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Review Article

Integrative Review on *Nyctanthes arbor-tristis*: Exploring its Botanical Identity, Bioactive Compounds, and Biomedical Applications

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ABSTRACT

Nyctanthes arbor-tristis or night-flowering jasmine (also called parijat) is a long-standing medicinal herb that is commonly used in Ayurveda, Siddha, Unani and various folk medicines of South Asia. The current integrative review will critically assess the botanical identity, ethnomedicinal property, phytochemical composition, pharmacological action, and mechanism of action of Nyctanthes arbor-tristis and also indicate its biomedical potential and future therapeutic potential. The plant has a clear botanical and pharmacognostic profile so that it is identified and evaluated with ease in terms of quality. The ethnobotanical record records that it has a wide range of applications in the treatment of fever, inflammation, arthritis, metabolic disease, infections and neurological disorders. Phytochemical studies indicate abundant levels of primary and secondary metabolites with the most significant ones being iridoid glycosides, flavonoids, phenolic compounds, terpenoids, steroids, and volatile compounds which are all involved in its therapeutic effects. The spectrum of pharmacological activity of experimental studies has shown the presence of an antioxidant, anti-inflammatory, immunomodulatory, antipyretic, analgesic, antimicrobial, antidiabetic, hepatoprotective, nephroprotective, neuroprotective, cardioprotective, and anticancer effects. Mechanistically, these effects are coupled by mediating the oxidative stress pathways, controlling the production of inflammatory mediators and cytokines, enzyme inhibition, receptor-based processes, and engagement of major molecular signal pathways. The variability in phytochemical composition, the

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absence of standardized processes of extraction and the absence of human studies are significant obstacles to translational development. To sum up, *Nyctanthes arbor-tristis* is a promising multi-target medicinal plant that has a high potential in the development of drugs in the future. Strict mechanistic research, standardized preparations, and properly structured clinical trials are needed to help in its evidence-based incorporation into the current healthcare systems.

INTRODUCTION

In many areas of the world medicinal plants still hold the key role in the health care structures with traditional medicine having a strong impact on the everyday life of the people living there. Even in the current biomedical paradigm, plant-based molecules have also played a significant role in drug discovery, as direct therapeutic agents or lead molecules to undergo synthetic modification [1]. Increased scientific interest in herbal medicines is fueled not only by their historical applicability but also by the rising concerns on the adverse effects, resistance rates as well as the economic cost of several common pharmaceuticals. As a result there has been a need to scientifically evaluate medicinal plants systematically in order to conciliate the traditional knowledge with evidence based biomedical research. *Nyctanthes arbor-tristis* has been the focus of continued interest in the current literature of herbal medicine because of its generalized therapeutic assertions and developing experimental support [2].

Nyctanthes arbor-tristis, or night-flowering jasmine or parijat, is a small tree or shrub that is traditionally worshipped because of its cultural and medicinal value. The plant is commonly found throughout the Indian subcontinent and some of Southeast Asia where it has long been utilized in Ayurveda, Siddha, Unani as well as other indigenous healing systems [3]. The plant has been used in traditional medicines to treat all its organs such as the leaves, flower, seeds, and even the

bark, among other ailments, such as fever and inflammation, and arthritis, hepatitis, and even neurological diseases. Although this has a long history of traditional use, scientific research on the plant has been historically disjointed, with some studies typically addressing a single pharmacological action or a tightly constrained phytochemical description [4]. This has produced a fragmented literature, which is not integrative and critically appraising. Modern literature has named various categories of bioactive constituents of the plant, such as those of iridoid glycosides, flavonoids, phenolic compounds, terpenoids, and fatty acids, many of which have been reported to regulate oxidative stress, inflammatory cascades and immune responses. The results have reinforced the scientific foundation of some of the traditional assertions as well as creating new possibilities to understand the potential of the plant in the treatment of chronic inflammatory diseases, metabolic disorders, infectious diseases, and neurodegenerative pathologies [5]. The absence of standard methodologies and variability of the plant material, and lack of translational studies still pose obstacles in its advancement to be no longer regarded as a traditional remedy to a clinically viable therapeutic agent. Historically, *Nyctanthes arbor-tristis* is in a special place in Indian medicine and culture. Ayurveda, in ancient times, talks of its application in the treatment of fever, especially those that are malarial fever and seasonal fever besides in the treatment of ailments that involve joint pains and inflammation. Classical literature also talks about the plant to balance doshas especially in disorders associated with vitiated vata and kapha. Besides the medicinal use, the plant is also symbolically important in mythology and religious beliefs, and many people related it to cleansing, piety, and healing [6]. This is what makes it a dual purpose medicinal and sacred plant, which has led to its intensive farming and production throughout the



centuries to maintain the continuity of knowledge and availability of raw material. *Nyctanthes arbor-tristis* as an ethnomedicine practiced in various geographical areas and cultural backgrounds is exceptionally diverse.

Traditional healers have used leaf decoctions to treat intermittent fever, arthritis and digestive discomforts and use flower extracts due to its weakly sedative and anti-inflammatory effects. Seeds and bark are also included in the formulations used to treat the parasitic infections and the skin disorders [7]. These procedures show that they have an empirical knowledge of the therapeutic versatility of the plant, which had been acquired over centuries of experience and observation. However, these ethnomedicinal practices need to be translated into conventional forms of therapeutic use but subjected to stringent scientific scrutiny, especially on issues of safety, optimal dosage, and mechanism-guided efficacy. There has been an upsurge in the pharmacological research on the validation of the traditional claims of *Nyctanthes arbor-tristis* in the recent decades through the use of modern experimental models. Antioxidant, anti-inflammatory, antipyretic, immunomodulatory, antimicrobial, hepatoprotective and neuroprotective effects have been reported. These works indicate that the plant influences its effect by means of regulating the important biochemical pathways such as the suppression of pro-inflammatory mediators, reactive oxygen species scavenging, cytokine production regulation, and stabilization of cellular membranes [8]. Although these results are encouraging, most of the data available are in vitro or animal based and there is still very little clinical evidence to aid translating them to therapies. In addition, variation in extraction methodology, phytochemical profiling and experiment design make comparison across studies difficult. The other serious area that needs a thorough

assessment is the safety profile of *Nyctanthes arbor-tristis*. Although the traditional usage may connote a level of safety, herb-drug interactions, long-term effects, and toxicity evaluation have not been scientifically evaluated. The need of systematic toxicological studies is demonstrated by isolated reports of dose-dependent adverse effects. In the absence of strong safety data, plant-based formulations cannot be fully integrated into mainstream healthcare [9]. A critical integrative review of both therapeutic potential and safety issues is thus necessary to give a relatively balanced view and lead all future research activities. The current integrative review is aimed to compile, analyze, and synthesize the current knowledge on *Nyctanthes arbor-tristis*, including its botanical identity, ethnomedicinal usage, phytochemical composition, and bio-medical uses. Contrary to narrative reviews which tend to give summary descriptions, this integrative method is expected to be critical in analysing the experimental evidence, find similarities and differences in the literature and reveal gaps in translation. The review aims to provide a unified picture of the therapeutic landscape of the plant by integrating information on the ethnobotanical records, phytochemical analyses, pharmacological research, and new biomedical studies [10].

BOTANICAL IDENTITY AND TAXONOMY

Nyctanthes arbor-tristis is a highly familiar medicinal plant whose botanical identity has been well defined with respect to classical taxonomical practices, regional flora as well as recent pharmacognostic studies. It is of the family Oleaceae, which is a family of aromatic and medicinally useful species. The genus *Nyctanthes* is not very large, although the most popular and used species is *N. arbor-tristis* [11]. The taxonomic position of the plant is reflected in its botanical name, which also describes its unique



biological behavior; the shedding of flowers with a sweet fragrance in the morning after nighttime blooming is called arbor-tristis, which means, sad tree. The species is not taxonomically unstable with a minor number of synonyms in accepted botanical treatment, making it easier to identify the species and diminishes confusion in medicinal plant research and trade. According to taxonomical perspective, *Nyctanthes arbor-tristis* belongs to the dicotyledonous group of angiosperm order Lamiales. The plant has characteristic features of the family Oleaceae, which includes opposite leaves, have flowers that are sympetalous, and a superior ovary. Proper taxonomic classification is of special interest to medicinal plant studies where misidentification or replacement by morphologically related plants can have a considerable impact on treatment effects and safety [12]. In both conventional medicine and in the modern phytopharmaceutical research, proper taxonomic identification of *N. arbor-tristis* is the basis of reproducible pharmacological and phytochemical studies. *Nyctanthes arbor-tristis* morphologically is a large shrub or small tree that normally grows to a height of 6-10 meters where the conditions are favorable. It has an erect stem and a rough, flaky, grayish-brown bark which fissures with age [13]. Branches are young and quadrangular and pubescent, but becoming terete and glabrous gradually. The leaves are plain, opposite, ovate or elliptical and with whole or slightly serrated margin and an acuminate tip. The leaf is dark green and scabrous on its upper surface with the lower surface being paler and pubescent a point that helps in identifying the species when one is using a macroscope Fig.1. Venation is eminent, reticulate, and easily observable, which is a part of the morphological characteristics of the plant diagnosis. One of the most notable things about *Nyctanthes arbor-tristis* is its flowers that are central to its cultural symbolism and its use as a medicine. Its inflorescence is usually cymose, with

small, fragrant, night-neutral, and abscising flowers. The flowers are made of a white corolla shaped into five or eight lobes and a tubular center of bright orange color, having carotenoid pigments. The ecological meaning of the nocturnal blooming pattern is that insects are pollinated by night species, and the fallen flowers are also an important element to the appearance under the canopy of the trees. The fruit is a two lobed, flattened, capsule with one seed in each lobe which gives another significant morphological feature of botanical identification. Its authentication and quality assessment is further enhanced by microscopic and pharmacognostic analysis of *Nyctanthes arbor-tristis* [14]. Transversal views of the leaf show a dorsiventral organization that is characterized by a distinct palisade layer at the bottom of the upper epidermis and a spongy mesophyll at the bottom of the lower epidermis. A significant diagnostic characteristic is the presence of multicellular trichomes especially on the abaxial surface. The stomata mostly belong to the anomocytic type, as is the case with many representatives of the Oleaceae family. Vascular bundles are developed and collateral, and secure effective water and nutrient flowing through the leaf tissue. These are microscopic characteristics that are regularly used in standardization of pharmacognostics to distinguish between true and adulterated plant material. Another diagnostic character that can be applied in the analysis of crude drugs is powder microscopy of dried plant parts and leaves.

The fine material usually contains fragments of epidermal cells having wavy anticlinal, trichomes, fibers, and xylem vessels having spiral and pitted thickening. In a few studies, the treatment of calcium oxalate crystals (not always constant) has been reported, and may act as the auxiliary identifying feature. Pharmacognostic parameters are also necessary in assuring consistency and



quality in herbal preparations especially when large-scale production is done where the macroscopic identification of a sample might be inadequate. Geographically, *Nyctanthes arbor-tristis* is still extensively found in the Indian subcontinent, extending to India, Nepal, Bangladesh and Sri Lanka with some extension into southeast Asia. It is widespread in India in its tropical and subtropical environments and even in the plains and the lower hilly parts. The plant is very flexible and can grow in different types of soils such as the loamy to slightly alkaline soils as long as the soil has excellent drainage. It is more tolerant to warm weather with average rains and can be grown under full sunlight but can also be grown under partial shade. This environmental adaptability has made it to be widely cultivated and naturalized in various agro-climatic regions [15].

The cultivation activity of *Nyctanthes arbor-tristis* is not so complicated and it can be successfully cultivated on a home garden and medicinal plantation. Propagation of the plant is usually by seed or a stem cutting with vegetative propagation being preferred to preserve a genetic homogeneity and target desirable characteristics. It does not need a lot of agronomic inputs, because the plant is resistant to a wide range of pests and diseases. Frequent pruning improves branching and flower growth, especially in case of harvesting flower, especially used in medicine or cultural functions. Its ease of growing and low maintenance needs

favor sustainability in the use and conservation of the species, particularly in areas where the species is ethnomedically relevant [16]. *Nyctanthes arbor-tristis* has a wide range of vernacular names, which is indicative of its popularity and usage across several regions in the world and various cultures. It is usually known as Harsingar or Parijat in Hindi and various North Indian languages, and in Sanskrit works as Shephalika or Mandara. The plant is called Shiuli in Bengali and in the southern Indian languages, the name of the plant is Paavizha Malli and Paarijatha. These local names are usually culturally and symbolically based and it stresses the fact that the plant is identified with religious ceremonies, seasonal celebrations, traditional medicine. Historical applications of *Nyctanthes arbor-tristis* reveal a great deal of regional diversity, due to local medical traditions and cultural values [17]. The Leaf preparations find extensive application in the treatment of fever, inflammations, and joint diseases, especially by the rural and tribal areas. Flower extracts and pastes are used due to their weak sedative, antipyretic, and anti-inflammatory effects, and seeds and bark have been used traditionally in the treatment of parasitic infections and skin conditions. In other areas, the plant is not only appreciated due to its medicinal value, but it is used in spiritual cleansing and sacrifice. Such a rich ethnomedicinal tradition is a good basis in modern scientific discovery and makes *Nyctanthes arbor-tristis* a useful medicinal plant whose medical use is of long-term interest [18].



Fig.1: Botanical and morphological identity of *Nyctanthes arbor-tristis*

ETHNOBOTANICAL AND TRADITIONAL MEDICINAL USES

Nyctanthes arbor-tristis holds a leading role in Indian ethnobotanical history, being a highly practiced multipurpose medicine since ancient times. Its extensive application throughout classical traditions, including Ayurveda, Siddha, and Unani, and its application in the folk medical traditions on the continent, demonstrate enormous empirical knowledge about its medicinal capabilities. In contrast to most medicinal plants that have only been utilized within a single medical tradition, the species exhibits incredible cross-cultural acceptance implying a wide range of bioactivity that has been effectively confirmed by experience use. Its ongoing use in different geographical areas and generations highlights its perceived effectiveness and safety in the framework of traditional healthcare [19]. Practitioners of Ayurvedic medicine believe that *Nyctanthes arbor-tristis* is a plant with notable therapeutic properties, especially in diseases that relate to fever, inflammation and musculoskeletal diseases. The classics of Ayurvedic medicine explain that its leaves were used in treating jwara (fever) particularly chronic and recurrent fevers,

and also in illnesses associated with aggravated vata and kapha doshas. Leaf decoctions are generally used in the treatment of joint pains, sciatica, inflammatory states, whereas flavored preparations are thought to be useful in the treatment of the nervous system as well as minor sleeping disorders. Also, the plant is cited as a detoxifier and the preparations are designed to enhance hepatic activity and the general metabolic status. These kinds of descriptions indicate an integrative treatment modality, in which the plant is applied not just to treat symptoms but to restore systemic balance [20].

Nyctanthes arbor-tristis is used in the Siddha system of medicine with its origin in South India and it is mostly used as an anti-inflammatory, antipyretic and analgesic agent. In the treatment of arthritis, rheumatic conditions and febrile illnesses, siddha preparations have long been used by siddha practitioners as leaf and bark preparations. It is commonly used as part of polyherbal preparations, in which the plant is thought to increase the effectiveness of other medicinal components by synergistic effects [21]. The focus is made on the capacity of the plant in reducing pain, swelling, and enhancing functional

mobility with reference to chronic inflammatory disorders. This would be very much in line with the Ayurvedic applications, which point to a commonality of therapeutic logic across classical systems even though the theoretical basis of each approach was different. *Nyctanthes arbor-tristis* is also known to have medicinal value in Unani medicine specifically in the treatment of inflammatory and infectious disorders. Under the Unani system, the plant is said to have properties which assist to moderate abnormal humoral imbalances, particularly those that are related to excess heat and inflammation. The leaves and flowers are prepared as the traditional remedies to treat fever, skin-related illnesses, and digestive conditions [22]. The Unani approach pays significant attention to the therapy of temperament, and the application of this plant is determined by a personal constitution and symptoms of a disease. This kind of personalized use goes further to show the richness of the traditional knowledge about the use of it as a medicine. In addition to classical systems, *Nyctanthes arbor-tristis* is also an important constituent of folk medicine in rural and tribal communities in India, Nepal, and Bangladesh. In such environments, the traditional healers usually use the locally available plant substances to treat the common diseases. Leaf juice/decoctions are very commonly used in intermittent fever, malaria like symptoms and in intestinal worms, topical use of leaf paste in skin infections and inflammatory swellings. It is occasionally used in mild preparations of sedation or as supportive therapy on headaches and anxiety related complaints [23].

The therapeutic indications that are assigned to *Nyctanthes arbor-tristis* in traditional systems are exceptionally wide-ranging to include inflammatory, infectious, metabolic, and neurological diseases. One of the most invariably reported signs is fever whereby traditional healers

normally highlight the plant efficacy in repeated or intractable febrile conditions. Another significant field of application is inflammatory disorders, especially arthritis and joint pain, which is the expression of the supposed anti-inflammatory and analgesic effects of the plant being used. Also, the conventional claims are spread to digestive disorders, liver diseases, skin disorders, and some disorders affecting the nervous system, indicating a systemic and not organ action. This broad indication is an indication of a complicated phytochemical make-up that can alter various physiological pathways [24].

PHYTOCHEMICAL PROFILE AND BIOACTIVE CONSTITUENTS

The broad spectrum of therapeutic applications of *Nyctanthes arbor-tristis* is deeply based on its highly complex phytochemical profile. Significant phytochemical studies have identified the plant to produce a large variety of primary and secondary metabolites that work together in producing biological activity [25]. Primary metabolites (carbohydrates, proteins, amino acids and lipids) have critical functions in cell metabolism and cell structure whereas secondary metabolites provide adaptive benefits and therapeutic properties. The nativistic medicine considers the synergistic action of a variety of bioactive constituents found in various parts of the plant, especially in leaves, flowers, seeds, and bark, is the therapeutic efficacy of the plant. The biochemical basis of the biosynthesis of secondary compounds in *Nyctanthes arbor-tristis* uses primary metabolites Fig.2. Sugars and polysaccharides are involved in storing the energy and cellular signaling whereas proteins and free amino acids are involved in enzymatic and regulatory functions. Lipid fractions, albeit in low amounts, are also important in seeds and flowers and are engaged in membrane stabilization, as well as precursors of bioactive



lipid-derived molecules. Though it is not generally the direct subject of pharmacological research, primary metabolites determine extract composition, bioavailability and stability thus indirectly affecting an outcome of the treatment [26-28]. In *Nyctanthes arbor-tristis*, the secondary metabolites are the most pharmacological chemical group of interest. These include iridoid and secoiridoid glycosides which have received much attention and are regarded as characteristic components of the species. The compounds are found mainly in leaves and seeds and the structure of the compounds is cyclopentanoid monoterpene skeletons. It is also known that iridoid glycosides have anti-inflammatory, antipyretic and immunomodulatory effects that are strongly implicated with the use of the plant in traditional medicine to treat fever and inflammatory diseases. The oxidative cleavage of the iridoid ring leads to the generation of secoiridoids, which are additional biological activity enhancers, adjusting the inflammatory mediator and oxidative stress systems. These compounds are found in a significant number, which gives the plant a strong chemical foundation of many of its ethnomedical uses. Another significant group of bioactive constituents in *Nyctanthes arbor-tristis* is flavonoids, phenolic acids and tannins. They are polyphenolic compounds, which are highly consumed in the leaves and the flowers and are also reported to have strong antioxidant effects. Flavonoids are also involved in free radical scavenging, chelation of metals and control of cell signaling pathways in inflammatory and apoptotic processes. Phenolic acids increase the ability of the plant to counter the oxidative damage and tannins provide astringent effects that can be involved in antimicrobial and anti-inflammatory effects. The abundance of phenolics in some of the extracts confirms the use of the plant in the past in the management of diseases linked with oxidative stress, including chronic inflammation and

metabolic diseases [29]. Alkaloids with rather lower concentration levels in relation to other phytochemical groups contribute to the pharmacological complexity of *Nyctanthes arbor-tristis*. These N-containing products usually show high biologic activity at low doses and can be associated with analgesic, antimicrobial, or neuromodulatory. Other major constituents are the terpenoids, such as mono-, sesqui-, and triterpenes, especially in the leaves and the bark. Terpenoids have been identified to have various interactions with diverse molecular targets, which affect the action of inflammatory signals, immune reactions, and the movement of cell membranes. The presence of steroidal compounds found in the plant also adds to the effects of anti-inflammatory and membrane-stabilizing effects, which supports the traditional application of the herb in inflammatory and degenerative diseases [30]. The volatile constituents and essential oils which are mainly extracted using the flowers of *Nyctanthes arbor-tristis* are crucial in its sensory and therapeutic uses. These volatile substances give the flowers their typical fragrance, and they consist of the complex combination of terpenes, aldehydes, and other aromatic structures. Along with their cultural and ritual value, essential oils have antimicrobial, anti-inflammatory and mild sedative properties. Seeds and other plant components contain fatty acids that add nutritional and pharmacological value to the plant and some of the unsaturated fatty acids have anti-inflammatory and cardioprotective actions [31]. The mixture of volatile and non-volatile compounds increases the general bioactivity of the plant, and contributes to its multi-purpose use as medicine. The phytochemical profile is compound, which requires the use of sophisticated methods in order to properly characterize and control quality. Classical qualitative tests offer a preliminary identification of the key groups of phytochemicals, but recent studies are based on chromatographic and



spectroscopic procedures. Separation and quantitation of iridoid glycosides, flavonoids and phenolic compounds are frequently separated and quantified using high-performance liquid chromatography (HPLC) and thin-layer

chromatography (TLC) techniques. Gas chromatography with mass spectrometry (GC-MS) is especially applicable to such volatile constituents and essential oils in order to identify each constituent accurately [32-34].

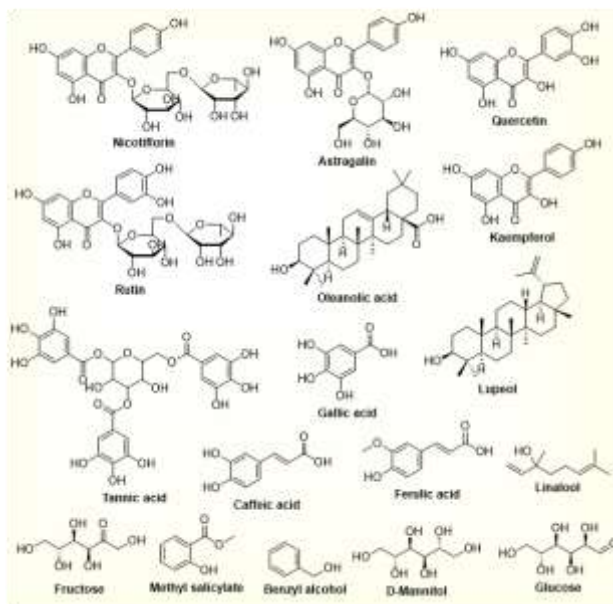


Fig.2: Phytochemical profile of *Nyctanthes arbor-tristis*

Pharmacological and biomedical activities

The pharmacological properties of *Nyctanthes arbor-tristis* indicate its abundant phytochemical structure and extensive history of traditional medical practices. The extensive scientific evidence of its various biomedical operations has been given in recent experimental studies, which

found out that the plant has multi-dimensional therapeutic properties based on antioxidant, anti-inflammatory, metabolic, and cytoprotective actions. The plant does not exert action on a single molecular target, but instead exhibits a pleiotropic mode of action, which is more so applicable in the treatment of complex and chronic diseases Fig.3.

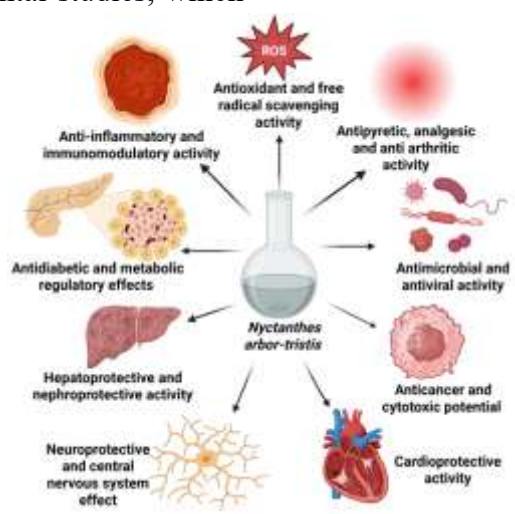


Fig.3: Pharmacological properties of *Nyctanthes arbor-tristis*

Antioxidant and free radical scavenging activity:

One of the most widely reported properties that *Nyctanthes arbor-tristis* exhibits is the antioxidant and free radical scavenging activity. Oxidative stress is one of the root causes of the pathogenesis of many diseases, and plant extracts have demonstrated considerable potential to counteract reactive oxygen species and prevent lipid peroxidation in test animals. These are attributed to a large extent due to the presence of flavonoids, phenolics, and iridoid glycosides, which elevate the endogenous defensive systems against antioxidative agents and guard the cellular components against oxidative damage. The plant supports cellular integrity and functional integrity in the various organ systems through redox homeostasis [35].

Anti-inflammatory and immunomodulatory effects:

The therapeutic value of *Nyctanthes arbor-tristis* is also characterized by anti-inflammatory and immunomodulatory effects. Among acute and chronic illnesses, inflammation is central and experimental research established that plant extracts inhibit inflammatory reactions by lowering the secretion of pro-inflammatory mediators and balancing out the cytokines. Besides modulating the excessive inflammation, the plant has the immunomodulatory effect by altering the activity of immune cells and preserving the immune homeostasis. This immunomodulatory, homeostatic maintenance of the immune response gives it good scientific foundation in its traditional application in inflammatory, autoimmune-like, and infection-related disease [36].

Antipyretic, analgesic, and anti-arthritic activities:

The analgesic, anti-arthritic and antipyretic properties of *Nyctanthes arbor-tristis* are more in line with its extensive ethnomedicinal use. Preclinical experiments have confirmed its anti-fever and analgesic properties, experimentally induced fever, and have shown that it acts on both central and peripheral pathways of thermoregulation and nociception. Plant extracts have been linked to the reduction of swelling and inflammatory markers and other beneficial effects in arthritis and joint inflammation models. These results support its past use in the treatment of fever, rheumatism, and chronic musculoskeletal disorders [37].

Antimicrobial and Antiviral properties:

The antimicrobial and antiviral effects of *Nyctanthes arbor-tristis* have become more and more popular in the background of emerging infectious diseases and antimicrobial resistance. It has been reported in laboratory studies that it has inhibitory activity against a variety of bacterial and fungal pathogens, indicating that the plant disrupts the integrity of microbial cells and vital metabolic functions. Even though the evidence of antiviral research is relatively minimal, the initial data points to its possible activity against some of the viral agents, which explains its conventional application in the treatment of febrile diseases of infectious etiology [38].

Antidiabetic and metabolic regulatory effects:

Nyctanthes arbor-tristis has antidiabetic and metabolic regulatory properties, which underscores its potential application in the treatment of metabolic conditions. It has been demonstrated through experimental studies that plant extracts can reduce blood glucose levels, enhance glucose tolerance and regulate enzymes that play a role in carbohydrate metabolism. It is believed that these effects occur due to increased



insulin sensitivity, decreased oxidative stress and metabolic pathway control. This kind of results gives the scientific confirmation of traditional assertions regarding metabolic balance and gives a preliminary study in the use of the plant as an adjunct in the management of metabolic diseases [39].

Hepatoprotective and Nephroprotective Activities:

Another dimension of the pharmacological profile of the plant is hepatoprotective and nephroprotective effects. Toxic and oxidative damage to the liver and kidney is especially prone to occur, and the experimental models have proved that extracts of *Nyctanthes arbor-tristis* are able to reduce organ damage caused by chemicals. There has been a consistent restoration of biochemical markers, and an improvement in tissue architecture as well as enhancement in antioxidant defenses. Such protective properties add to the customary application related to the detoxification and support of organs [40].

Neuroprotective and Central Nervous System Effects:

Nyctanthes arbor-tristis neuroprotective and central nervous system effects are a new focus of biomedical research. It has been experimentally indicated that the plant can minimize neuroinflammation and oxidative stress in neural tissues, which can protect neural tissues against neuronal harm. Conventional reports of mild sedative and calming effects can be associated with metabolism of neurotransmitter networks. The given area is still in need of further mechanistic and clinical research; nevertheless, the existing evidence suggests that it may be relevant to neurodegenerative and stress-related conditions [41].

Cardioprotective and vascular protective effects:

There is also cardioprotective and vascular protective effects indicating that the plant has a capacity to regulate the oxidative stress and inflammatory pathways that are associated with cardiovascular disease. There are experimental studies which indicate that lipid metabolism, vascular and cardiac injury markers are improved after using plant extracts. These results indicate a supportive effect in preserving cardiovascular health but extensive clinical research is required by establishing the therapeutic utility [42].

Anticancer and Cytotoxic Potential:

Nyctanthes arbor-tristis has gained a growing scientific interest in the area of drug discovery, especially natural product-derived drugs due to its anticancer and cytotoxic activity. In vitro research has shown that some extracts and isolated compounds have the potential to prevent cancer cell growth and induce cell death via cell cycle and oxidative stress signal transduction. Notably, there are reports of selective cytotoxicity against malignant cells, which implies the potential of application in therapy. Nevertheless, these results should be translated to clinical practice with a lot of in vivo validation and safety analysis [43].

Mechanisms of Action of Major Bioactive Compounds

Complex and interconnected multiple molecular mechanisms that allow the different phytochemical constituents to act as complexes determine the therapeutic efficacy of *Nyctanthes arbor-tristis*. The bioactive compounds found in this plant have pleiotropic effects due to the ability of these compounds to influence various biochemical pathways unlike single-molecule drugs that bind to specific targets. Such multi-



targeted mechanism of action becomes of special importance in chronic and multifactorial pathologies, when oxidative stress, inflammation, metabolic dysregulation, and cellular damage are present in combination [44]. These mechanisms are critical to understand in order to match the traditional therapeutic claims to the current biomedical evidence as well as the rational development of drugs. One of the main processes that lead to the development of the pharmacological effect of *Nyctanthes arbor-tristis* is the regulation of oxidative stress pathways. Oxidative stress is caused by the lack of balance between the generation of reactive oxygen species and their neutralization by endogenous antioxidant systems. Flavonoid, phenolic acid, iridoid glycoside and other bioactive compounds are key in restoring such equilibrium [45-47]. These compounds function as direct free radical scavengers as they donate electron or hydrogen atoms to neutralize the reactive species. Moreover, they increase the activity of endogenous antioxidant enzymes, hence improving the defense mechanisms of cells. These compounds help maintain cell integrity and inhibit the induction of pathological cascades mediated by oxidative stress by decreasing lipid peroxidation, protein oxidation, and DNA damage. In addition to direct antioxidant effects, constituents of *Nyctanthes arbor-tristis* impact redox-regulated signaling pathways that mediate cell survival and stress responses. Transcriptional regulators such as modulation of antioxidants defense result in the upregulation of cytoprotective enzymes and genes. This indirect antioxidant activity is most significant in chronic disease, where chronic oxidative stress is also a cause of progressive tissue damage [48]. These activities enable the bioactive compounds in the plant to present a mechanistic description of its protective actions in inflammatory, metabolic, neurodegenerative and cardiovascular disorders. Another important

mechanism of action is regulation of inflammatory mediators and cytokines. Inflammation is a highly controlled physiological reaction, which when poorly controlled causes damage to tissues and chronic illness. Isolated compounds and extract of *Nyctanthes arbor-tristis* are proven able to inhibit the synthesis of pro-inflammatory mediators, such as cytokines, chemokines and inflammatory enzymes. This inhibition diminishes the process of recruiting and activating immune cells in locations of inflammation, and thus tissue damage. Notably, the plant does not seem to induce a generalized immunosuppression, on the contrary, the plant enhances an immune homeostasis by inhibiting an overproduction of inflammatory responses, but it does not disrupt the primary immune functions. This immunomodulatory effect of the plant is also validated by the fact that the plant can alter cytokine profiles. The plant helps in resolution of inflammation by altering the balance between the pro-inflammatory cytokines and the regulatory or anti-inflammatory mediators. This process is in line with the classical descriptions of the plant as a medicine that reinstates systemic balance other than the symptom suppression. This equilibrium of immunomodulation is especially useful in diseases in which there is chronic inflammation of low grade or immune dysregulation. Another significant detail with regard to the pharmacological activity of the plant is enzyme inhibition and receptor actions. Some of the bioactive compounds in *Nyctanthes arbor-tristis* can suppress main enzymes of the inflammatory and metabolic process. Enzyme inhibition lowers inflammatory mediator and metabolic intermediate production which leads to disease development [49].

Simultaneously, some of its constituents engage with cellular receptors, interfering with downstream signaling events that control pain sensations, immunological reactions, and



metabolic homeostasis. These receptor-mediated activities aid in the explanation of analgesic, antipyretic, and metabolic regulatory activities of the plant seen to be effective in experimental research. The interaction of the *Nyctanthes arbor-tristis* bioactives with intracellular signaling pathways at the molecular level affects cell survival, apoptosis and stress responses. These pathways are typically related and can be affected by the modulation of one node in many of the downstream effects. The plant coordinates the action of protective and regulatory mechanisms through the regulation of inflammatory, oxidative stress, and cell proliferation signaling cascades. This type of pathway-level modulation is especially pronounced in the literature dealing with its anticancer and cytoprotective actions where antagonism of aberrant signaling results in diminished cell proliferation and increased programmed cell death of aberrant cells. The discovery of certain molecular targets has also increased the knowledge about the mechanism of action of the plant even more. The bioactive compounds bind to transcription factors, kinases and other regulatory proteins that regulate gene expression and cellular responses. The plant, through the modulation of these targets, can affect processes of cytokine production, antioxidant enzyme expression and apoptotic signaling. The scientific validity of the traditional use of medicinal plants is supported by these molecular interactions which present a mechanistic link between the phytochemical composition and the observed pharmacological effects [50]. The synergistic action between the phytoconstituents of *Nyctanthes arbor-tristis* is a characteristic feature of this species. Instead of acting, various compounds collaborate to increase therapeutic effectiveness and minimize possible toxicity. Synergism can be either complementary, e.g., antioxidant and anti-inflammatory act simultaneously, or pharmacokinetic, e.g.,

enhancing bioavailability and stability of active compounds. This synergy has shown why whole plant preparations can be more biologically active than single constituents and why the traditional use of complex herbal preparations has been favored. The advantage of a wide spectrum of therapeutic effects of the plant is also due to synergistic effects. The phytochemical ensemble, which acts on a variety of pathways at the same time, is capable of meeting various disease pathology conditions, such as oxidative damage, inflammation, metabolic imbalance and dysfunction of cells. The multi pronged one is especially applicable in chronic illnesses in which single target interventions tend to be of little help. The principle of synergy therefore, is an important strength of plant therapeutics and underscores the need to maintain phytochemical complexity in the process of extraction and formulation.

FUTURE PROSPECTIVES

The clinical translationalism of *Nyctanthes arbor-tristis* is in the systematic combination of tradition with the modern frameworks of biomedical research. Though there is significant preclinical evidence that supports its pharmacological relevance, future research should focus on translational research that will help in filling the gap between experimental results and clinical use. Effective human studies need to be designed to determine efficacy, safety, optimal dosage, and therapeutic duration, especially in chronic inflammatory, metabolic and neurodegenerative disease in which long-term administration may be necessary. Further studies on the bioactive profile of *Nyctanthes arbor-tristis* can be prospective with the problems of phytochemical and molecular research. Further studies are required in the field of the detailed metabolomic and proteomic analysis to detect minor components that can be significant to either therapeutic activity as a result



of synergistic interactions. Standardization of extracts with validated chemical markers will be very important in reproducibility and uniformity between studies and formulations. This standardization will also aid in making the products acceptable by the regulatory bodies and the formulation of evidence based herbal products that can be used in a broader application in the clinical context. The other direction that is important entails mechanistic studies to establish specific molecular targets and signaling pathways that the bioactive compounds of the plant modify. Such knowledge, on both cellular and genomic levels, will not only contribute to scientific validation but will also assist in determining which therapeutic niches the plant can be beneficial in as compared to current therapies. Simultaneously, pharmacokinetic, bioavailability, and herb-drug studies should be conducted to provide safety in combination with conventional treatments, particularly in patients who are undergoing prolonged pharmacological therapy. In pharmaceutical development terms, new formulation mechanisms can be used to increase the clinical usefulness of *Nyctanthes arbor-tristis*. New drug delivery vehicles, such as nanoformulations and controlled-release formulations, might enhance drug stability, bioavailability, and delivery of active constituents to the location of action. They can also lower the necessary doses and decrease the adverse effects that can occur, which enhances the compliance of patients. Also, the importance of sustainable cultivation methods and conservation policies should be pointed out to provide the supply of the high-quality plant material regularly without the disruption of the ecological balance. To sum up, *Nyctanthes arbor-tristis* is a prospective candidate in the future therapeutic development, in case the research directions would shift their focus to mechanism-based, clinically focused studies, rather than remaining at the descriptive approach

of pharmacology. The synergy of sophisticated analytical methods, clinical testing and sustainability of use would enable the research in the future to unlock the full biomedical potential of this traditionally sacred medicinal plant and enable its responsible introduction into modern health care systems.

CONCLUSION

Nyctanthes arbor-tristis is a medicinal plant of significant ethnopharmacological and biomedical significance that has a long history of traditional use, which is beginning to be supplemented by modern scientific data. Its multifacetedity of the therapeutic profile due to antioxidant, anti-inflammatory, immunomodulatory, metabolic, and cytoprotective activity is examined by integrative evaluation of its botanical identity, phytochemical composition, and pharmacological activities. All these properties justify the vast variety of classic indications of the plant due to its use in the treatment of inflammatory, febrile, metabolic, and degenerative diseases. Phytochemical studies have also determined that the therapeutic effect of *Nyctanthes arbor-tristis* arises as a result of the synergistic effect of various bioactive constituents, which include iridoid glycosides, flavonoids, phenolic compounds, terpenoids, and volatile constituents. Instead of working via one molecular target, the compounds influence various interrelated mechanisms associated with oxidative stress, inflammation, immunoregulation, and homeostasis of cells. The diversity of pharmacological actions of the plant is scientifically explained by this multiple-target mode of action, and the traditional use of whole-plant or multi-component preparations. The translation of *Nyctanthes arbor-tristis* into clinically validated therapeutics has not been done extensively, despite positive preclinical results. The inconsistency of phytochemical content,



unstandardized extracts, and a shortage of clinical information are some of the most critical issues that should be resolved in further studies. Active quality control, mechanism driven research, and structured clinical trials are required to determine the safety, efficacy, and therapeutic concentration in human populations. Moreover, the investigation of the advanced formulation approaches and eco-friendly cultivation will play a significant role in guaranteeing the stable quality and sustainability. To sum up, *Nyctanthes arbor-tristis* is an important promising source of bioactive compounds that can be applied in the contemporary healthcare sphere. A highly integrative and evidence-based research methodology that honors traditional knowledge without being disrespectful to the traditional one and applies state-of-the-art scientific standards will be critical to unlocking its potential as a therapeutic agent and to help implement it into the modern healthcare systems in a responsible way.

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