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Mechanisms of action of *Nyctanthes arbor-tristis* in the treatment of chronic diseases

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Abstract
Nyctanthes arbor-tristis (Night-flowering Jasmine), a revered plant in traditional Indian medicine, has shown immense potential in the treatment of various chronic diseases, including arthritis, malaria, cancer, and liver disorders. The therapeutic effects of this plant are attributed to its rich phytochemical profile, which includes flavonoids, alkaloids, glycosides, and tannins. This paper examines the mechanisms of action of *Nyctanthes arbor-tristis* in managing chronic diseases, providing a comprehensive review of its pharmacological activities and potential biomedical applications. The review emphasizes its anti-inflammatory, antioxidant, anti-arthritic, and anticancer properties, which contribute to its broad-spectrum therapeutic uses.

Keywords: *Nyctanthes arbor-tristis*, medicinal plants, rheumatoid arthritis, anticancer, phytochemicals, anti-inflammatory

Introduction
Chronic diseases are a significant global health challenge, accounting for approximately 60% of all deaths worldwide, as reported by the World Health Organization (WHO) (World Health Organization, 2020) [3]. These diseases, which include cancer, arthritis, cardiovascular conditions, liver disorders, and autoimmune conditions, are characterized by their long duration and slow progression. The increasing prevalence of these ailments is primarily driven by factors such as aging populations, sedentary lifestyles, and unhealthy dietary habits. Conventional treatments for chronic diseases often involve pharmacological interventions, which, while effective, may be associated with side effects and resistance. This has led to growing interest in alternative and complementary approaches, particularly the use of herbal medicines, which are often viewed as safer and more holistic (Sharma *et al*., 2023) [1].

Herbal medicines have been integral to traditional healing systems, such as Ayurveda, Traditional Chinese Medicine (TCM), and Unani, for thousands of years. These systems utilize plant-based therapies for the prevention and treatment of various diseases, and they are increasingly being incorporated into modern healthcare practices. The renewed interest in phytotherapy is supported by scientific research that validates the efficacy of many plant-derived compounds in managing chronic conditions (Rathore *et al*., 2014) [4]. Among the numerous plants studied, *Nyctanthes arbor-tristis* (NAT) has gained attention for its wide range of pharmacological activities, making it a promising candidate for managing chronic diseases (Sharma *et al*., 2023) [1].

N. arbor-tristis, commonly known as the night-flowering jasmine or parijat, is a deciduous shrub that belongs to the Oleaceae family. It is native to South Asia and is widely distributed in tropical and subtropical regions. In traditional Ayurvedic medicine, NAT is considered a divine and medicinal plant, with each part of the plant-leaves, flowers, bark, seeds, and roots-used for therapeutic purposes. The plant is revered for its multifaceted medicinal properties and has been employed in traditional remedies for ailments ranging from fever and cough to serious conditions such as arthritis, cancer, and malaria (Rathore *et al*., 2014; Sharma *et al*., 2023) [4, 1].

NAT has been extensively studied for its bioactive phytochemicals, which include flavonoids, alkaloids, glycosides, tannins, and essential oils (Sharma *et al*., 2023) [1].

These compounds have demonstrated a variety of pharmacological activities, including anti-inflammatory, antioxidant, antipyretic, and anticancer effects. The plant's rich phytochemical profile contributes to its ability to target multiple pathways involved in chronic diseases, making it an attractive option for integrative therapy (Rathore *et al*., 2014) [4].

Chronic inflammation is a key factor in the progression of many chronic diseases, including arthritis and cardiovascular diseases (Godse *et al*., 2016) [2]. *N. arbor-tristis* has been shown to inhibit inflammatory mediators such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and cyclooxygenase-2 (COX-2), which are implicated in inflammatory processes. By modulating these pathways, NAT reduces inflammation and protects tissues from damage, particularly in conditions such as rheumatoid arthritis and osteoarthritis (Rathore *et al*., 2014) [4]. Furthermore, its antioxidant properties help neutralize free radicals, thereby reducing oxidative stress, which is a major contributor to chronic diseases like cancer and liver disorders (Sharma *et al*., 2023) [1].

In addition to its anti-inflammatory and antioxidant effects, *N. arbor-tristis* has been found to possess immunomodulatory properties (Godse *et al*., 2016) [2]. This makes it particularly useful in autoimmune conditions, where an overactive immune response causes damage to healthy tissues. Studies have shown that NAT can regulate immune cell activity, reducing the severity of autoimmune responses while promoting healing. These properties have made it a focus of research in the context of chronic diseases such as rheumatoid arthritis and systemic lupus erythematosus (Rathore *et al*., 2014) [4].

Moreover, NAT's anticancer potential has been demonstrated in several *in vitro* and *in vivo* studies. The plant's bioactive compounds, particularly flavonoids like quercetin and kaempferol, have been shown to induce apoptosis (Programmed cell death) in cancer cells and inhibit cell proliferation (Sharma *et al*., 2023) [1]. This has sparked interest in its use as an adjunctive treatment in cancer therapy, particularly for cancers that are resistant to conventional treatments. For instance, studies have reported that NAT can inhibit the growth of breast, colon, and liver cancer cells, potentially offering a natural alternative or complement to chemotherapy (Sharma *et al*., 2023) [1].

The hepatoprotective properties of NAT have also been well-documented. Liver disorders, including hepatitis, cirrhosis, and fatty liver disease, are prevalent chronic conditions that significantly impair quality of life (Godse *et al*., 2016) [2]. The liver is susceptible to damage from oxidative stress and inflammation, both of which can be mitigated by NAT's antioxidant and anti-inflammatory effects (Rathore *et al*., 2014) [4]. Several studies have demonstrated that NAT extracts can protect liver cells from damage induced by toxins or oxidative stress, thereby maintaining liver function and promoting detoxification processes (Godse *et al*., 2016) [2].

In traditional medicine, *Nyctanthes arbor-tristis* has also been used as a remedy for parasitic infections, particularly malaria. The plant's antimalarial properties have been studied, and it has been shown to inhibit the growth of *Plasmodium falciparum*, the parasite responsible for malaria (Godse *et al*., 2016) [2]. This makes NAT an important plant in regions where malaria is endemic, and where access to modern antimalarial drugs may be limited. Its potential use in combination therapies for malaria has been suggested as a way to enhance the efficacy of conventional treatments and reduce the development of drug resistance (Godse *et al*., 2016) [2].

Overall, the increasing body of scientific evidence supports the traditional use of *Nyctanthes arbor-tristis* in the management of chronic diseases. Its broad pharmacological profile and ability to target multiple disease mechanisms make it a valuable candidate for integrative medicine (Sharma *et al*., 2023) [1]. This review aims to explore the mechanisms of action of NAT in chronic disease treatment, highlighting its potential as a therapeutic agent for conditions such as cancer, arthritis, liver disorders, and autoimmune diseases.

Phytochemical profile of *Nyctanthes arbor-tristis*

The medicinal properties of *Nyctanthes arbor-tristis* (NAT) are largely attributed to its rich phytochemical composition. The plant contains a diverse array of bioactive compounds, including flavonoids, glycosides, alkaloids, tannins, and essential oils. These compounds exhibit various pharmacological properties that make NAT a powerful therapeutic agent in the treatment of chronic diseases, such as cancer, arthritis, and liver disorders.

Flavonoids

Flavonoids are one of the most significant groups of phytochemicals found in *Nyctanthes arbor-tristis*. These compounds include quercetin, astragalin, kaempferol, and rutin. Flavonoids are known for their potent antioxidant, anti-inflammatory, and anticancer properties. Quercetin, in particular, has been studied extensively for its ability to neutralize free radicals, reduce oxidative stress, and inhibit the proliferation of cancer cells (Sharma *et al*., 2023) [1].

Glycosides

N. arbor-tristis is rich in iridoid glycosides, including nyctanthoside and arbortristoside. These glycosides have been shown to possess anti-inflammatory, antimicrobial, and hepatoprotective activities. Iridoid glycosides are believed to inhibit the production of pro-inflammatory cytokines and reduce the inflammatory response in chronic conditions like arthritis and liver disease (Rathore *et al*., 2014) [4].

Alkaloids

Alkaloids, such as arborine, are another important class of compounds found in *Nyctanthes arbor-tristis*. These phytochemicals are known for their antimicrobial, anti-inflammatory, and analgesic properties. Alkaloids are believed to contribute significantly to NAT's ability to manage pain and inflammation in diseases like rheumatoid arthritis (Godse *et al*., 2016) [2].

Tannins

Tannins are polyphenolic compounds that possess astringent, antimicrobial, and anti-inflammatory properties. In *N. arbor-tristis*, tannins play a key role in modulating immune responses and reducing oxidative stress, making them valuable in the treatment of chronic inflammatory diseases (Sharma *et al*., 2023) [1].

Table 1: Key Phytochemicals in *Nyctanthes arbor-tristis* and Their Functions

Phytochemical	Category	Functions
Quercetin	Flavonoid	Antioxidant, anti-inflammatory, anticancer
Kaempferol	Flavonoid	Anti-inflammatory, antioxidant
Astragalin	Flavonoid	Antioxidant, anticancer
Rutin	Flavonoid	Antioxidant, anti-inflammatory
Nyctanthoside	Iridoid glycoside	Anti-inflammatory, antimicrobial, hepatoprotective
Arbortristoside	Iridoid glycoside	Anti-inflammatory, analgesic
Arborine	Alkaloid	Antimicrobial, anti-inflammatory, analgesic
Tannins	Polyphenol	Astringent, antimicrobial, anti-inflammatory

Pharmacological activities and mechanisms of action

N. arbor-tristis exhibits a wide range of pharmacological activities, making it a potent candidate for the treatment of several chronic diseases. Its phytochemicals exert anti-inflammatory, antioxidant, anticancer, anti-arthritic, and hepatoprotective effects.

Anti-inflammatory and Antioxidant Properties

Inflammation is a key factor in the pathogenesis of many chronic diseases, including arthritis, cardiovascular diseases, and liver disorders. *Nyctanthes arbor-tristis* is rich in compounds like quercetin and iridoid glycosides, which have demonstrated strong anti-inflammatory effects. These compounds act by inhibiting key inflammatory pathways, including the NF-κB signaling pathway, which is responsible for the production of pro-inflammatory cytokines such as TNF-α, IL-6, and COX-2 (Rathore *et al*., 2014) [4].

NAT's antioxidant properties are primarily due to its high flavonoid content. Flavonoids like quercetin scavenge reactive oxygen species (ROS), which are responsible for oxidative damage in cells. This antioxidant action helps protect tissues from oxidative stress, which is a major contributor to conditions like arthritis and liver fibrosis (Sharma *et al*., 2023) [1].

Mechanism of Action

N. arbor-tristis inhibits the NF-κB signaling pathway and downregulates pro-inflammatory cytokines, reducing inflammation. Its flavonoids neutralize ROS, which reduces oxidative stress and protects tissues from damage.

Anti-arthritic Mechanisms

Arthritis, particularly rheumatoid arthritis, is characterized by chronic inflammation of the joints, leading to pain, swelling, and eventual joint destruction. NAT has been traditionally used to manage arthritis, and recent studies have provided scientific evidence of its effectiveness. Animal studies have shown that NAT extracts reduce joint swelling, cartilage degradation, and immune cell infiltration in inflamed tissues (Rathore *et al*., 2014) [4].

Mechanism of Action

NAT reduces the release of pro-inflammatory cytokines, including TNF-α and IL-6, and inhibits matrix metalloproteinases (MMPs), which are enzymes responsible for the degradation of joint cartilage. Inhibition of these cytokines and enzymes leads to reduced inflammation and cartilage protection. Additionally, NAT modulates immune cell activity, leading to decreased pain and inflammation in arthritic patients (Sharma *et al*., 2023) [1].

Table 2: Anti-arthritic Mechanism of *Nyctanthes arbor-tristis*

Effect	Mechanism
Reduction in joint swelling	Inhibition of pro-inflammatory cytokines (TNF-α, IL-6)
Protection of cartilage	Inhibition of matrix metalloproteinases (MMPs)
Reduction in immune cell infiltration	Modulation of immune responses

Anticancer Properties

The anticancer potential of *Nyctanthes arbor-tristis* has been demonstrated in several studies, particularly in relation to breast, liver, and colon cancers. NAT's anticancer activity is attributed to its ability to induce apoptosis (Programmed cell death) in cancer cells, inhibit cell proliferation, and reduce angiogenesis (The formation of new blood vessels that supply tumors) (Sharma *et al*., 2023) [1].

Mechanism of Action

NAT exerts its anticancer effects through multiple mechanisms. Flavonoids like quercetin arrest the cell cycle in cancer cells, leading to apoptosis via the activation of the caspase pathway. Additionally, NAT inhibits the PI3K/AKT signaling pathway, which is often dysregulated in cancer, thereby reducing cancer cell survival and proliferation (Rathore *et al*., 2014) [4].

Table 3: Anticancer Mechanisms of *Nyctanthes arbor-tristis*

Effect	Mechanism
Induction of apoptosis	Activation of the caspase pathway
Inhibition of cell proliferation	Arrest of the cell cycle via flavonoids
Reduction of angiogenesis	Inhibition of PI3K/AKT pathway

Hepatoprotective Effects

Liver diseases such as hepatitis, cirrhosis, and non-alcoholic fatty liver disease (NAFLD) have been traditionally treated with *Nyctanthes arbor-tristis*. Scientific studies have shown that NAT provides hepatoprotective effects by reducing liver enzymes, such as ALT (alanine aminotransferase) and AST (Aspartate aminotransferase), which are indicators of liver damage (Godse *et al*., 2016) [2].

Mechanism of Action

The hepatoprotective effects of NAT are largely due to its antioxidant properties. By neutralizing free radicals, NAT

prevents lipid peroxidation in liver cells, protecting them from oxidative damage. Additionally, NAT modulates detoxification enzymes in the liver, promoting the elimination of toxic substances and reducing liver injury (Sharma *et al*., 2023) [1].

Table 4: Hepatoprotective Mechanisms of *Nyctanthes arbor-tristis*

Effect	Mechanism
Reduction in liver enzymes (ALT, AST)	Protection from oxidative damage by neutralizing free radicals
Protection from lipid peroxidation	Inhibition of oxidative stress in liver cells
Enhancement of detoxification	Modulation of liver detoxification enzymes

Antiparasitic and Antimalarial Properties

N. arbor-tristis has also been shown to possess antiparasitic properties, particularly in the treatment of malaria. Extracts of NAT have demonstrated inhibitory effects on *Plasmodium falciparum*, the parasite responsible for malaria. The plant's traditional use in antimalarial therapies is supported by scientific evidence that shows its ability to reduce parasitic load and improve patient outcomes (Godse *et al*., 2016) [2].

Mechanism of Action

The antimalarial effects of NAT are attributed to its ability to interfere with the life cycle of *Plasmodium falciparum*, thereby reducing parasitemia. NAT also modulates the immune system, enhancing the body's ability to fight parasitic infections (Godse *et al*., 2016) [2].

Biomedical applications of *Nyctanthes arbor-tristis*

The versatile bioactive compounds found in *Nyctanthes arbor-tristis* (NAT) contribute to its wide range of biomedical applications, particularly in managing chronic diseases. Several studies have highlighted its anti-inflammatory, antiparasitic, anticancer, and hepatoprotective effects. These properties make NAT a valuable candidate in the treatment of conditions like rheumatoid arthritis, malaria, cancer, and liver disorders. This section delves deeper into the biomedical applications of NAT, supported by scientific evidence and relevant mechanisms of action.

Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by persistent joint inflammation, pain, and degradation of cartilage and bone. Conventional treatments often focus on reducing inflammation and slowing disease progression, but they can have side effects. As a result, the search for safer, alternative therapies has led to the investigation of natural compounds like NAT.

In clinical studies, NAT has been shown to significantly reduce the symptoms of RA, owing to its strong anti-inflammatory and antioxidant properties. A study conducted by Rathore *et al*. (2014) [4] demonstrated the efficacy of NAT in a mouse model of arthritis. The study showed that NAT extracts led to a reduction in joint swelling and inflammation. These effects were attributed to the inhibition of pro-inflammatory cytokines like TNF-α and IL-6 and the reduction of oxidative stress due to its antioxidant activity.

Mechanism of Action

NAT's anti-arthritic effects are primarily driven by its ability to modulate immune responses. It inhibits the activity of matrix metalloproteinases (MMPs), which are responsible for cartilage degradation, and downregulates pro-inflammatory cytokines. Additionally, its antioxidant properties neutralize reactive oxygen species (ROS), protecting joint tissues from oxidative damage.

Table 5: Effect of *Nyctanthes arbor-tristis* on Rheumatoid Arthritis

Effect	Mechanism
Reduction in joint swelling	Inhibition of pro-inflammatory cytokines (TNF-α, IL-6)
Cartilage protection	Inhibition of matrix metalloproteinases (MMPs)
Reduction in oxidative stress	Antioxidant activity, neutralizing reactive oxygen species (ROS)
Reduced immune cell infiltration	Modulation of immune response, reducing infiltration of inflammatory cells in joints

Malaria and Parasitic Infections

Malaria is a life-threatening disease caused by *Plasmodium* parasites, transmitted through the bites of infected mosquitoes. The increasing resistance to conventional antimalarial drugs has prompted the exploration of alternative therapies, including herbal remedies like *Nyctanthes arbor-tristis*. In traditional medicine, NAT has long been used as an antimalarial agent, and recent scientific studies have supported this application. A study by Godse *et al*. (2016) [2] demonstrated the antiparasitic potential of NAT. The plant's extracts were found to be effective in inhibiting the growth of *Plasmodium falciparum*, the parasite responsible for malaria. The study also suggested that NAT has disease-modifying effects that go beyond simple parasite inhibition, offering potential as part of an integrative treatment approach for malaria.

Mechanism of Action

NAT exerts its antiparasitic effects by interfering with the life cycle of *Plasmodium falciparum*, thereby reducing parasitemia. Additionally, it modulates the immune system, enhancing the body's ability to clear the parasite. Its anti-inflammatory properties also reduce the inflammatory damage caused by the parasitic infection.

Table 6: Effect of *Nyctanthes arbor-tristis* on Malaria

Effect	Mechanism
Inhibition of parasite growth	Interference with the life cycle of *Plasmodium falciparum*
Modulation of immune response	Enhancement of immune clearance of the parasite
Reduction of inflammation	Inhibition of pro-inflammatory cytokines

Cancer

The search for novel anticancer agents has increasingly turned towards natural products, due to their ability to target multiple pathways involved in cancer progression. *Nyctanthes arbor-tristis* has attracted considerable attention for its potential as an anticancer agent. Several studies have demonstrated its cytotoxic effects on cancer cells, making it a promising candidate for adjunctive cancer therapies.

A study by Sharma *et al*. (2023) [1] highlighted the anticancer potential of NAT. The plant's bioactive compounds, particularly flavonoids like quercetin and kaempferol, have shown strong anticancer activity, particularly against breast and liver cancer cells. These compounds induce apoptosis (Programmed cell death) in cancer cells and inhibit their proliferation. Furthermore, NAT has been found to reduce angiogenesis (The formation of new blood vessels that supply tumors), which is critical in preventing tumor growth and metastasis.

Mechanism of Action

NAT exerts its anticancer effects through multiple mechanisms. It induces apoptosis in cancer cells via the activation of the caspase pathway, arrests the cell cycle, and inhibits angiogenesis by downregulating the PI3K/AKT signaling pathway. This combination of actions makes it effective in slowing cancer progression.

Table 7: Effect of *Nyctanthes arbor-tristis* on Cancer

Effect	Mechanism
Induction of apoptosis	Activation of the caspase pathway
Inhibition of cell proliferation	Arrest of the cell cycle
Reduction in angiogenesis	Inhibition of the PI3K/AKT signaling pathway, reducing tumor vascularization

Hepatoprotective Effects

Liver diseases, including hepatitis, cirrhosis, and non-alcoholic fatty liver disease (NAFLD), are chronic conditions that impair liver function and quality of life. *Nyctanthes arbor-tristis* has been used traditionally in treating liver disorders, and recent studies have provided scientific backing for its hepatoprotective properties. NAT has been shown to reduce levels of liver enzymes such as ALT (Alanine aminotransferase) and AST (Aspartate aminotransferase), which are markers of liver damage.

Mechanism of Action

NAT's hepatoprotective effects are largely due to its antioxidant properties, which protect liver cells (Hepatocytes) from lipid peroxidation and oxidative stress. By reducing the generation of free radicals, NAT prevents oxidative damage to liver tissues. It also modulates detoxification enzymes, enhancing the liver's ability to metabolize and eliminate toxic substances, thus preventing further injury.

Table 8: Hepatoprotective Effects of *Nyctanthes arbor-tristis*

Effect	Mechanism
Reduction in liver enzymes	Decrease in ALT and AST levels
Protection from oxidative stress	Antioxidant properties that neutralize free radicals
Enhanced detoxification	Modulation of liver detoxification enzymes to eliminate toxins

Conclusion

The therapeutic potential of *Nyctanthes arbor-tristis* in the treatment of chronic diseases is supported by its broad pharmacological activities, including anti-inflammatory, antioxidant, anti-arthritic, anticancer, and hepatoprotective properties. Its bioactive compounds-such as flavonoids, iridoid glycosides, alkaloids, and tannins-offer promising avenues for further research and development in modern medicine. While current studies have laid a strong foundation for understanding the mechanisms of action of NAT, more clinical trials are required to fully elucidate its efficacy and safety profile, particularly in human populations.

The future of NAT in biomedical applications appears promising, especially as part of integrative therapeutic approaches for managing chronic diseases. With further research, NAT has the potential to become a key component of natural, holistic therapies aimed at reducing the global burden of chronic diseases such as arthritis, cancer, liver disorders, and parasitic infections.

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