International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 1614-1630 www.ijprajournal.com ISSN: 2456-4494

Effect of Leaves of Nyctanthes Arbor-Tristis Linn on Hyperglycaemic and Glucose Loaded Rats

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Submitted: 15-08-2022 Accepted: 23-08-2022

ABSTRACT:
Diabetes mellitus is characterized by abnormally high levels of sugar (glucose) in the blood. There is a growing interest in focusing on the beneficial role of "alternative therapeutics" in the treatment of diabetes.Nyctanthes arbor-tristis Linn is native to India, distributed widely in sub-Himalayan regions and southward to Godavari (Das S et al., 2010). It is also distributed in Bangladesh, Indo- Pak subcontinent and South-East Asia (Khatune NA et al., 2003), tropical and sub-tropical South East Asia. It grows in Indo-Malayan region and distributed across Terai tracts as well as Burma and Ceylon. It tolerates moderate shade and is often found as under growth in dry deciduous forests The leaves of Nyctanthes arbor-tristis Linn are used extensively in Ayurvedic medicine for the treament of various diseases such as sciatica, chronic fever, rheumatism and internal worm infections and as a laxative, diaphoretic and diuretic.

Keywords: Diabetes, Hyperglycemia, Nyctanthes arbor-tristis, sciatica, rheumatism, laxative, diaphoretic, diuretic.

I. INTRODUCTION

In people with diabetes, blood sugar levels remain high. This may be because insulin is not being produced at all, is not made at sufficient levels, or is not as effective as it should be. Gestational diabetes is a form of diabetes that occurs in pregnancy, and other forms of diabetes are very rare and are caused by a single gene mutation.

For many years, scientists have been searching for clues in our genetic makeup that may explain why some people are more likely to get diabetes than others are. "The Genetic Landscape of Diabetes" introduces some of the genes that have been suggested to play a role in the development of diabetes.

The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and

failure of different organs, especially the eyes, kidneys, nerves, heart and blood vessels. Diabetes is classified on the basis of the pathogenic process that leads to hyperglycemia, as opposed to earlier criteria such as age of onset or type of therapy. The two broad categories of diabetes mellitus are designated as type 1 and type 2. Type 1 diabetes mellitus results from autoimmune beta cell destruction, which leads to insulin deficiency. Type 2 diabetes mellitus is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion and increased glucose production. Although type 1 diabetes mellitus most commonly develops before the age of 30, autoimmune beta cell destruction can develop at any age. Type 2 diabetes mellitus develops more rapidly with increasing age, but it also occurs in children, particularly in obese individuals.[2] The global prevalence of diabetes is estimated to increase from 4% in 1995 to 5.4% by the year 2025 and the number of people with DM are set to rise from an estimate of 150 million in 2008 to 220 million in 2010 and 300 million in 2025. The countries with the largest number of diabetic people are and will be in the year 2025, India, China and United States. Despite the availability of insulin and many oral hypoglycemic drugs diabetes mellitus still remains a major health concern for humans. The leaves of Nyctanthes arbor-tristis Linn are used extensively in Ayurvedic medicine for the treament of various diseases such as sciatica, chronic fever, rheumatism and internal worm infections and as a laxative, diaphoretic and diuretic.Leaves are used in cough.
The extracted juice of leaves acts as a cholagogue, laxative and mild bitter tonic. The expressed juice of leaves (10 ml BD × 5 days) is a native remedy for intermittent fever.

Classification:

Diabetes is classified by underlying cause. The categories are: type 1 diabetes—an autoimmune disease in which the body's own immune system attacks the pancreas, rendering it unable to produce insulin; type 2 diabetes—in which a resistance to the effects of insulin or a

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 1614-1630 www.ijprajournal.com ISSN: 2456-4494

defect in insulin secretion may be seen; gestational diabetes; and "other types". There are many underlying factors that contribute to the high blood glucose levels in these individuals. An important factor is the body's resistance to insulin in the body, essentially ignoring its insulin secretions. A second factor is the falling production of insulin by the beta cells of the pancreas. Therefore, an individual with type 2 diabetes may have a combination of deficient secretion and deficient action of insulin.

In contrast to type 2, type 1 diabetes most commonly occurs in children and is a result of the body's immune system attacking and destroying the beta cells. The trigger for this autoimmune attack is not clear, but the result is the end of insulin production.

Historyof Diabetes:

Physicians have observed the effects of diabetes for thousands of years. For much of this time, little was known about this fatal disease that caused wasting away of the body, extreme thirst, and frequent urination. It wasn't until 1922 that the first patient was successfully treated with insulin.

One of the effects of diabetes is the presence of glucose in the urine (glucosuria). Ancient Hinduwritings, many thousands of years old, document how black ants and flies were attracted to the urine of diabetics.

Around 250 B.C., the name "diabetes" was first used. Mellitus is Latin for honey, which is how Willis described the urine of diabetics ("as if imbued with honey and sugar").Up until the mid-1800s, the treatments offered for diabetes varied tremendously. Various "fad" diets were prescribed, and the use of opium was suggested, as were bleeding and other therapies. The most successful treatments were starvation diets in which calorie intake was severely restricted. Naturally, this was intolerable for the

What is Type 1Diabetes?

Type 1 diabetes is called as juvenile diabetes, that is most severe form of the disease. About 5% of people who have diabetes have type 1 diabetes, or insulin- dependent diabetes. it is usually develops in children and teenagers. But people of all ages can develop type 1 diabetes. The islet cells sense glucose in the blood and produce the right amount of insulin to normalize blood sugars. This attack on the body's own cells is known as autoimmune disease. Scientists are not sure why the autoimmune attack happens.

What are the Warning Signs of Type 1Diabetes?

• Increased thirst
• Increase amount of Urine
•Rapid and unexplained weight loss
•Extreme hunger
•Extreme weakness or fatigue
•Unusual irritability
•Blurred vision
•Nausea, vomiting and abdominal pain
• Itchy skin

Type1DiabetesTreatment

Type 1 diabetes is treated by insulin injections. The challenge with taking insulin is that it's tough to know precisely how much insulin to take. The amount is based on many factors, including:

- Food
- Exercise
- Stress
- Emotions and general health

What is Type 2 Diabetes?

The most common form of diabetes is called type 2 diabetes, or non-insulin dependent diabetes. About 90% of people with diabetes have type 2. Type 2 diabetes is also called adult onset diabetes, since it typically develops after age 35. However, a growing number of younger people are now developing type 2 diabetes.

People with type 2 diabetes are able to produce some of their own insulin. Often, it's not enough. And sometimes, the insulin will try to serve as the "key" to open the body's cells, to allow the glucose to enter. But the key won't work. The cells won't open. This is called insulin resistance. Type 2 diabetes is typically tied to people who are overweight with a sedentary lifestyle.

What are the Warning Signs of Type 2 Diabetes?

The symptoms of type 2 diabetes are similar to those of type 1 diabetes. But the onset of type 2 diabetes is usually slower and the symptoms are not as noticeable as those for type 1 diabetes. For these reasons, many people mistakenly overlook the warning signs. They also might think that the symptoms are the signs of other conditions, like aging, overworking or hot weather.

Type 2 Diabetes Treatment

Treatment for type 2 diabetes focuses on improving ways to better use the insulin the body already produces to normalize blood sugar levels. Treatment programs for type 2 diabetes focus on

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diet, exercise and weight loss. If blood sugar levels are still high, medications are used to help the body use its own insulin more efficiently. In some cases, insulin injections are necessary.

Etymology:-

Etymology of Parijata is "Paarinaha Samudrath jaatho va parijatah":- It is called Parijata, because of it's origin from samudra (Ocean) as a result of (parinaha) extensive searching.

Habit and Habit at:-Habit:

- Leaves decussately opposite, ovate, subcordate at base, acute at apex, margin entire or with a few teeth.
- Anthers are 2, sub-sessile and inserted near the mouth of corolla tube. Ovary is two celled with one ovule in each cell.
- The fruit is a flat brown heart-shaped to round, capsule 2 cm diameter, with two sections each containing a single seed. Seeds are erect, orbicular and flattened.
- The tree begins to flower from late September onwards till December. Flowers open late in the evening.

Habitat:

Night jasmine is native to the subtropical Himalayas of Nepal and India; it is more found in southern parts of India, and in South- East Asian country such as Thailand, Malaysia and Indonesia.

Plant Description

Coral jasmine, commonly known as night jasmine, is an aboriginal small tree, with a gray or greenish, rough and peeling bark. The shrub grows to a height of 10 meters. The simple leaves are opposite, with an entire edging about 6 to 12 cm long and 2 to 6.5 cm wide. The flowers are fragrant with a five-to-eight lobed corolla and orange-red center, often seen in a cluster of two to seven. The petals are snow white with dew drops sitting on them. The fruit is plane, brown and heart-shaped to round capsule, around 2 cm in diameter with two sections, each containing a single seed.

Growing season and type

This tree grows well in a variety of loamy soils and in soils found in average garden situations, with pH 5.6-7.5.

Ecological and distribution

It is also widely distributed in Bangladesh, Indo-Pak subcontinent and South-East Asia, tropical and sub-tropical South East Asia. It grows in the Indo-Malayan region and distributed across Terai tracts as well as Burma and Ceylon. It tolerates moderate shade and is often found as undergrowth in dry deciduous forests. It is also found in Thailand.

Taxonomical classification Kingdom: Plantae Division: Magnoliophyta Class:
Magnoliopsida
Order: Lamiales Family: Oleaceae Genus: Nyctanthes Species: arbor-tristis
Binomial name: Nyctanthes arbor-tristis

OVERVIEW OF FAMILY OLEACEAE

Oleaceae is a family containing 24 extant genera and around 600 species of mesophytic shrubs, trees and occasionally twiners. As shrubs, members of this family may be twine climbers, or scramblers.

Somegenerawithcommonnamesof Oleaceaefamily GeneraForsythia	Commonname
Abeliophyllum	WhiteForsythia
Chionanthus	Fringetree
Forester	Swamp-privet
Forsythia	Forsythia
Fraxinus	Ash

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Jasminum	Jasmine
Ligustrum	Privet
Osmanthus	Osmanthus
Olea	Olive
Failure	Mock-privet
Syringa	Lilac

The plant is named in different vernacular languages. Unani: Harasingaar.
Sanskrit: Parijatha.
Siddha: Pavazha motif.
Hindi: Harsingar.
Ayurvedic: Paarijaata, Shephaali, Shephaalikaa, Mandaara. English: Tree of Sorrow,
Night Jasmine, Coral Jasmine.
Punjabi: Harsinghar.
Sanskrit: Parijata, Parijatah, Parijataka, Sephalika.
Thai: Karanikaa.
Filipino: Coral Jasmine.
Indonesian: Srigading (Sundanese, Javanese).
Vietnamese: Iai Tau.
Gujarati: Jayaparvati, Parijatak.

Characteristic Features of Nyctanthes arbor-tristis
Morphology:

Leaves

Leaves are opposite, 5 -10 of 2.5 – 6.3 cm, ovate, acute or acuminate, entire or with a few large, distant teeth, short bulbous hairs rounded or slightcuneate; main nerves few, conspicuous beneath; petiole 6cm long, hairy [4]. Leaves are simple, petiolate and stipulate The lamina is ovate with acute or acuminate apex, the margin entire or serrate, somewhat undulated, particularly near the base, Nyctanthes arbor-tristis venation is unicostate, reticulate with an average of 12 lateral veins leaving the midrib. The petioles are about 5–7.7–10 mm long with adaxial concavity.

Fruits

Fruits of Nyctanthes arbor-tristis are a capsule of 1-2 cm diameter, long and broad, obcordate orbicular, compressed, 2-celled, separating into 2 flat 1- seeded carpels, reticularly veined, glabrous [6]. The macroscopic character of the fruit: The fruit is flat, brown and heart cordite-shaped to rounded-capsule, around 2 cm in diameter with two celled opening transversely from the apex, each containing a single seed.

Seed

The seed is compressed and is 1 per cell Seeds is exalbuminous, testa thick; the outer layer of large transparent cells and heavily vascularised. phytosterols, phenolic compounds, tannins, flavonoids, cardiac glycosides, saponins and alkaloids all are found in seeds of N. arbortristis .

Traditional Uses:
Traditional Uses flowers

Different parts of Nyctanthes arbortristis Linn are known to possess various ailments by tribal people of the Indian subcontinent with its use in Ayurveda, Sidha and Unani systems of medicines. The bright orange corolla tubes of the flowers contain a colouring substance nyctanthin, which is identical with ά- Crocetin from Saffron. The corolla tubes were formerly used for dyeing silk, sometimes together with Safflower or turmeric. The flowers of Nyctanthes arbortristis are used in India, Indonesia (Java) and Malaysia to provoke menstruation.

Traditional Uses of leaves

The leaves are also used in fungal skin infection and in a dry cough. The young leaves are used as female tonic and in alleviating gynecological problems [12]. Leaves of Nyctanthes arbortristis Linn is used extensively in Ayurvedic medicine for the treatment of various diseases such as sciatica, chronic fever, rheumatism, and internal worm infections, and as a laxative, diaphoretic and diuretic. Leaves are used in cough reduction. Leaf juice is mixed with honey and given thrice daily for the treatment of cough. Paste of leaves is given with honey for the treatment of fever, high blood pressure and diabetes. The juice of the leaves is used as digestives, antidote to reptile venoms, mild bitter tonic, laxative, diaphoretic and diuretic. The

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extracted juice of leaves acts as a cholagogue, laxative and mild bitter tonic. It is given with little sugar to children as a remedy for intestinal ailments [13]. Here is the Ayurvedic remedies supply indicative relief and prevent from complications of Nipah virus.

- Take 6–7 leaves, put in 200 ml of water and boil it and make into 100 ml decoction, at the end add pepper powder and 3 drops of lemon.
- Drink the Kashaya 3–4 times a day .

Traditional Uses of Stems

- In rheumatic joint pain
- In treatment of malaria
- also used as an expectorant

Chemical constituents of Nyctanthes arbortristis Linn Phyto-constituents from leaves

Leaves contain D-mannitol, β-sitosterole, Flavanol glycosides, Astragaline, Nicotiflorin, Oleanolic acid, Nyctanthic acid, Tannic acid, Ascorbic acid, Methyl salicylate, resinous substances, Amorphous glycoside, Amorphous resin, Trace of volatile oil, Carotene, Friedeline, Lupeol, Mannitol, Glucose, Fructose, Iridoid glycosides, Benzoic acid. All the important phytoconstituents are being used in Ayurvedic medication and reported for sciatica, arthritis, fevers, and various painful conditions and as a laxative.

Phyto-constituents from flowers

Flowers contain modified diterpenoid nyctanthin, flavonoids, anthocyanins and an essential oil which is related to that of jasmine. Flowers have modified essential oil, Nyctanthin, d-mannitol, Tannin, Glucose, Carotenoid, Glycosides, βmonogentiobioside ester of α-crocetin (or crossing-3), βmonogentiobioside, β-D monoglucoside ester of α-Christian, β-digentiobioside ester of α- crocetin (or crossing- 1). 1, anthocyanins and essential oil which is similar to jasmine19 Nyctanthin, tannin and glucose, carotenoid, glycosides viz. β- monogentiobioside ester of α- crocetin (or crossing-3), βmonogentiobioside -β-D monoglucoside ester of αcrocetin, β- digentiobioside ester of α-crocetin (or crossing-1), 4- hydroxy hexahydrobenzofuran–7-one also reported in flowers. The orange tubular calyx of the flower contains carotenoids. It also contain an antiplasmodial cyclohexylethanoid, rengyolone, a new iridoidglucoside 6-O -trans-cinnamoyl-7- O-acetyl-6-β-hydroxyloganin and three known iridoidglucosides, arborside-C, 6-β-hydroxyloganin and nyctanthoside.

Phyto-constituents from seeds

Seeds contain Arbortristoside A&B, Glycerides of linoleic acid, oleic acid, lignoceric acid, stearic acid, palmitic and myristic acids, nyctanthic acid, 3-4 secotriterpene acid, a water soluble polysaccharide tranquil of D-glucose and D mannose. The seed of Nyctanthes arbortristis contains 15% of pale yellow brown oil, nyctanthic acid, nyctoside A, b-sitosterol, arbortristoside A & B, glycerides of linoleic oleic, lignoceric, stearic, palmitic and myristic acids, 3-4 secotriterpene acid and A water soluble polysaccharide composed of Dglucose and D mammals and used as an immunostimulant and hepatoprotective .

Phyto-constituents from stem

Stem contain β-sitosterol, Glycoside-naringenin-4-0-β-glucapyranosyl-αxylopyranoside and Flower oil Flower oil contains p-cymene α-pinene, 1- hexanol methyl heptanone, phenyl acetaldehyde, 1- deconol and anisaldehyde. β-Amyrin, arbortristoside-a, oleanolic acid, nyctoside-a, nyctantic acid and 6- β-hydroxyloganin .

Phyto-constituents from the Roots

The root part of the plant composed of alkaloids, tannins and glucosides. From the chloroform extract of the root β-Sitosterol and oleanolic acid has been isolated .

Phyto-constituents present invariouspartsofplant[28]Part Used	PharmacologicalEffect
Bark	Antimicrobial

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FlowerOil	Perfume

Flowers	Ant-BiliousAntifilarial Anti-Inflammatory AntioxidantDiuretic Dyspepsia OphthalmicSedative
Leaves	Anthelmintic Antibacterial LAntifungal Anti-Inflammatory AntioxidantAntipyretic Arthritis Asthma BronchitisCholecystagogueConstipationCough Dyspepsia FlatulenceHeartburn HepatoprotectiveImmunopotentia L NauseaReptile VenomRheumatismRingwormSciatica

Seeds	Antibacterial AntifungalAlopeciaAntileishmanialHairTonic ImmunomodulatoryPiles
Stem	AntioxidantAntipyreticBronchitisSnakebite

Bio-prospection undertaken for Nyctanthus arbor-tristis

Anti Allergy Activity

Petroleum ether, chloroform, ethyalacetate, ethanolandaqueous extracts of Nyctanthus arbor-tristis bark were examined, of which petroleum ether extract at 50 and 100 mg/kg showed maximum protection against mast cell degranulation by clonidine and resisted contraction (bronchodilation) induced by histamine at 50and 100 mg/kg [29]better than other extracts which they proposed, might be due to B- sitosterol. Though the toxicity studies have not been reported in any of this work , but other reports of toxicity in similar extracts indicate a much safer level. The pretreatment of guinea pigs exposed to histamine aerosol with a water soluble portion of the alcoholic extract of N. arbor- tristis leaves offered significant protection against the development of asphyxia. Arbortristoside A and arbortristoside C are present in N. arbortristis were reported to be anti- allergic .Anti Anxiety.

Hydroalcoholic extracts of N. arbortristis (NAT) have anxiolytic potential. Using hydro-alcoholic mixture, dried plant parts of N. arbortristis was extracted, concentrated by distilling off the solvent and then evaporated to dryness on the water bath and then stored in an airtight container in a refrigerator till used .

Anti-Inflammatory activity

The aqueous extract of the whole plant, alcoholic extract of stem and seeds and water soluble portion of the alcoholic extract of leaves of N. arbortristis were reported to have acute and sub-acute anti-inflammatory activity. The acute

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antiinflammatory activity is evaluated in inflammatory models using different phlogistic agents' viz. carrageenan, formalin, histamine, 5-hydroxytryptamine and hyaluronidase in the hind paw of rats. In the sub- acute models, N. arbortristis was found to check granulation tissue formation considerably in the granulomapouch and the cotton pellet test. N. arbortristis is also found to inhibit the inflammation produced by
immunological methods that are Freund's adjuvant arthritis and purified tuberculin reaction.

Hepatoprotective activity

Ethanolic leaf extract of Nyctanthes arbortristis protects against carbon tetrachloride – induced hepatotoxicity in rat. For this investigation rats were pretreated with extract (1000mg/kg body weight/day, p.o. For 7 days) prior to the administration of a single dose of CCl4 (1.0ml/kg, s.c.). The samples of blood were collected at 48 h after CCl4 administration (9 day) from the abdominal aorta under pentobarbitone anesthesized (350mg/kg i.p.). Silymarin (70mg/kg body weight/day, p.o. For 7 days) were used as a reference standard. In this study the leaf extract of Nyctanthes arbortristis and silymarin restored all serum and liver parameters which were altered by (CCl4) from the normal level, also prevent loss of body weight; both candidates are also protected against (CCl4) induced increase in liver weight and volume. These effects may be mediated by the antioxidant present in the plant. In another investigation, the ethanolic and aqueous extract of the leaf of Nyctanthes arbortristis (500mg/kg oral route for 10 days) reversed the rise in serum AST and total bilirubin in (CCl4) induced hepatotoxicity in animal models .

Antiviral activity

The ethanolic extract, n-butanol fractions and two pure compounds, arbortristoside A and arbortristoside C, isolated from the Nyctanthes arbortristis possess pronounced inhibitory activity against encephalomyocarditis virus (EMCV) and Semliki Forest Virus (SFV). The in- vivo ethanolic extract and the n-butanol fraction at daily doses of 125 mg/kg weight protected EMCV infected mice against SFV by 40 and 60% respectively 30, 30. Khatu na, haue me, mosaddik ma. Laboratory evaluation of Nyctanthes arbo-rtristis Linn. Flower extract and its isolated compound against common floral vector, Culex quinquefasciatus say (dip. The fresh juice obtained from the leaves of the plant was found to have antimalarial activity. The 50% ethanolic extract of the seeds, leaves, roots, flowers and stem of the plant is proven to posses antiamoebic and antiallergic properties. Leaf extract of the plant showed antiinflammatory, analgesic, antipyretic and allergenic activities. The leaves, seeds and flowers of the plant were reported to exert immunostimulant activity. The water soluble fraction of the ethanolic extract is proven to posses tranquilizing, antihistamines, purgative effects and depletion of tumor necrosis.

Anti-Filarial activity

The chloroform extract of the flowers and a pure compound isolated from N. arbortristis plant exhibit larvicidal activity against Culex quinquefasciatus, a common floral vector.

Antibacterial activity

Infectious diseases are the world's leading cause of premature death. Resistance to antimicrobial agents is conferred in a wide variety of pathogens and multiple drug resistance is becoming more common in diverse organisms such as Staphylococcus aureus, Staphylococcus epidermis, Salmonella typhi, Salmonella paratyphi A. In a study, it was reported that methanolic extract of leaves of N. arbortristis exhibited significant antibacterial activity against Staphylococcus aureus, Staphylococcus epidermis, Salmonella typhi, Salmonella paratyphi A with MIC value ranging between 1-8 mg/ml. The zone of inhibition and the Minimum Inhibitory Concentration (MIC) of the extracts were determined and compared with the standard drugs ciprofloxacin and fluconazole. The chloroform extract was found to have both antibacterial and antifungal activities, whereas the
petroleum ether and ethanol extracts hold only antibacterial activity.

Antioxidant activity

Plants produce potent antioxidants and the use of N. arbortristis leaves as a decoction in Ayurvedic medicine for various ailments 8. can be linked to the anti-oxidant activity of classes of compounds which aid in scavenging the free radicals mostly responsible for the pathogenesis. An initial report by Sunil Kumar and Muller (1999) evaluated the effect of the methanolic extract from the leaves of N. arbortristis on free radical induced lipid peroxidation using bovine brain phospholipid liposomes and found good activity with IC50 values of 20 mg/ml. The aqueous extracts from the leaves of the plant have been first reported to have DPPH radical, hydroxyl radical scavenging activity, lipid peroxidation preventive property.

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Thangavelu and Thomas (2010) indicated that ethanolic extracts of the leaves and stem of the plant are a potent source of antioxidants through assays like di-phenyl picryl hydrazyl (DPPH) radical scavenging assay. A study of the antioxidant activity of aqueous extract from the flower and its parts indicated that the DPPH radical scavenging activity is in the order of calyx4flower4petal. A further study on the fractioned alcoholic extract of the leaves showed antioxidant activity in the order of butanol (95.22%) 4 ethyl acetate (84.63%) 4petroleum ether (82.04%) at 100 mg/ml as compared to 93.88% of ascorbic acid at 10 mg/ml. A study by on acetone soluble fraction of ethyl acetate extract from leaves showed impressive antioxidant activity through DPPH, hydroxyl and superoxide radicals as well as H2O2 scavenging assays. The fractions have been compared with standard antioxidants like a-tocopherol, BHT, monitor and found to be comparable. Methanolic extracts of the flowers also exhibit high phenolic content and antioxidant activities, interestingly aqueous extracts showed high enzymatic antioxidants. Methanol extract and flavonoid fraction of leaves exhibited DPPH scavenging activity and strong ferric reducing activity with an IC50 value of 63.670.29 and 61.970.15 mg/ml, respectively.Summarizing the antioxidant activity, it may be concluded that leaves, stem and flower extracts containing phenolics and flavanoids are responsible for the antioxidant activity which overall were detected in extracts derived solvents of lower polarity. The report on an aqueous extract (higher polarity) conclusively indicated lower antioxidant activity.

Anticancer activity

With 86% inhibition of breast cancer cell lines free of pathogens. A high degree of against human breast cancer cell lines (MDA-MB 231) was observed with N. arbortristis dried fruit methanol and the IC50 values were calculated to be 9.72mg and 13.8mg. The phytochemicals isolated from N. arbortristis dried fruit methanol are glycosides, tannins, phenols and steroids and are predicted to be responsible for this anticancer activity.

Anti-Diabetic activity

The anti-diabetic activity of methanol extract of root of N. arbortristis is comparable to that of diabetic control animals. The extract poses safe and strong anti-diabetic activity. The extract was prepared by extracting 50g root powders with 400mL of methanol for 18 hours by hot continuous extraction method. It reduces blood glucose levels after seven days at the 500 mg/Kg in rats compare with standard drug. It was found that methanolic extract of N. arbortristis roots were more effective in reducing the blood glucose level compared to the standard drug.

Antimalarial activity

Clinical study on 120 patients of malaria. Administration of fresh paste of medium sized 5 leaves of N. arbortristis thrice a day for 7-10 days has cured the disease in 92 (76.7%) patients within 7 days. Another 20 patients were cured by 10 days while the remaining 8 patients did not respond to the treatment.

Anti-Parasitic activity

A crude 50% ethanolic extract of the leaves has been reported to exhibit trypanocidal activity at 1000 g/ml concentration. However, it is also reported that as soon as the treatment with the extract is discontinued, the parasitemia increases and results in the death of the experimental animals. N. arbortristis extract has also exhibited potent anti-leishmanial activity in Leishmania donovani infected hamsters. The 50% ethanolic extracts of the seeds, leaves, roots, flowers and stem of the N. arbortristis have been found to clear Entamoeba histolytica infections in rat cecum. However, the extracts were not active in vitro. The water soluble portions of ethanolic extract of flowers, bark, seeds and leaves of N. arbortristis were found to possess anthelmintic activity which is suggested due to inhibition of motility by relaxing and depression responds to contractile action of acetylcholine.

Anti-Trypanosomal Potential Antitrypanosomal

The potential of a crude 50% ethanol extract of Nyctanthus arbortristis leaves were evaluated in vitro and in vivo. However, as soon as the treatment with the extract was discontinued, the parasitemia increased and resulted in the death of the experimental animals .

Anti-Leishmanial Activity

The anti-leishmanial activity of N. arbortristis has been attributed to iridoid glucosides, arbortristosides A, B, and C and 6-b-hydroxyloganin.The arbortristosides A, B, C, and 6- beta- hydroxy-loganin exhibited both in vitro and in vivo anti-leishmanial activity against amastigotes in macrophage cultures and hamsterstest systems, respectively .

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Anti-Histaminic and Anti-Tryptaminergic activity

The aqueous solubility of the alcoholic extract of N. arbortristis leaves (4.0 and 8.0g/kg oral) significantly protect against histamine aerosol - induced asphyxia (2% at 300 mm Hg) in guinea pigs. arbortristosid A and arbortristosid C present in N. arbortristis was reported to be anti-allergic.

Anti-Cholinesterase activity

The aqueous extract of N. arbortristis stimulated the activity of acetylcholine esterase in mice; it antagonizes the inhibition of this enzyme by malathion. The higher effects were seen in the serum than in the brain. The low anti muscarinic activity against acetylcholine induced contractions of isolated rabbit ileum was already reported .

Anti-Nociceptive and Antipyretic activity

The aqueous soluble fraction of ethanolic extract of the leaves exhibited significant aspirin-like anti-nociceptive activity which was evidenced by inhibition of acetic acid induced writhing in albino mice, but fails to elicit morphine like analgesia which was tested via the rat tail flick and mouse tail- clip method .

Anti-Anemic Activity

A research was performed as a hematological study on the ethanolic extracts of the flowers, barks, seeds and leaves of the plant and noticed the dose dependent rise in hemoglobin content and red blood cells count in rats. The extracts also protect the decline of hemogram profile in anemic rats.

CNS depressant activity

It was reported that the leaves, flowers, seeds and barks (600 mg/kg) of N. arbortristis exhibited significant and dose dependent prolongation of onset and duration of sleep and found to cause a decrease in dopamine and increase serotonin level from which it can be resolved that the CNS depressant activity of the ethanol extracts of seeds, leaves and flowers may be due to the decrease in dopamine and increase in serotonin level.

Essential oils

The essential oil in the fragrant flowers, which is similar to the oil in N. arbortristis, is used as a perfume.

Membrane Stabilizing Activity

From a research work of N. arbortristis isolated a carotenoid Anglican Ag-NY1 from the orange colored tubular calyx of flowers. The compound exhibited a good membrane stabilizing activity as compared to the corresponding glycoside crossing .

Sedative Activity

In this test, male rats exhibited a dose dependent conscious sedative activity while female rats remained unaffected. At these doses, muscle strength and cardio Nyctanthes arbortristision were not affected, nor was blood glucose levels affected even at the highest dose. However, glucose absorption from the small intestine was significantly reduced. The sedation was attributed, in part, to the antioxidant and membrane stabilizing activity of the extract .

Treatment of Piles, Gout, Dry Cough

The seeds of N. arbortristis are used in the treatment of piles. The decoction of N. arbortristis flowers are used in the treatment of gout. Leaves are used against dry cough. The aqueous paste of the leaves is used externally in the treatment of skin related troubles specifically in the treatment of ringworm. The young leaves are used as a female tonic. N. arbortristis also has hypoglycemic effect, potentiating action of exogenous insulin and streptozotocin- induced diabetic rat model .

Toxicity

N. arbortristis showed the toxic effect of ethanol extract of leaves in rats. The median lethal dose (LD) 16 GM/kg was observed in rats. No mortality was at 2.0 mg/kg, while 75% mortality was seen at a 32 mg/kg dose. An administration of ethanol extract of the leaves (1, 2 and 4 mg/kg/day) orally for 6 consecutive days is produced gastric ulcers in rats. When extract installed into the rabbit‘s eye produced conjunctival congestion with edema, while the person who grounded the dried leaves developed vesicles on both palms.

Other activities

80.73% ovicidalaction was observed at 100% concentration of the extract. Petroleum ether extract of N. arbortristis also exhibits insecticidal activity against Bagrada cruciferarum. The ethanolic extract of N. arbortristis leaves, seed and roots were screened in humoral and cell-mediated immune responses against Candida albicans and Salmonella antigens. The water soluble portion of an ethanol extracts of the leaves exhibits significant aspirin like anti-nociceptive activity but failed to produce morphine like analgesia. It was also found to possess anti- pyretic activity against brewer’s

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yeast induced pyrexia in rats. An Ethanolic extract of the whole plant has been reported to initiate hair growth .

PARTS OF THE NAT REPORTED FOR VARIOUS PHARMACOLOGICALACTIVITIES:

Reported activity	Partused	Extract	Illation
Anti-arthritic	Seeds,leavesandfruitswholeplant	Ethanolic	Seedextractineffective;Leavesand fruits extracts reduced TNF α,IL-1,IL-6.Extractofleavesandfruitpossessanti-arthritic properties[20].
Antibacterial	Leaves	Methanolic	Antibacterialactivity againstStaphylococcusaureus,Staphylococcus epidermis,Salmonellatyphi, Salmonella paratyphiA[28].
Antidiabetic	StemBark	Ethanolic	Serumcholesterolandtriglycerides getlowered;Antidiabetic[4].
	Whole plant	Ethanolic	SubduedTBARS;Antidiabetic antioxidant[31].
	Leaves andflowers	Chloroform	IncreaseinSODandCAT enzymaticantioxidant action[20].

PARTS OF THE NAT REPORTED FOR VARIOUS PHARMACOLOGICALACTIVITIES:

Reported activity	Partused	Extract	Illation
Anti-inflammatory	Leaves	Ethanolic	Inhibit inflammation produced by Freund's adjuvantarthritisandPPDinducedtuberculin reaction[32].
		Ethanolic	Inhibitacuteinflammatoryedema producedby carrageenan, formalin, histamine, 5-hydroxytryptamineandhyalouronidaseinhind

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			pawofrats.Italso reducedacuteinflammatory swellingin thekneejoint induced byturpentine oil[47].
	Seeds	Ethanolic	Isolatedarbortristoside-Asubduedthehistamine, serotoninand carrageenan-induced edema[30]

PARTS OF THE NAT REPORTED FOR VARIOUS PHARMACOLOGICALACTIVITIES

Reportedactivity	Partused	Extract	Illation
Antileishmanial	Leaves	Methanolic	Isolatedcalceolarioside Awhichseemedt obe potentagainst visceralleishmaniasis[34].
	Flowers	Chloroform	Larvicidal against Culexquinquefasciatus [36].
Antioxidant	Leaves	Ethanolic	DPPHassay,freeradicalscavengingacti vity,reducingpowerassay,totalantioxid ant capacityresolved it to stronglypossessantioxidant[18].
	Leaves	Ethyl-acetate	Potentantioxidant[32].
Antispasmodic	Fresh flowers, Dried leaves,stem,bar k	Ethanolic	Inhibit contractile response ofacetylcholine[29].

PARTS OF THE NAT REPORTED FOR VARIOUS PHARMACOLOGICALACTIVITIES

Reported activity	Partused	Extract	Illation
Antiviral	Whole plant	Ethanolicextract; n-butanol fraction	Ethanolicextractsandn-butanolfraction protected EMCV infected miceto theextent of40 and 60% respectivelyagainstSFV[37].
Cytoprotective	Flowers	Chloroform	No adverse effects on central nervoussystem[39].

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CNSdepressant	Seeds, leaves, Flowers,Bark	Ethanolic	Dose-dependentaction [38].
Hepatoprotective	Leaves	Alcoholic, Aqueous	Significanthepatoprotective activityby reducingtheelevatedlevelsofbiochemicalparameters [40].
		Methanolic	Hepatoregenerative potentialin acetaminophen-induced hepaticdamage[40].
	Seed	Aqueous	Hepatoprotective against CCl4inducedhepatotoxicity[42,43].

PARTS OF THE NAT REPORTED FOR VARIOUS PHARMACOLOGICALACTIVITIES:

Reported activity	Partused	Extraction	Illation
Immunostimulant	Whole plant	Ethanolic	EnhancedtotalWBCcountand DTHreaction[21,22].
Antihelmintic	Freshflowers, driedleaves,stem, bark	Ethanolic	Seedsandflowerspossessmorepotent activity than bark and leaves.Alsopotentiatedantihelminticactivityof atropine [29].

Marketed formulations:

- Hersingar herbal memory nectar, by Chandi, LLC, USA
- Jasmine- enchanting light massage oil, by Sadatan Pure Ayurveda Pvt. Ltd, India

PLAN OFWORK

The aim of our study is to investigate the effect of leaves of Nyctanthes arbor-tristis on adrenaline induced hyperglycaemic rats, glucose loaded rats and normoglycemic rats.

The objectives of present study are as follows-

- Collection of leaves of plant material.
- Hydro-alcoholic Extraction of dried leaves of plant by maceration.
- Pharmacological evaluation
- Study of effect of extract on normoglycemic rats.
- Study of effect of extract on glucose loaded rats.

Study of effect of extract on adrenaline induced hyperglycemiaMATERIALS AND METHODS

Preparation of plant extract

The leaves were shade dried and then powdered. The powder was taken for maceration with 60% ethanol at a room temperature. The filtrate was evaporated to dryness and then used. The dose of 200 mg/kg was selected for the study .

Animals

Albino wistar male rats weighing 150-200g was used for the present study. They were mai ntained in the animal house of Sheat College of Pharmacy, Varanasi Sambalpur, for

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experimental purpose. The animals were maintained under controlled condi tions of temperature (23 ± 2°C), humidity (50 ± 5%) and 12-h light-dark cycles. All the an imals were acclimatized for seven days before the study.

Animals were habituated to laboratory conditions for 48 ho urs prior to experimental protocol to minimize if any of non-specific stress. All the studies conducted were approved by the Institutional Animal Ethical Committee (IAEC) of Sheat College of Pharmacy, Varanasi. Plant material Nyctanthes arbor-tristis Linn is native to India, distributed widely in sub- Himalayan regions and southward to Godavari (Das S et al., 2010)..

Preparation of dry powder of nyctanthes arbor-tristis leaves:

Collection of fresh leaves of Nyctanthes arbor-tristis from the local area. Clean the leaves by using distilled water. Leaves are dried at room temperature for a few days. The hot air oven is used for the complete drying of leaves. The dried leaves are collected and grind in a mixer to make a fine powder.

Experimental design no. 1

Effect of the extract on normal rats

Twenty-four albino rats weighing 150-200g were fasted for 18h and were divided into four groups of six animals in each. The groups included

1. Vehicle control- received 5% gum acacia in normal saline, 2ml/kg rat.
2. Test drug- received 200mg/kg, p.o. N. arbor leaf extract, and 2ml/kg rat.
3. Standard- received Glibenclamide (0.5 mg/kg p.o. 10% w/v, 2ml/kg g rat).

Blood from the tail of each rat was collected at '0' hour. Blood samples were collected again at 1, 3, 5 and 7 h after administration of drugs from the treated animals and blood glucosewas estimated by glucometer (one touch select).

Experimental design no.2:

Effect of extract on glucose loaded rats (OGTT)

In Oral Glucose Tolerance Test (OGTT), glucose (2 gm/kg b.w.) was given orally to the fasted rats 2 hr of drug administration and blood samples were collected from tail vein after 30 min, 60 min, 90 min and 120 min of glucose treatment.

Group-1: Normal group, receive solvent (5% gum acacia). Group-2: Glucose loaded group, receive Glucose+ Solvent. Group-3: Test group, receive Glucose +test drug (200 mg/kg).

Group-4: Standard group, receive Glucose + standard drug (Glibenclamide (0.5 mg/kg p.o)).

Experimental design no.3:

Effect of extract on adrenaline induced hyperglycemia.

Animals are divided into four groups of six rats per group. Test groups are administered extracts at a dose of 200 mg/kg body wt by oral route. Control groups are administered Normal saline at a dose 2ml/kg body wt. Hyperglycaemic control groups are administered Adrenaline at a dose of 0.8mg/kg body weight after 1hr of drug treatment. Standard groups were administered Glibenclamide orally at a dose of 0.5mg/kg body wt.

The experimental designs were as follows:

Group I – Normal Control (saline)

Group II – Hyperglycaemic control (Adrenaline 0.8 mg/kg body wt)

Group III – Test drug group (Adrenaline 0.8 mg/kg + extracts of Nyctanthes arbor-tristis leaves (200 mg/kg body wt)).

Group IV – Standard drug group (Adrenaline 0.8 mg/kg + Glibenclamide (0.5 mg/kg p.o)). Blood glucose levels were estimated at 1, 3, 5 and 7 h after administration of drugs.

II. RESULT

Table-1: Effect of hydro-alcoholic extracts of leaves of Nyctanthes arbor-tristis **onnormoglycemic rats.**

Group	**Treatment (Dosemg/kg)**	**Initial Glucose(mg/dl)**	**FinalGlucoseLevel(mg/dl)**			
			1hr	3 hr	5hr	7 hr
I	Control (solvent5ml/kg)	90.17 ±7.54	85.50 ±7.25	88.13 ±5.56	85.73 ±6.71	87.67 ±6.45
II	Extractof	92.33 ±8.31	82.24	79.50	71.62	73.12

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	N.arbor-tristis(200 mg/kg)		±7.00	±6.77	±6.06*	±7.10*
III	Glibenclamide(0.5 mg/kg)	91.15 ±6.29	70.40 ±5.37*	67.52 ±5.76*	60.57 ±6.18*	67.67 ±5.31*

Values are mean± SEM (Standard error of mean); Statistical analysis by Students t-test.pvalue <0. 01.
*GroupII, III compared with Group I.

Table-2: Effect of hydro-alcoholic extracts of leaves of Nyctanthes arbor-tristis onglucoseloadedrats

Group	**Treatment(mg/kg)**	**Initial glucoselevel(mg/dl)**	**Finalglucoselevel(mg/dl)**			
			30min	**60min**	**90min**	**120min**
Group1	Solvent	88.6±6.62	85.0±7.4	80.3±7.3	82.0±6.5	81.4±6.3
Group2	Glucose(2gm/kg)	87.5±5.75	202.0±9.4	160.3±10.3	142.0±8.5	108.4±7.5
Group3	Glucose+Extract(200)	84.5±7.53	192.4±8.5	154.4±8.4	126.6±7.5*	95.4±5.3*
Group4	Glucose+Glibenclamide(.5)	85.7±6.74	126.0±9.9*	98.3±7.3*	102.2±7.5*	80.4±6.4*

Values are mean± SEM (Standard error of mean); Statistical analysis by Students t-test.pvalue <0. 01.
*GroupII compared with Group I,Group III,IV compared to GroupII.

Table 3: Effect of hydro-alcoholic extracts of leaves of Nyctanthes arbor-tristis onadrenalineinduced hyperglycaemicrats.

Groups	**Treatment(Dose mg/kg)**	**Initial glucose(mg/dl)**	**Finalglucose(mg/dl)**			
			1hr	**3hr**	**5hr**	**7hr**
I	Normalcontrol (Solvent5ml/kg)	86.12 ±5.12	85.62 ±5.51	87.11 ±5.82	84.62 ±5.61	86.15 ±5.22
II	Hyperglycaemic control(Adrenaline)	87.33 ±6.91	191.01 ±9.12*	212.52 ±9.34*	193.31 ±9.43*	142.43 ±7.11*
III	Adrenaline+Extract (200)	85.41 ±5.83	177.43 ±8.43	194.24 ±7.21	155.60 ±6.45*	124.62 ±6.23*

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IV	Adrenaline+ Glibenclamide(0.5mg/kg)	88.64 ±5.24	162.33 ±8.42	166.52 ±9.34*	148.31 ±8.64*	121.43 ±7.02*

III. DISCUSSION

Plants may act on blood glucose through different mechanisms, some of them may have insulin-like substances and some may inhibit insulinase activity, Stimulation of β-cells to produce more insulin Therefore, the pan creas is especially susceptible to the action of alloxan induced free radical damage.

Recently, it was reported that the Nyctanthes arbortristis linn extract, exhibited significantly radical scavenging activity and thus antioxidant acti vity and the present finding indicates that administration of Nyctanthes arbortristis linn root confirms the possibility that the major function of the extract is on the protect ion of vital tissues including the pancreas, thereby reducing the causation of diabetes in animals .

In the present study, an attempt was made to establish the effect of plant Nyctanthes arbor-tristis on adrenaline induced hyperglycaemia and glucose loaded rats. It was found that the leaves of the plant Nyctanthes arbortristis can be used in the treatment of many diseases.

The oral dose of 200 mg/kg was selected for studies.

In normoglycemic rats, the drug reduces blood glucose level significantly after 5 hr of administration. So it shows significant glucose lowering activity in 5hr and 7hr time points. In normoglycemic glucose loaded rats also it reduces blood glucose level significantly when administered 2hr before administration glucose.

In adrenaline induced hyperglycaemic rats, the extract in the dose of 200 mg/kg also reduces blood glucose level significantly in comparison to solvent (control) groups after 5 hr of administration. The adrenaline induces hyperglycaemia by the release of glucocorticoids which alter glucose metabolism in liver. It also inhibits insulin release from pancreas and increase blood glucose level.

The results of our study showed that, the standard drug glibenclamide in the dose of 0.5 mg/kg, p.o. and the extract, in the dose of 200 mg/kg reduces the blood glucose level of glucose loaded rats significantly.

The leaves contain D-mannitol, β-sitosterole, Flavanol glycosides-Astragaline, Nicotiflorin, Oleanolic acid, Nyctanthic acid, tannic acid, ascorbic acid, methyl salicylate, carotene, friedeline, lupeol, mannitol, Glucose and fructose, iridoid glycosides, benzoic acid. These compounds have antioxidant, hepatoprotective, antiinflammatory and other action.

IV. CONCLUSION

Based on the results of this study, it may be concluded that N. arbortristis leaves extracts show interesting possibilities as a source of oral hypoglycemic agents. We believe that this plant must be considered as an excellent candidate for future studies on determining the mechanisms of its hypoglycemic activity, as well as for the isolation and identification of active hypoglycemic substances.

In summary, the present study demonstrated that administration of ethanolic extract of leaves of N. arbortristis significantly improved systemic insulin sensitivity and glucose homeostasis in normoglycemic rats. Our results support overall in vivo antihyperglycemic activity and activity on impaired glucose tolerance of the extract that may prove to be of clinical importance in improving the management of type 2 diabetes.

In the light of our pharmacological studies we can assume that further experiment should be carried out for isolating the possible hypoglycemic compounds and then explain the actual mechanism of hypoglycemic actions of the plant fractions. The present study has given some preliminary idea of the hypoglycemic compounds present in the reported plant fractions.

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