. Rangi Keerthirathna, Chamalika Kanthini Manawadu, Indeewarie Hemamali Dissanayake, Rizwan Ali, Abdullah Mashhour, Hajar Alzahrani, Pahan Godakumbura, Mohamed Boudjelal, 2019). Antiproliferative studies were made on the following 3T3-L1 cells, primary peripheral blood mononuclear cells (PBMC) isolated from healthy and adult acute myeloid (AML) Moreover, chronic lymphocytic leukemia (CLL) patients, recombinant Jurkat T cells, and MCF7 cell lines revealed that NAT exerted a high specific activity against anti-AML and anti-CLL PBMC cells, especially by the hexane and ethyl acetate fractions. The ethyl acetate and chloroform fractions inhibited the differentiation of 3T3-L1 cells, followed by hexane fractions. In this study, further investigation was done to detect the presence of 1- heptacosanol (hexane fraction), 1-octadecene (hexane and chloroform fractions), and other organic substances. Molecular docking revealed the specificity of phenol,2,5-bis(1,1-dimethyl ethyl), and 4-hydroxypyridine 1-oxide compounds for survivin protein, indicating the possibility of NAT creating new therapeutic leads against leukemia(Saumya Nishanga Heendeniya, Lakshika. Rangi Keerthirathna, Chamalika Kanthini Manawadu, Indeewarie Hemamali Dissanayake, Rizwan Ali, Abdullah Mashhour, Hajar Alzahrani, Pahan Godakumbura, Mohamed Boudjelal, 2020). On treatment with different concentrations (50, 100, and 200 μg/ ml) of floral extracts, the GSH level has been significantly enhanced while decreasing GST activity in lymphocytes(Chikati et al., 2021; Santhi Latha Pandrangi, Sarangadhara Appala Raju Bagadi, Navin Kumar Sinha, Manoj Kumar, Rima Dada, Meena Lakhanpal, Abha Soni, Shreshtha Malvai, Sheeba Simon, Chintamani Chintamani, Ravindar Singh Mohil, Dinesh Bhatnagar, 2014). Also, the LDH activity reduced considerably in cell-free media. Compared to cells treated with H_2O_2 alone, cells that have been pre-treated with floral extract have been protected lymphocytes from H_2O_2- induced oxidative stress by

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significantly increasing GSH levels and reduced LDH activity(Hanan et al., 2018; Hassan et al., 2012).

In a study where betulinic acid was first isolated from ethyl acetate extract of NAT leaves via Bioactivity-guided fractionation. The anticancer efficacy was tested on various human cancers, including liver-HepG2, lung-A549, Leukaemia-HL-60, breast-MCF-7, colon-HCT-116, prostrate-PC-3, and cervix-HeLa cell lines. Betulinic acid was cytotoxic to several cancer cell lines with IC50 values of 6.53 (HepG2), 9.34 (A549), 14.92 (HL-60), and 16.90 (MCF-7), 17.07 (HCT-116), 13.27 (PC-3), and 12.55μM (HeLa). This is the first report on the isolation and identification of the lupane-type triterpenoid, betulinic acid, which has not been reported before and has shown to have substantial anti-inflammatory, antiproliferative, and antioxidant activities in vitro. In LPS- stimulated RAW 264.7 cells, betulinic acid inhibited the cyclooxygenase (COX-1, COX-2), lipoxygenase (5-LOX) enzyme activity, and NO and TNF-α production. On further investigation through the DPPH assay, it was proven to show good antioxidant activity alongside significant anticancer activity on various cancer cell lines(Karan et al., 2019). In a study (Pandeti, Sharma, Bathula, & Tadigoppula, 2014)two compounds, arbortristoside- A and 7-O-trans-cinnamoyl 6-hydroxyloganin(Omkar et al., 2006), were isolated and identified from the seeds of NAT. The n-Butanol fraction (80g) has been eluted with chloroform and methanol in increasing polarity. Two sub-fractions were collected based on Rf values and rechromatographed with chloroform– methanol(96:4); recrystallization from methanol to give compound 1 and chloroform–methanol (90:10); recrystallization from methanol afforded compound 2 These compounds displayed moderate in vitro anticancer activity. They prepared thirteen derivatives from compound 2 and tested them for anticancer activity. Of the derivatives, 8 and 15 were identified to be effective anticancer agents. T7his mechanistic study revealed that these derivatives cause apoptosis and cell cycle arrest against three cancer cell lines HepG2(human hepatocellular carcinoma), MCF-7, and MDA-MB-231. Chemical modification of compound 2 resulted in significantly improved activity against HepG2 and MCF7 cells, and in HepG2 cells, compounds 8 and 15 were also capable of cell cycle arrest and caspase-dependent death. Caspase 3 is said to trigger apoptotic activation. Nevertheless, more work needs to be done on the iridoid class to produce potent anticancer drugs from NAT(Omkar et al., 2006; Pandeti et al., 2014).

Conclusion: According to the in-vitro and in vivo studies so far conducted, Nyctanthes arbor-tristis has been proven to be a worthy colossal therapeutic in the field of natural medicine, particularly in the treatment of illnesses such as malaria, fevers, arthritis, and also protozoan infections like leishmaniasis. It is also proven that every portion of this plant has medicinal value. The only available study that has undergone clinical trials was for the treatment of malaria, despite the usage of the crude extract. In addition, more extensive safety data on acute, subacute, cardio, and immunotoxicity for crude extracts and pure extracts needs to be obtained.

A bird's eye perspective of the literature reveals a gap in the scientific investigation, which requires immediate attention in collaborative studies with the traditional medical system.

However, several studies indirectly associated biological activities such as intestinal worms with anthelmintic activity, gout via analgesic and anti-inflammatory, and anxiety and restlessness via CNS modulatory activity. Some of the traditional medicine beliefs, such as antiviral, ophthalmic difficulties, bronchitis, an antidote to snake venom, piles, and gynecological effects of NAT, have to be investigated and validated. Further studies are needed to investigate the anticancer activity to convert NAT into a potential therapeutic agent to treat cancer and other diseases.

Conflict of Interest: None declared

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Author Contributions: Wrote the manuscript: SSC. Tabulation and arranging the data: SG and PC. Conceptualized the study: SLP. Overall supervision of the study: SLP

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