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A REVIEW OF CLASSIC CURES FOR CONTEMPORARY MARVELS: UNVEILING THE MEDICINAL SECRETS OF *PIPER BETLE LINN. LEAVES* AND *NYCTANTHES ARBORTRISTIS*

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ABSTRACT:

Modern pharmacology finds inspiration from the rich legacy of traditional medicinal herbs. This examination explores the therapeutic possibilities of *Nyctanthes arbortristis* and *Piper betel Linn.* In recent times, scientists have been intrigued by these plants for their diverse applications in traditional medical practices. *Nyctanthes arbortristis*, commonly known as the 'Night-flowering Jasmine,' contains a plethora of bioactive compounds. Our analysis focuses on its analgesic, immunomodulatory, and anti-inflammatory properties, shedding light on its potential for treating various diseases. Additionally, we delve into the historical uses of *Nyctanthes arbortristis,* aligning them with contemporary knowledge. Piper betel Linn, known as the 'Betel Leaf,' plays a significant role in traditional medicine, especially in Asia. This examination highlights the pharmacological effects of Piper betel, encompassing its antibacterial, antioxidant, and anticancer attributes. By connecting traditional wisdom with modern research, we underscore the medicinal applications of these plants. The examination also addresses the challenges and opportunities associated with unlocking the medical potential of *Nyctanthes arbortristis* and *Piper betel Linn* in the twenty-first century. This thorough investigation serves as a valuable resource for academics, professionals, and enthusiasts seeking insights into these botanical wonders and their integration into contemporary medicine.

Keywords: *Nyctanthes arbortristis*, *Piper betel Linn,* medicinal herbs

I. INTRODUCTION:

The World Health Organization (WHO) defines traditional medicine as the collective knowledge, skills, and practices rooted in the theories, beliefs, and experiences indigenous to diverse cultures. These practices are employed in the maintenance of health, as well as in the prevention, diagnosis, improvement, or treatment of physical and mental illnesses. This includes practices whether or not they are based on explicable theories, beliefs, or experiences. Indian Traditional Medicine stands out as the world's oldest system of medicine, making substantial contributions to the care and well-being of people throughout its extensive history. Ayurveda, Siddha, Unani, Yoga, Naturopathy, and Homoeopathy represent six ancient medical traditions in

India, with Ayurveda being the most prominent among them. Over 70% of India's rural population relies on ancient Ayurvedic remedies. The historical use of plants for medicinal purposes is well-documented in ancient literary works, providing essential insights into traditional knowledge about medicinal plants that have contributed significantly to modern drug development. An example is Nyctanthes arbor-tristis L., an important medicinal plant with a rich history of uses in local and traditional medicine, offering various medicinal benefits according to ancient practices.

Nyctanthes arbor-tristis Linn.

Division	*Magnoliophyta*
Class	*Magnoliopsida*
Order	*Lamiales*
Family	*Oleaceae*

Widely recognized as Parijat and Night Jasmine, Nyctanthes arbor-tristis (NAT) is traditionally employed for managing Rheumatism and Inflammatory conditions. Various plant components, such as seeds, leaves, flowers, bark, and fruit, possess medicinal properties and are utilized in traditional remedies. Scientific studies consistently indicate the potential of NAT in treating various conditions, including persistent fever, biliary disease, liver disorders, rheumatism, intractable sciatica, malaria, bronchitis, wound healing, skin problems, stomachic issues, astringency, and menstruation. Recognized as one of the most effective conventional medicinal plants in India, NAT is considered significant for producing both unique medical formulations and essential industrial items. Higher plants like NAT are often referred to as "storehouses of chemo-therapeutants" due to their extensive collection of biochemicals. Piper betel Linn, another notable religious and traditional medicinal plant, belongs to the Piperaceae family and is an evergreen and perennial creeper featuring glossy heart-shaped leaves. With over 90 different types of betel vine globally, 45 of them are found in India, and 30 in West Bengal alone. Extracts from Piper betle leaves have demonstrated beneficial effects against various human diseases. The most valued part of the plant is the betel leaf, traditionally chewed for centuries to combat bad breath, containing tannins, chavicol, phenyl, propane, sesquiterpene, cyneole, alkaloid, sugar, and essential oils. These compounds offer diverse medicinal benefits, including aiding digestion, acting as appetizers, providing aromatics, acting as expectorants, serving as stimulants, and exhibiting antibacterial properties, among others.

Fig. 1 Nyctanthes Arbor-tristis **(Parijat) Fig. 2** ***Piper Betel Linn*** **(Nagarbael)**

II. DETAILED PLANT STUDIES:

A) *Nyctanthes arbor-tristis*:

a) Taxonomical Classification: [15]

Kingdom	*Plantae*
Division	*Magnoliophyta*
Class	*Magnoliosida*
Order	*Lamiales*
Family	*Oleaceae*
Genus	*Nyctanthes*
Species	*arbor-tristis*
Binomial Name	*Nyctanthes arbor-tristis*

b) Vernacular Names of *Nyctanthes arbor-tristis*: [15]

• Sanskrit: Parijata, Parijatah, Parijataka, Sephalika

• Hindi: Harsinghar, Harsingur, Seoli, Sheoli, Sihau

• Gujarati: Jayaparvati, Parijatak

• English: Coral Jasmine, Night Jasmine

c) Geographical Distributions:

Nyctanthes arbortristis Linn is typically located on rocky terrain in arid hillsides and serves as undergrowth in dry deciduous forests. Indigenous to the Indo-Pak subcontinent, this plant naturally thrives in the Indo-Malayan region, including Burma, Thailand, Ceylon, South Asia, and Southeast Asia. In India, it is prevalent in the outer Himalayas and spans areas from Jammu and Kashmir to Nepal, extending to the east of Assam, Bengal, Tripura, and through the central region up to the Godavari in the south. Nyctanthes arbortristis Linn can be found at altitudes ranging from sea level to 1500 meters, exhibiting adaptability to a diverse range of rainfall patterns, from seasonal to non-seasonal. Moreover, it demonstrates tolerance to moderate shade. Flowering typically takes place between July and October. Nyctanthes generally thrives in secluded, semi-shaded environments

d) Botanical Description:

Nyctanthes Arbor-tristis, commonly known as the Linn tree, is a deciduous shrub or small tree characterized by stiff white hairs and irregular bark, reaching heights of up to 10 meters. The young branches exhibit a distinct quadrangular shape.

Bark:

The bark of Nyctanthes Arbortristis features quadrangular branches and rough, grey or greenish-white bark. Scaling off of circular barks has left the bark surface dipped, with grayish-brown patches creating a patchy appearance. Circular flakes are shed from the bark, revealing a creamy white, soft-textured non-collapsed phloem zone in the inner bark.

Leaves:

The leaves are simple, opposite, petiolate, and range from 5-10 cm in length and 2.5-6.3 cm in breadth. They are oval or wedge-shaped, occasionally with distant teeth, and have a dusky green top surface and a light green bottom surface covered with dotted glands. The venation is unicostate and reticulate, with approximately 12 lateral veins. The plant sheds its leaves annually between October and March.

Flowers:

The small, fragrant flowers appear in clusters of 2–7 at the tips of the main stem and branches or in the axil of the leaves. They have 4-angled peduncles, pedunculate bracteate fascicles, ovate or suborbicular attached modified leaf structures (bract), and a calyx with fine hairs on the outside. The 6–10 mm flowers consist of 5-8 white lobes with a reddish-orange core and typically bloom from July through October.

Fruits:

The fruit is a brown capsule, 1-2 cm across, with a distinctive pattern of two locules, each containing two ovules. It is a compressed, glabrous, obcordate structure that divides into two carpels, each bearing one seed. Large elliptical cavities, serving as anatomical indicators, are common in NAT fruits. Fruit ripening occurs in February and March.

Seeds:

Each fruit contains one brown, compressed seed. These seeds are ex-albuminous, with a thick testa and a strongly vascularized surface layer composed of large transparent cells. Seed harvesting typically takes place between September and October.

Fig. 3 a) Bark b) Leaves c) Flowers

Fig. 4 a) Fruits b) Seeds

e) Phytochemical Profile:

Phytochemicals are chemicals of plant origin. Phytochemicals (from Greek *phyto*, meaning "plant") are chemicals produced by plants through primary or secondary metabolism. They generally have biological activity in the plant host and play a role in plant growth or defense against competitors, pathogens, or predators.

Plant Parts	Chemical Constituents
Leaves	D-mannitol,sitosterole, astragaline, nicotiflorin, oleanolic acid, nyctanthic acid, tannic acid, ascorbic acid, methyl salicylate, carotene, friedeline, lupeol, mannitol, glucose and fructose, iridoid glycosides, benzoic acid.
Flowers	Essential oil, nyctanthin, d-mannitol, tannin and glucose, carotenoid, glycosides viz β-monogentiobioside ester of α-crocetin (or crocin-3), β-monogentiobioside-β-D monoglucoside ester of α-crocetin, β-digentiobioside ester of α-crocetin.
Seeds	Arbortristoside A&B, Glycerides of linoleic oleic, lignoceric, stearic, palmitic and myristic acids, nyctanthic acid, 3-4 secotriterpene acid.
Stem	Glycoside-naringenin-4'-0-β-glucapyranosyl-α-xylopyranoside and β-sitosterol.

Bark	Glycosides and alkaloids.

III) Pharmacological Profile of *Nyctanthes Arbor-tristis*:

i) Anticancer Activity:

Methanol extracts from N. arbortristis fruit, leaf, and stem were evaluated for in vitro anticancer properties. At a concentration of 30 mg/ml, moderate anticancer activity was observed. The dried N. arbortristis leaf methanol extract exhibited 71% inhibition, with the least inhibitory efficacy observed at 10 mg/ml. Remarkably, the dried fruit methanol extract demonstrated high effectiveness against human breast cancer cell lines (MDA-MB 231), showing 86% inhibition with IC50 values of 9.72 mg and 13.8 mg. The presence of glycosides, tannins, phenols, and steroids in the dried fruit methanol extract is believed to contribute to its anticancer effects.

ii) Anti-Parasitic Activity:

A 50% ethanolic extract of N. arbortristis leaves displayed trypanocidal activity at a concentration of 1000 µg/ml. The extract also exhibited strong anti-leishmanial action in hamsters infected with Leishmania donovani. Additionally, infections caused by Entamoeba histolytica in rat cecum were cured by 50% ethanolic extracts from N. arbortristis seeds, leaves, roots, flowers, and stem. Water-soluble components of the ethanolic extract from flowers, bark, seeds, and leaves showed anthelmintic effects by inhibiting motility in response to acetylcholine's contractile action**.**

iii) Antimalarial Activity:

A clinical investigation involving 120 malaria patients revealed that a fresh paste made from five medium-sized N. arbortristis leaves, administered three times daily for seven days, resulted in a positive response in 76.7% of patients. No serious adverse effects were observed, and the paste was well-tolerated.

iv) Anti-Diabetic Activity:

Oral administration of chloroform and ethanolic leaf and flower extracts significantly increased superoxide dismutase (SOD) and catalase (CAT) levels while decreasing liver lactoperoxidase (LPO), serum SGPT, SGOT, alkaline phosphatase, cholesterol, and triglyceride levels in diabetic controls. The stem bark's ethanol extract demonstrated notable anti-diabetic effects, reducing blood glucose levels depending on the dosage.

v) Anti-Allergy Activity:

Guinea pigs exposed to histamine aerosol, pre-treated with a water-soluble component of an alcoholic extract of N. arbortristis leaves, showed prevention of asphyxia. Arbortistosides A and C in N. arbortristis were identified for their anti-allergic properties.

vi) Antianemic Activity:

In a rat study, ethanolic extracts from N. arbortristis flowers, barks, seeds, and leaves increased hemoglobin and red blood cell count in a dose-dependent manner. The extracts also prevented deterioration of hemogram profiles in anemic rats**.**

vii) Anti-Leishmanial Activity:

Iridoid glucosides, including arbortristosides A, B, and C, and 6-b-hydroxyloganin, were associated with N. arbortristis' anti-leishmanial action. Both in vitro and in vivo studies demonstrated efficacy against amastigotes in macrophage cells and hamster test systems.

viii) Anti-Inflammatory Activity:

The aqueous extract of the whole plant, alcoholic extract of the stem and seeds, and water-soluble component of the alcoholic extract of the leaves exhibited acute and subacute anti-inflammatory effects. N. arbortristis significantly inhibited granulation tissue development in inflammatory models using various agents. It also demonstrated anti-inflammatory activity against immunological techniques such as Freund's adjuvant arthritis and pure tuberculin response.

ix) Anti-Oxidant Activity:

N. arbortristis leaves are used in Ayurvedic medicine for their strong antioxidant properties. The methanolic extract from the leaves exhibited significant antioxidant activity against free radical-induced lipid peroxidation, with IC50 values of 20 mg/ml. Aqueous extracts from the leaves were found to have anti-DPPH radical, anti-hydroxyl radical, and anti-lipid peroxidation properties.

B) *Piper Betel Linn:*

a) Taxonomical Classification: [46]

Synonyms	Chavica Beta, Arthanthe Hixagona
Kingdom	Plantae
Order	Piperales
Family	*Piperaceae*
Genus	*Piper*
Species	*P. Petle*
Taste	Pungent Taste
Division	Magnoliphyta

b) Vernacular Names of *Piper Betle Linn:* [46]

Sanskrit: Tambool, Mukhbhushan, Varnalata

Hindi: Paan leaf

Gujarati: Nagarbael, Paan

English: Betle, Betle pepper, Betle-vine

c) Geographical Distributions:

The Betel vine, commonly cultivated in India and various countries in South and Southeast Asia, is believed to have originated in Malaysia. It is predominantly found in regions with hot and humid climates, where the woods are typically damp. The piper beetle is said to have initially emerged in tropical Asia and later migrated to Madagascar and East Africa. The betel plant has a rich history dating back over 2000 years, with references to its presence in India, Sri Lanka, Bangladesh, Indonesia, Nepal, Pakistan, Vietnam, Thailand, Laos, Kampuchea, Philippine Islands, Burma, Malaysia, Taiwan, and other Southeast Asian countries. It is found in Indian states such as Bengal, Bihar, Orissa, Andhra Pradesh, Karnataka, Uttar Pradesh, and Tamil Nadu. There are more than 100 varieties of betel plants, with 40 produced in India and an additional 30 in Bangladesh and

West Bengal. Growing betel vines is a common form of farming, with suitable locations for cultivation being highlands with fertile sandy, sandy clay, or sandy loam soil, good drainage, and a pH range of 5.6-8.2. Unsuitable conditions include saline and alkali soils with water logging issues. The optimal weather conditions for betel cultivation include 2250-4750 mm of rainfall, relative humidity between 40-80%, and temperatures ranging from 15 to 40°C.

d) Botanical Description:

The plant is a dioecious root climber, and its shoots can reach heights ranging from 3 to 10 meters, depending on the available climbing infrastructure. The plant features lateral branches along its entire length, sprouting a few feet above the ground.

Stems:

The stems exhibit dichotomous branching with roots at the nodes, characterized by a large and articulate structure. In its youth, the stems display a light green color with short, elevated white streaks and pinkish stripes along the nodes. They are thick, almost terete, and somewhat flattened. The internodes typically achieve a diameter of 1.2 cm and a length of approximately 12 cm.

Leaves:

The leaves are simple blades, arranged alternately in a spiral pattern, and lack stipules. The petioles measure 2–5 mm in length, are hairy, and possess a channelled structure. The leaf blades are entire, slightly recurved, glabrous, coriaceous, fleshy, and range in color from green to yellowish. They are shiny, broadly ovate, with a width of 7-8.5 cm and a length of 9-11 cm. The venation is reticulate, featuring 7-9 veins in two or three pairs originating from the midrib, with an additional pair rising from the base.

Fruits:

The mature flower's rachis bears fruiting spikes that are 3-5 cm long, displaying an orange color and a drooping appearance.

Fig. 5 a) Stem b) Leaves c) Fruits

e) Phytochemical Profile:

Phytochemicals are chemicals of plant origin. Phytochemicals (from Greek *phyto*, meaning "plant") are chemicals produced by plants through primary or secondary metabolism. They generally have biological activity in the plant host and play a role in plant growth or defense against competitors, pathogens, or predators.

Chemical Compounds	Bioactive Constituents
Phenolic	Chavicol, Hydroxychavicol, Chavibetol, Chavibetol Acetate and Eugenol.
Ethanolic	Steroids, Diterpenes, Tannin, Cardiac Glycosides, Flavonoids, Saponin, Phenols, Coumarin and Alkaloids.
Methanolic	Steroids, Diterpenes, Tannin, and Saponin
Butanolic	Steroids, Diterpenes, Tannin, Flavonoids, Emodins and Alkaloids.
Acetone	Steroids, Diterpenes, Tannin, Flavonoids, Saponin and Coumarin.
Aqueous	Steroids, Diterpenes, Tannin, Cardiac Glycosides, Flavonoids, Saponin, Phenols, Coumarin and Alkaloids.

IV) Pharmacological Profile of*Piper Betle Linn:*

i) Antioxidant Activity:

The ethyl acetate extract of Piper betle demonstrated robust antioxidant activity due to its high phenolic content. This extract exhibited strong ferric reducing activity and effective radical scavenging against DPPH, superoxide anion, and NO radicals. Analyses revealed the presence of catechin, morin, and quercetin in the leaves. Moreover, the plant extract significantly inhibited the growth of MCF-7 cells, accompanied by increased catalase and superoxide dismutase activity.

ii) Anticancer Activity:

An evaluation of the aqueous extract of Piper betle leaves in cytotoxicity studies on Hep-2 cell line indicated a mean CTC50 of 96.25 µg/ml, suggesting potent cytotoxicity and potential anticancer properties. The extract also displayed significant LC50 values (>100 µg/mL) towards A. salina, implying the presence of cytotoxic compounds with possible antitumor or anticancer effects.

iii) Wound Healing:

The study observed significant healing of NSAID-induced peptic ulcers in albino rats with the use of Piper betle plant extract. The therapeutic effect was attributed to the extract's capacity to scavenge free radicals. In Sprague-Dawley rats, APC, a phenolic component, significantly reduced indomethacin-induced ulcers, demonstrating antioxidative and mucin-protecting qualities linked to the protective effect.

iv) Antifungal Activity:

Hydroxychavicol, obtained from the chloroform extraction of the aqueous extract of Piper betle, exhibited antifungal activity against 124 strains of selected fungi. The inhibitory effects were observed in clinically significant fungi, suggesting potential applications as a topical antifungal drug and a gargle for oral candida infections. Additionally, it demonstrated prolonged post-antifungal action and prevention of mutant emergence**.**

v) Anti-malaria Activity:

Piper betle essential oil showed superior protection against Anopheles stephensi and Culex fatigans mosquitoes compared to citronella oil. Sprayed at 20 µ/cm2, piper betle oil provided almost 4 hours of protection, while citronella oil only offered 2.2 and 2.6 hours of protection, respectively. This establishes the plant's efficacy as a mosquito repellent.

vi) Anti-allergic Activity:

Extracts of Piper betle significantly reduced histamine and GM-CSF levels during an IgE-mediated hypersensitivity reaction. They also suppressed the release of exotoxin and IL-8 in allergic reactions triggered by TNF- and IL-4. These findings suggest that Piper betle may present a novel treatment strategy for managing allergic illnesses by reducing the generation of allergic mediators.

V) CONCLUSION:

In conclusion, the thorough examination of Parijat and Betel has revealed a profound historical legacy of ancient remedies alongside their contemporary wonders. These plants, known for their medicinal attributes, have been integral to traditional medicine for centuries. Presently, scientific research is delving into their therapeutic potential, presenting promising prospects for novel treatments and a deeper comprehension of their health advantages. By connecting ancient wisdom with modern scientific exploration, these plants hold significant promise for the future of medicine. Further investigations are imperative to fully unravel their authentic medicinal properties.

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