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Review Article

Beyond Beauty: A Multidimensional Review of the Sacred Lotus (*Nelumbo nucifera*) in Culture, Ecosystems, and Medicine

Mamta Kumari[1,2], Anubhav Dubey[3], Niladry Sekhar Ghosh[1,*]

[1]Faculty of Pharmaceutical Science, Assam Down Town University, Guwahati, Assam, INDIA.
[2]Department of Pharmaceutical Sciences, Harcourt Butler Technical University, Kanpur, Uttar Pradesh, INDIA.
[3]Department of Pharmacology, Maharana Pratap College of Pharmacy, Kanpur, Uttar Pradesh, INDIA.

ABSTRACT

Lotus (*Nelumbo nucifera* Gaertn.) is grown worldwide. It has seeds, leaves, roots, and flowers. Lotus leaves (pronounced "He-Ye") provide minerals and phytochemicals for food and medicinal. Pharmacokinetic information on *Nelumbo nucifera* Leaves' (NLEs) health benefits was examined. Nutrition and diet of NLEs are investigated. Including extensive tissue distribution, NLEs and critical components have good pharmacokinetics. Nelumbinis Folium fights obesity, diabetes, neuropathy, inflammation, cancer, liver protection, and more. The industrial uses of NLEs include meat, egg, dairy, pasta, drinks, fruit preservation, rice and meat zong, food packaging membranes, and health products. Further research and long-term clinical trials are needed to examine its physiochemical processes, safety, and bio-effects due to its unknown therapeutic efficacy and usefulness. Indian Ayurveda and Traditional Chinese Medicine eat and treat numerous diseases using Poddo (*Nelumbo nucifera*). Numerous phytochemistry and pharmacology studies have been published in the last two decades. We will research *N. nucifera*'s neuropharmacological effects, psych activities, active constituents, and probable route of action, which have not been thoroughly studied. The survey uses Google Scholar, PubMed, Web of Science, ScienceDirect, and Scopus. *N. nucifera* may affect *in vivo* animal models and *in vitro* cells or enzymes via 5-HT2A receptor blockage, the GABAergic system, NCAM and GAP-43 expression modulation, skolin-stimulated cAMP generation, and more. Depressive, sedative-hypnotic, anxiolytic, analgesia-potentiating, anticonvulsant, antipsychotic, and memory-enhancing *N. nucifera* alkaloids. Although human clinical trial research is sparse, various studies have shown this plant and its constituents' neurotherapeutic potential.

Keywords: Analgesia-potentiating, Anticonvulsant, Antipsychotic, Anxiolytic, GABAergic, Memory-enhancing, Sedative-hypnotic.

Correspondence:
Niladry Sekhar Ghosh
Faculty of Pharmaceutical Sciences,
Assam Down Town University,
Guwahati-781026, Assam, INDIA.
Email: niladry_chem@yahoo.co.in

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INTRODUCTION

Indigenous medicine, often known as traditional medicine, refers to medical practices created by local ethnic groups using natural minerals and herbs. Ayurvedic medicine started in India, and Acupuncture and TCM have their roots in China, but Southeast Asian and Unani medicine have their roots in the Arab world and the Middle East. The practice of traditional medicine has a long and varied history around the globe (Andjelković *et al.*, 2017; Abraham *et al.*, 2015). Herbal plants sometimes contain secondary metabolites, including tannins, steroids, alkaloids, glycosides, terpenes, flavonoids, and so on. Some compounds include sulfur or nitrogen, while others are phenols or oxygen-substituted derivatives of these, such as tannins, which are physiologically active and advantageous for maintaining human and animal health and preventing disease. Antioxidant properties of polyphenols result in numerous health advantages (Li *et al.*, 2014). These compounds serve as plant defense systems against their predators in addition to their biological activity in humans. Since ancient times, several of these spices and herbal products have been used as beneficial medical sources for humans (Figure 1) (Li *et al.*, 2015).

History

Indigenous medicine, often known as traditional medicine, refers to medical practices created by local ethnic groups using natural minerals and herbs. Ayurvedic medicine started in India, and Acupuncture and TCM have their roots in China, but Southeast Asian and Unani medicine have their roots in the Arab world and the Middle East. The origins of traditional medicine vary greatly

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around the globe (Chen *et al.*, 2024). The secondary metabolites found in herbal plants include compounds including tannins, steroids, alkaloids, glycosides, terpenes, and flavonoids. Phenols and their oxygen-substituted derivatives, such as tannins, are one type of chemical. Other compounds may contain physiologically important elements like sulfur or nitrogen and advantageous for maintaining human and animal health and preventing disease. Antioxidant properties of polyphenols result in numerous health advantages (Li *et al.*, 2017). These compounds serve as plant defense systems against their predators in addition to their biological activity in humans. Since ancient times, several of these spices and herbal products have been used as beneficial medical sources for humans (Figure 2) (Li *et al.*, 2020).

Plant-Based Compounds and Phytochemicals

Here are the chemical components of *Nelumbo nucifera* that have been described in different parts of the plant (Figure 3 and Table 1) (Li *et al.*, 2020).

Using phytochemical analysis, ten molecules were found from the seed extract of *N. nucifera*. These included five simple phenolic compounds, two indole derivatives, a flavonoid glycoside, and two abscisic acid derivatives. Lotus seeds contain a variety of compounds that have medicinal properties. These include alkaloids, flavonoids, polysaccharides, essential oils, glycosides, polyphenols, triterpenoids, and more chemical (Li *et al.*, 2020).

- Lotus: (*Nelumbo nucifera*).
- Family: Nelumbonaceace.

Local tribal names - (*Nelumbium nelumbo, N. speciosa, N. speciosum*, and *Nymphaea nelu*) and a plethora of botanical names (Chinese water lily, Indian lotus, sacred lotus, and bean of India) (Tables 2-9).

Plant Profile

Even at depths of 2.5 M (8 feet), the sacred lotus can still flourish. There must be water a depth of at least 30 cm (12 in). The tubers are more protected and the plant often grows and flowers more when the water is deeper in colder climates. The sacred lotus starts to blossom when the temperature rises above 13°C (55°F). Depending on the variety, most types can withstand year-round outdoor conditions in USDA hardiness zones 6-11 (though some farmers have reported success in zones 4-5). The higher the number of zones, the more adaptable the plants (Li *et al.*, 2022). The average daily temperature needed for growth is 23 to 27°C (73 to 81°F) and it occurs from April to September in the Northern Hemisphere. The sacred lotus enters a dormant period in winter in areas with low light levels. Although the tubers will not survive temperatures below 0°C (32°F) when left exposed to air, they can withstand cold weather when submerged in soil and stored underwater. The tubers and roots must be kept in a secure, frost-free place, such as a garage, preferably in a cardboard box or container that is well packed with vermiculite or perlite, if the plants are removed from the water for winter storage (which is typically done in really cold locations). Care must be taken to fully insulate the tubers (Li *et al.*, 2022b).

Planting

The loamy, nutrient-rich soil is ideal for the sacred lotus. A tiny in the northern hemisphere, the spring (March-May) is the time to plant portions of rhizomes that have at least one eye, either in ponds or directly into a flooded field. Seeds or buds can also be propagated in a variety of other ways. Additionally, tissue culture shows potential as a future method of propagation for producing huge amounts of consistent, disease-free, true-to-type materials. Plowing the arid field is the initial stage of agriculture. After ten days, a single application of manure is made before the field is flooded. The water level is kept relatively low to facilitate rapid early development and rises as plants develop. Then, with a grid spacing of 1.2 by 2 M (3 ft 11 in × 6 ft 7 in), a maximum of about 4,000 plants per hectare (1,600/acre) are planted straight into the mud 10 to 15 cm (3+7⁄8-5+7⁄8 in) below the soil surface (Li *et al.*, 2023).

Harvest

The stage of development of the lotus blossom bud is more advanced. Two to three months after planting, the stolon is ready for harvest. It needs to be picked before it blooms. Hand labor is used to harvest the stolon. The field is not drained during this stage. To get the stolon out of the water, we take the young leaves floating in the shallows and shake them. The initial crop of leaves and flowers is ready for picking three months following sowing. You can pick flowers every two days in the summer and every three days in the winter (Tables 1-9). The peak of flower output occurs four months following planting. Typically, flower harvesting takes three to four months and is done by hand (Li *et al.*, 2023).

Bioactive and pharmacological action

Numerous Research in the field of pharmaceuticals has shown that this substance has a variety of useful effects, such as reducing blood pressure, preventing cancer, fighting viruses, reducing obesity, breaking down fat cells, lowering blood sugar, protecting the liver, preventing diarrhoea, killing fungal and bacterial infections, reducing inflammation, and increasing urine output. Alkaloids, flavonoids, glycosides, triterpenoids, and many more chemical classes of compounds have been isolated from this plant, each with its own unique medical use. All parts of *N. nucifera* are therefore recognized to have their own unique active components and pharmacological effects. Because of this evaluation, it is easier to learn about all of the previous scientific studies and will give the essential details about *Nelumbo nucifera* Garten's vast pharmacological activities. This will encourage researchers to conduct more research in order to protect people

from a variety of diseases and possibly even use it as a natural resource to advance humankind (Anekonda and Reddy, 2005).

Plant-Based Compounds and Phytochemicals

Here are the chemical components of *Nelumbo nucifera* that have been described in different parts of the plant (Figure 4).

Antioxidant Activity

Scavenging DPPH, ABTS, and nitric oxide free radicals. Boosts antioxidant enzymes (SOD, CAT, GPx) and inhibits oxidative stress-induced cell damage. Active components include neferine, catechins, kaempferol, and quercetin. Both *in vitro* and *in vivo* tests were conducted to determine the antioxidant activity of a Hydroalcoholic Extract of *Nelumbo nucifera* (HANN) seeds. *In vitro*, HANN demonstrated notable free radical scavenging activity against Nitric Oxide (NO) and 1,1-Diphenyl-2 Picrylhydrazyl (DPPH) with IC_{50} values of 84.86±3.56 µg/mL and 6.12±0.41 µg/mL, respectively. These results were better than average. The *in vivo* model showed that compared to the control group that received only CCl_4, the group that received 100 and 200 mg/kg body weight of HANN four days prior to CCl_4 administration had significantly higher levels of catalase and SOD and lower levels of TBARS in the kidney and liver. Both the 50 mg/kg and 100 mg/kg doses of tocopherol produced comparable effects. *Nelumbo nucifera* seeds include saponins, alkaloids, polyphenolics, and carbohydrates, which boost HANN's antioxidant activity (Chang, 2012). Lee *et al.* examined the antioxidant effects of Korean Traditional Lotus Liquor made from lotus blossoms and leaves in 2005. Above 25 µg of lotus liquor, dose-dependent antioxidant actions reached their apex, inhibiting around 80% of the target substance. The DPPH scavenging effect of the liquor was substantial, with an IC_{50} value of 17.9 µg (Chen *et al.*, 2022). Researchers Yen *et al.* discovered in 2006 that reactive nitrogen species may be removed from lotus seeds. To find out whether extracts from lotus seeds could inhibit RNS in RAW264.7 macrophage cells, researchers looked at water, ethyl acetate, and hexane. The generation of NO is inhibited in lipopolysaccharide-activated RAW 264.7 cells by all lotus extracts. The Sodium Nitroprusside (SNP) breakdown-induced reduction of NO buildup, which is dose-dependent. The order of potency was LSEAE > LSWE > LSHE. In the comet assay, it was demonstrated that lotus extracts prevent DNA damage in SNP-stimulated macrophage RAW264.7 cells. At a concentration of 0.2 mg/mL, LSWE and LSEAE decreased peroxynitrite-induced DNA damage by 63%, LSHE by 59%, and LSEAE by 38%. Each of the extracts inhibited tyrosine nitration by acting as a peroxynitrite scavenger (Chen *et al.*, 2018). Procyanidins were isolated from lotus seedpods by Ling *et al.* in 2005 by means of Me_2CO/H_2O extraction. Although catechin and epicatechin were the primary building blocks, the extract had a high proportion of procyanidin dimers, tetramers, and monomers. Additionally, the procyanidins were evaluated for their ability to scavenge reactive free radicals, inhibit lipoxygenase enzyme activity, and test lipid peroxidation. The superoxide radical scavenging IC_{50} of lotus pod procyanidin is 17.6 mg/L, which is four times lower than that of ascorbic acid, which is 4.1 mg/L. When it came to antioxidant properties in soybean oil, 0.1% procyanidins were superior to Butylated Hydroxytoluene (BHT) at a concentration that was similar (Deng *et al.*, 2022). An 80% methanol extract of *Nelumbo nucifera* seed embryo was discovered by Kim *et al.* (2014) to decrease ROS production in HT22 cells found in the mouse hippocampus and to eliminate the free radicals DPPH (IC_{50}: 240.51 µg/mL) and H_2O_2 (IC_{50}: 1769.01 µg/mL) (Bae *et al.*, 2014).

Neuroprotective and Anti-Alzheimer's Activity

Enhances learning and memory inhibits the activity of Acetylcholinesterase (AChE). Prevents neurotoxicity caused by β-amyloid Neferine and liensinine are active alkaloids. An important bioactive alkaloid with an aromatic ring, nuciferine, has been demonstrated to have anti-inflammatory, anti-apoptotic, and neuroprotective properties. Because of these characteristics, nuciferine can help prevent stroke by controlling the body's metabolic equilibrium. Significant pathways pertaining to energy metabolism (glycolysis, gluconeogenesis, and the TCA cycle), lipid metabolism, metabolic stress, and other metabolic processes that may assist prevent stroke development have been discovered to be influenced by nuciferine. These findings provide a starting point for investigating nuciferine as a possible stroke treatment (Wu *et al.*,2010). Clinical research has focused Following MCAO, a characteristic of ischemic stroke that is associated with high rates of occurrence, recurrence, death, and impairment (Lee *et al.*, 2012).

In MCAO rats, Chen Chang and associates showed that nuciferine considerably reduced brain damage. According to transcriptomic data, nuciferine may have a therapeutic effect via controlling lipid metabolism, particularly the metabolism of phospholipids, arachidonic acid, and pathways linked to PPAR signaling. This offers a fresh viewpoint on the use of nuciferine in the management of MCAO. Cerebral edema, cerebral infarction, and neurological function impairment scores are all markedly improved with nuciferine. To investigate variations in serum endogenous metabolism among groups and find indicators

Table 1: Plant-Based Compounds and Phytochemicals (Li *et al.*, 2020).

Plant-Based Compounds and Phytochemicals	
Embryo	Phytochemicals found in *Nelumbo nucifera* embryos
Stamen	Stamen of the *Nelumbo nucifera* Plant Contain Phytochemicals
Flower	The compounds found in *Nelumbo nucifera* flowers
Leaf	The compounds discovered in *Nelumbo nucifera* leaves
Seed	The *Nelumbo nucifera* seed phytochemicals

of nuciferine's influence on ischemic stroke, multivariate data analysis was utilized. The therapeutic effects of nuciferine in stroke treatment were linked to about 19-metabolites and 7 -metabolic pathways, suggesting that nuciferine modulates metabolism to positively influence cerebral ischemia. According to observational research, nuciferine shares receptor properties with antipsychotic medications such as aripiprazole. It inhibits dopamine transporters and functions as an agonist on 5-HT1A and D4 receptors, a partial agonist on D2, D5, and 5-HT6 receptors, and an antagonist on 5-HT2A, 5-HT2C, and 5-HT2B receptors. Nuciferine has demonstrated effectiveness in rodent models of antipsychotic drug action by blocking head twitch responses, blocking the discriminative stimulus effects of 5-HT2 agonists, replacing the discriminative stimulus of clozapine, increasing amphetamine-induced locomotor activity, blocking Phencyclidine (PCP)-induced locomotor activity, and rescuing PCP-induced prepulse inhibition disruption without causing catalepsy. This implies that nuciferine has atypical antipsychotic-like effects, even though its chemical properties are comparable to but distinct from those of a number of licensed antipsychotic medications. Because it hydrolyzes Acetylcholine (ACh) quickly, Acetylcholinesterase (AChE) is essential for stopping neurotransmission at cholinergic synapses. By generating many subtypes of aporphine alkaloids that function as AChE inhibitors, nuciferine has been recognized as a necessary natural AChE inhibitor. Because of this characteristic, nuciferine shows promise in treating Parkinson's disease, myasthenia gravis, Alzheimer's disease, and ataxia.

Antisteroids

Research on the anti-steroidogenic effects of *N. nucifera* seed

Table 2: Scientific classification of *Nelumbo nucifera* Gaertn. (Li *et al.*, 2021).

Botanical Name	*Nelumbo nucifera* Gaertn.
Synonyms	Asian lotus, Indian lotus
Kingdom	Plantae
Division	Angiosperms (Flowering Seed Plants) (Dicotyledon)
Angiosperm	Flowering Plant
Class	Magnoliopsida
Order	Proteales
Family	Nelumbonaceace
Genus	Nelumbo
Species	*Nelumbo nucifera*
Habitat	Slow moving water, Ponds, Lakes, flowering
Ayurvedic name	Padma or Kamala
Hindi name	Lotus, Teratai, Sacred Lotus, East Indian Lotus
Origin	It is currently widely dispersed (wild or cultivated) from northeastern Africa to northeastern Australia, encompassing Southeast Asia, China, and Japan, as well as continental Asia (including India). It has been regarded as a sacred flower in Indian culture and religion for at least 6000 years.

Table 3: Cultivation and Planting Process (Li *et al.*, 2023).

Sl. No.	Cultivation	Planting	Harvest
1.	Deep water up to 2.5 M (8 feet).	Requires anutrient-rich andloamy soil	Lotus bud in advanced stage of bloom
2.	12 inches (30 cm). When winter rolls along	The season of summer has arrived, which in the northern hemisphere lasts from March to May.	Two to three months after planting, Stolon is ready for harvest.
3.	At temperatures higher than 13°C (55 °F), lotus seeds can germinate.	Seeds and buds are the two main methods of propagation.	Collecting just before blossoming
4.	When the sun is directly overhead from April to September	Planting directly into the mud 10-15 cm (3+7⁄8-5+7⁄8 in) below the soil surface requires 4,000 per hectare (1,600/acre) with grid spacing of 1.2 by 2 M (3 ft 11 in × 6 ft 7 in).	Firstleaves and flowers can be harvested three months after planting.
5.	23 to 27°C (73 to 81 °F) Colder season	-	Depending on the season, you can harvest flowers as often as every two days in the summer or every three days in the winter.
6.			The flower harvest typically takes three to four months and is done by hand.

Table 4: Overview of different lotus species and their distinctive attributes (Lin *et al.*, 2019).

Common name	Scientific name	Origin	Characteristics	Habitat
Sacred Lotu	*Nelumbo nucifera*	Asia and Australia	Huge, fragrant blossoms in shades of pink or white; broadly oval leaves	Wetlands, lakes, and ponds
American Lotus	*Nelumbo lutea*	North America	Blossoms of yellow; big, spherical leaves with a unique notch	Lakes and rivers that move slowly
White water lily from Egypt	*Nymphaea lotus*	Egypt	Flowers that bloom at night; white with a golden center	Seas that are neither moving nor very slow
Pygmy Water-lily	*Nymphaea tetragona*	Eurasia	Miniature, spherical leaves; delicate, white or pink blossoms	Cold, still freshwater bodies
Blue Lotus	*Nymphaea caerulea*	Ancient Egypt	Vibrant blue flowers; used in traditional medicine and for ornamental purposes	Freshwater habitats; ornamental ponds

Table 5: Pharmacological and bioactive action of Plant (Baldissera *et al.*, 2017).

Class	Representative Compounds	Occurrence (Part of Plant)	Pharmacological Activity / Function
Alkaloids	Nuciferine, Neferine, Liensinine, Isoliensinine, Roemerine, Armepavine	Leaves, seeds, embryo, and stamens	Sedative, anti-obesity, anti-inflammatory, antioxidant, antidiabetic, antiarrhythmic
Flavonoids	Quercetin, Kaempferol, Isoquercitrin, Myricetin	Leaves, flowers, and seed embryos	Antioxidant, hepatoprotective, anti-aging, anti-cancer
Tannins	Ellagic acid, Gallic acid	Seed coat, rhizome	Antimicrobial, antioxidant, astringent
Phenolic compounds	Ingredients: Vanillic acid, Catechol, Syringic acid, and p-hydroxybenzoic acid	Leaves, rhizome, seeds	Free radical scavenging, anti-inflammatory
Saponins	Nelumboside A, Nelumboside B	Seeds, rhizomes	Immunomodulatory, cholesterol-lowering
Terpenoids	Linalool, β-sitosterol, Lupeol	Flower, rhizome	Anti-inflammatory, antimicrobial
Glycosides	Nelumbinis glycoside, Quercetin-3-glucoside	Leaves, seeds	Antioxidant, hypoglycemic
Sterols	Campesterol, Stigmasterol	Rhizome, seed	Cardioprotective, cholesterol metabolism
Polysaccharides	Lotus seed polysaccharides	Seeds, embryo	Immunostimulant, anti-fatigue
Fatty acids and oils	Linoleic acid, Palmitic acid, Oleic acid	Seeds	Nutritional value, skin health



Figure 1: *Nelumbo nucifera.*

Table 6: *Nelumbo nucifera*: the medicinal plant's many uses (Calugi *et al.*, 2017).

Part of plant	Traditional uses	Active compounds	Anti-inflammatory properties	Antioxidant properties	Other medicinal benefits
Seed	Sedative, astringent, antidiarrheal	Phenols, quinones	Yes	Yes	Resolves sleeplessness and promotes heart health
Rhizome	Digestive health, skin conditions	Polyphenols, alkaloids	Yes	Yes	Skin health, gastrointestinal aid
Leaf	Cooling effect, treatment of sunstroke	Flavonoids, polyphenols, alkaloids	Yes	Yes	Stress relief, anti-anxiety
Flower	Heart tonic, treatment of diarrhea	Flavonoids, glycosides	Yes	Yes	Stress relief, menstrual disorders

Table 7: Pharmacological Activity of *Nelumbo nucifera* (Calugi *et al.*, 2017).

Pharmacological Action	Primary Bioactive	Target/Effect
Antioxidant	Flavonoids, alkaloids	Scavenges ROS, boosts antioxidant enzymes
Anti-inflammatory	Neferine, quercetin	↓ TNF-α, IL-6; inhibits NF-κB
Antidiabetic	Alkaloids, flavonoids	↓ Blood glucose, ↑ insulin sensitivity
Anti-obesity	Leaf extract	↓ Lipogenesis, inhibits lipase
Neuroprotective	Neferine, liensinine	↑ Memory, ↓ AChE, anti-amyloid
Hepatoprotective	Polyphenols	↓ Liver enzymes, oxidative damage
Anticancer	Neferine, flavonoids	Apoptosis, anti-proliferative
Cardioprotective	Flavonoids, alkaloids	↓ Lipids, protects myocardium
Antimicrobial	Phenolics, alkaloids	Bacteriostatic and fungistatic effects
Wound Healing	Polyphenols	Regeneration, antioxidant effect

extract on the testes and ovary of rats. This investigation involved giving sexually immature female rats and mature male rats an oral dose of petroleum ether extract fraction on alternate days for a maximum of fifteen days. According to Evidence-Based Complementary and Alternative Medicine, a significant delay in sexual maturation was noted in prepubertal patients. Male rats showed a decrease in sperm motility and count, whereas female rats showed indications of first estrus and the age of vaginal opening (cornified smear). Furthermore, ascorbic acid and cholesterol were found to accumulate after the extract was administered, and the ovary and testis showed a reduction in the activity of δ-5-3-β-hydroxysteroid dehydrogenase and glucose-6-phosphate dehydrogenase. The goal of this study is to determine whether or not a petroleum ether extract can inhibit steroid production in rat reproductive organs. The three hypotheses put up by Thangkaboworn and Munglue (2014) on the infertility-preventive effects of *N. nucifera* seed extract on male rats are as follows: producing testosterone; (2) reducing the number of gonadotropins released by the pituitary gland; or (3) reducing the number of gonadotropic hormones produced by the pituitary gland (including FSH, LH, and others) (Li *et al.*, 2021; Lee *et al.*, 2006). By administering *N. nucifera* to female rats, proved that estrogen suppression occurred due to the antiestrogenic properties of the plant (Karki *et al.*, 2013).

Antipyretic Activity

Using a rat as an *in vivo* model, both normal body temperature and yeast-induced pyrexia were found to be alleviated by the antipyretic properties of lotus stem ethanol extract, as reported by Sinha *et al.* (2000). A 3-hr. cooling effect at 200 mg/kg and a 6-hr. cooling effect at 400 mg/kg of lotus extract are reported in the literature (Harer, 1985). Lotus extract dramatically reduced central body temperature in this yeast culture over 4hr. at both dosages, and the findings were similar to those of paracetamol, a common fever medication, at 150 mg/kg (Pham-Huy *et al.*, 2008; The Wealth of India, 1948).

Anti-inflammatory Activity

Blocks the production of inflammatory cytokines (such TNF-α and IL-6) as well as COX-2 and iNOS. The process involves changing the signaling pathways of NF-κB and MAPK. Tissue

inflammation, a harmful reaction that damages tissues, can cause serious illnesses such as rheumatoid arthritis, atopic dermatitis, and asthma (Anila, 2003). New evidence suggests that cytokines including IL-4, IL-10, and INF-γ, which are generated by T cells in reaction to antigen activation, impact atopic dermatitis, lung inflammation, and asthma (Badami *et al.*, 2005). The ethanol extract of *Nelumbo nucifera* included a phytochemical (NN-B-4) that significantly decreased the proliferation of PMBCs stimulated by phytohemagglutinin, IL-4, IL-10, INF-γ, and the cdk-4 gene, according to a bioassay-based screening approach. A key mechanism by which NN-B-4 inhibits the activation of PBMCs is by stopping them from progressing through the cell cycle (Beers & Sizer, 1952). Edema in rat paws caused by serotonin and carrageenan were tested to determine the potent anti-inflammatory effects of the triterpenoid betulinic acid, which was isolated from a methanol extract of *Nelumbo nucifera* rhizome. Two doses of 200 and 400 mg/kg p.o. of the anti-inflammatory properties were demonstrated by the methanol extract. Oral dosages of 50 and 100 mg/kg of betulinic acid significantly reduced inflammation in animal models of inflammation. When compared to the powerful anti-inflammatory medications phenylbutazone and dexamethasone, betulinic acid and extract are equally effective (Bhattacharya *et al.*, 2000). A well-known fact is that very reactive molecules called free radicals can destroy cells. DNA, proteins, and cell membranes can be damaged by an overabundance of free radicals. Free radicals damage cells and are associated with the development of certain diseases like cancer; they are an essential part of oxidative stress in humans and other animals.

Anti-obesity and Hypolipidemic Effects

Levels of bad cholesterol (LDL), triglycerides, and serum cholesterol can be reduced by slowing the development of body fat and weight. inhibits pancreatic lipase activity The active components consist of extracts from seeds and leaves. By inducing lipolysis in the adipose tissue of mice, Ohkoshi *et al.* (2007) demonstrated that active components derived from *Nelumbo nucifera leaves* were efficacious. The acquired component showed anti-obesity activity via the beta-adrenergic receptor pathway. In A/J mice given a high-fat diet, *Nelumbo nucifera* significantly reduced body weight. Several flavonoids were isolated from NN by using fractionation and chromatography. Flavonoids such as isoquercitrin, hyperoxide, catechin, and astragalin have demonstrated lipolytic activity in visceral adipose tissue (Bhattacharya *et al.*, 2001). In their study on diabetic rats and mice, Ono *et al.* (2006) detailed the possible pharmacological mechanism of an *N. nucifera* (NNE) leaf extract. Levels of β-amylase, lipase activity, lipid metabolism, and UCP3 mRNA expression in C2C12 myotubes were reduced in a concentration-dependent manner in mice that were administered the extract for five weeks. The NNE showed inhibitory activity against lipase and β-amylase *in vitro* as well. The results demonstrated that NNE had a higher lipase inhibitory activity (IC_{50}, 0.46 mg/mL) than β-amylase (IC_{50}, 0.82 mg/mL). Both the amount of weight gained and the amount of fat in the abdominal region were significantly reduced by the extract. Furthermore, the extract reduces liver triacylglycerol level and suppresses UCP3 mRNA expression in skeletal muscle, both of which are caused by a high-fat diet in rats (Baliyan *et al.*, 2022). Velusami *et al.* (2013) also investigated the efficacy of methyl alcohol and sequential water extracts of *N. nucifera* petals in alleviating ant obesity. Adipogenesis, adipolysis, lipase, serotonin (5-HT2C), Cannabinoids (CNR2), Melanocyte Concentrating Hormone (MCHR1), and Melanocortin (MC4R) receptors were among the factors the researchers investigated. An increase in lipolysis and a decrease in adipocyte lipid storage was seen in response to methyl alcohol and later water extracts of *N. nucifera* petals. The methyl alcohol extract from *N. nucifera* petals also showed that it could decrease lipase activity, with an IC_{50} value of 47 µg/mL, which was dose-dependent. Furthermore, the 5-HT2C and CNR2 receptors are both activated by *N. nucifera* flower extracts (Ling *et al.*, 2005). Also unaffected are the MCHR1 and MC4R receptors. Results showed that compared to the following water extract, the methyl alcohol extract of *N. nucifera* petals showed more promise in regulating obesity (Nabih *et al.*, 1968).

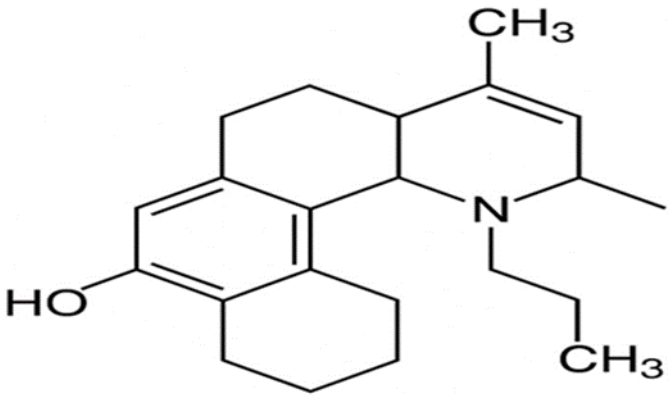
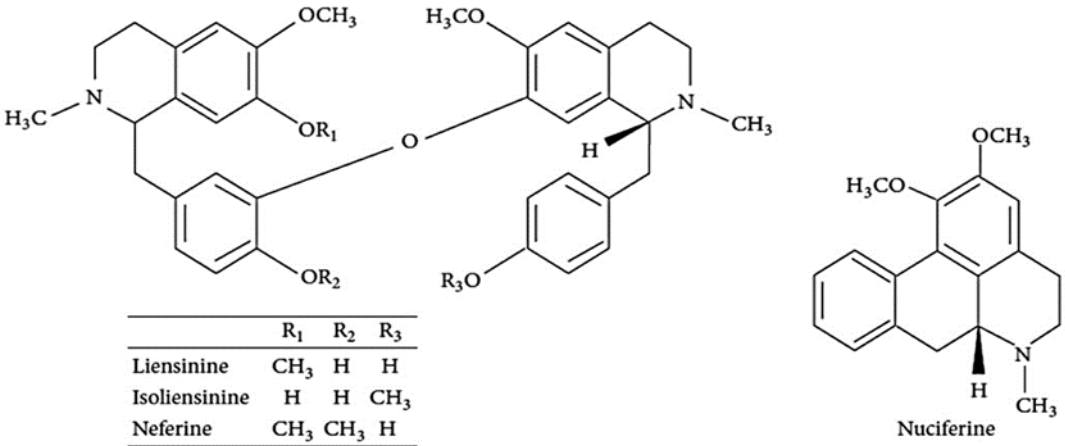


Figure 2: The chemical structure of *nuciferine*.



	R_1	R_2	R_3
Liensinine	CH_3	H	H
Isoliensinine	H	H	CH_3
Neferine	CH_3	CH_3	H

Figure 3: Key chemical components of the embryo of the *Nelumbo nucifera*.

Antidiabetic Activity

Improves glucose tolerance, inhibits the enzymes α-glucosidase and α-amylase, and raises insulin sensitivity and secretion (Glick, 1988).

Mechanism: AMPK pathway activation

Researchers looked studied the effects of a glucose-fed ethanolic extract of the rhizomes of *N. nucifera* on rats that had diabetes caused by streptozotocin. Improved glucose tolerance was seen in the extract. The extract was also found to enhance the effects of exogenous insulin. The antidiabetic effects of the extract were compared to those of tolbutamide in both healthy and sick rats (Marcocci *et al*., 1994). An example of this impact is the attenuation of glucose absorption in the intestines, which occurs when plant fiber is administered orally with glucose (Parola *et al*., 1992). One possible culprit in the development of diabetes and its complications is aldose reductase, an enzyme essential to the polyol pathway (Raji and Bolarinwa, 1997). A methanolic extract of *Nelumbo nucifera* stamens was found to inhibit rat lens aldose reductase. One of the thirteen flavonoids found in the extract was kaempferol, which has a carbon ring containing 3-O-alpha-1-rhamnopyranosyl-1(1→6)-beta-d-glucopyranoside groups. Isorhamnetin 3-O-alpha-1-rhamnopyranosyl-1(1→6)-beta-d-glucopyranoside and beta-d-glucopyranoside inhibit rat lens aldose reductase the most *in vitro* (Ross, 2001).

Hepatoprotective Effects

Shields liver cells from harmful substances such as Carbon tetrachloride (CCl_4). *Nelumbo nucifera*'s hepatoprotective activity was reported by Sohn *et al.* in 2003. In order to determine whether the ethanol Extract from *Nelumbo nucifera* (ENN) seeds protected primary cultured rat hepatocytes from CCl_4-induced cytotoxicity, the Aspartate Transaminase (AST) cellular leakage and cell survival rate were utilized (Misra and Fridovich, 1972). There was a dose-dependent reduction in AST cellular leakage and CCl_4-induced cell death at ENN doses ranging from 10 to 500 μg/mL. Also tested was ENN's capacity to ward off the hepatotoxin Aflatoxin B1 (AFB1). At 250 and 500 μg/mL, ENN produced a significant hepatoprotective effect of 74.5% and 94.6%, respectively, in comparison to the AFB1 controls (48.9%) (Prabhakaran *et al*., 2016). *Nelumbo nucifera* Butanol Extract (NNBE) against hepatocellular injury in cultured hepatocytes produced by H_2O_2. The hepatoprotective effects of NNBE were associated with the overexpression of many enzymes, such as HO-1 (2.4 times), CAT (0.42%), and SOD-1 (0.62%). Similarly, nuclear factor erythroid 2-related factor 2 (Nrf2) accumulation in the nucleus increased 8.1-fold after NNBE pretreatment, suggesting that Nrf2 is responsible for the increased expression of SOD-1, CAT, and HO-1 (Ke *et al*., 2018). In a separate study, Yuan *et al*. evaluated the hepatoprotective effect of ethyl acetate (NUEA) and n-butanol (NUBU) extracts from *N. nucifera* leaves against acute liver injury in mice that was produced by CCl_4. The levels of aspartate and alanine aminotransferases (AST and ALT, respectively) decreased significantly across all treatment groups except for the NUEA group (Roessner *et al*., 2008). There was also a significant decrease in Malondialdehyde (MDA) and Superoxide Dismutase (SOD) levels in the livers of all groups (Onodera *et al*., 2015). Similarly, in an *in vivo* model of experimental alcoholic steatohepatitis, Tang *et al*. assessed the mechanisms of *Nelumbo nucifera* Leaf Extract's (NLE) hepatoprotective activity. By modifying the levels of Triglycerides (TG) and Cholesterol (TC) in both plasma and hepatic content analysis, the results demonstrated the inhibitory effect of NLE on lipid accumulation (Bishayee *et al*., 2022). Additionally, NLE increased the levels of the receptors PPAR-α and p-AMPK/AMPK, which are responsible for the oxidation of fatty acids and their transport via Microsomal Triglyceride transfer Protein (MTP) and Carnitine Palmitoyltransferase-1 (CPT1), respectively (Mukherjee *et al*., 2009). These results demonstrate the several ways in which the NLE can avoid alcoholic steatohepatitis (Rusu *et al*., 2018). lowers serum levels of liver enzymes (ALT, AST),

reduces the liver tissue's lipid peroxidation (Scientific Basis for Ayurvedic Therapies, 2004).

Anticancer Activity

Stops the cell cycle from continuing and kills cancer cells while preventing their growth in certain types of cancer (such as colon, liver, and breast). Reduces the process of blood vessel formation. Mechanisms: Regulation of Bcl-2 family proteins and activation of caspases. A number of *N. nucifera* component extracts and isolated chemicals demonstrate anticancer activity in both laboratory and animal models (Durairaj and Dorai, 2010). The most powerful lethal impact of the three main alkaloids is exhibited by isoliensinine, which mainly causes triple-negative breast cancer cells to undergo apoptosis by activating p38 MAPK/JNK and producing ROS (Wu *et al*., 2010). When nicotine was present, *N. nucifera* significantly reduced the growth of Non-Small-Cell Lung Cancer (NSCLC) cells, decreased Wnt/β-catenin signaling activity, increased Axin stabilization, and triggered death. The levels of β-catenin and its downstream targets, such as c-myc, cyclin D, and Vascular Endothelial Growth Factor (VEGF), were reduced by *N. nucifera*. The proapoptotic impact of nuciferine may be explained by the fact that *N. nucifera* also reduced the ratio of B-cell lymphoma 2/Bcl-2-associated X protein (Bcl-2/Bax) (Rai *et al*., 2006). 7-Hydroxydehydronuciferine was one of 15 chemicals that were extracted from *Nelumbo nucifer*a leaves, and it dramatically reduced the growth of gastric, prostate, and melanoma cancer cells (Sohn *et al*., 2003). Cao *et al.* investigated the reversal impact of neferine on the human gastric cancer cell line (SGC7901), which is resistant to multiple drugs. Neferine and VCR were administered either in combination or separately to SGC7901 and its Vincristine-Resistant (VCR) variant. Neferine reverses the multidrug resistance of SGC7901/VCR cells in human gastric cancer by reducing the production of permeability glycoprotein (P-gp) and Multidrug Resistance-associated Protein (MRP) in SGC7901/VCR cells. In a separate study, it was suggested that neferine could promote cell death in A549 lung cancer cells. Nuclear factor kappa and B-cell lymphoma 2 (Bcl-2) are downregulated, Bcl-2-associated X protein (Bax) and Bcl-2-AssociatedDeath promoter (BAD) are upregulated, cytochrome C is released, the caspase cascade is activated, and DNA is fragmented as a result of neferine treatment. In addition, neferine caused G1 cell cycle arrest by downregulating cyclin D1, inducing p53, and its effector protein p21 (Qamar *et al*., 2022). One such way nuciferine stopped human osteosarcoma cells from growing was by causing them to get stuck in the G1 phase of the cell cycle (Ruan *et al*., 2008). While p53 and RB (retinoblastoma-associated protein) were determined not to be required for the induction of G1 arrest, p21 (WAF1/CIP1). P21 overexpression occurred as a result of neferine's effect on the p21 protein's half-life. According to studies that examined four kinases that are believed to affect the stability of p21, it was found that neferine increased p38 MAPK and JNK (Subashini and Sumathi, 2012; Valko *et al*., 2007). They showed that the p38 inhibitor (SB203580) could reduce p21 overexpression in response to neferine, but not the JNK inhibitor (SP600125) (Ho *et al*., 2010). Neferine enhanced p21 phosphorylation at Ser130, which was reliant on p38. These findings demonstrated neferine's direct antitumor effect, indicating that it has potential as a cancer preventive and cancer treatment (Wijeratne *et al*., 2005).

Cardioprotective Effects

Reduces blood pressure. Improves lipid profile. Protects cardiac tissue from ischemia damage. Active compounds: Flavonoids and alkaloids. Antiarrhythmia. Phytochemicals, dauricine, and neferine, derived from *N. nucifera* seeds have pharmacological effects on the heart (Ott *et al*., 2007). *N. nucifera* phytochemicals inhibited the cardiac transmembrane currents of Ca^{2+} and Na^{+}/K^{+}. Neferine, a notable chemical, has antiarrhythmic effects and dramatically reduces platelet aggregation in rabbits (Chang *et al*., 2013). Antiarrhythmic effects are attributed to the primary alkaloid derived from *N. nucifera*, neferine. A few *in vivo* experiments have shown this (Xu *et al*., 2021). An investigation was conducted on the electrical and mechanical activities of neferine in the guinea pig's atrium and pedal smooth muscles. At a concentration of 0.1 mmol/L, the effect of neferine was to reduce the contractile force, reduce the amplitude and *X*max of the Action Potential (AP), and lengthen the duration of the Action Potential at 50% (APD50), 90% (APD90), and the Effective Refractory Period (ERP). Furthermore, neferine (30 µmol/L) partially mitigated the impact of acetylcholine (10 µmol/L) (Yang *et al*., 2024). Thirty micromoles per liter of neferine reduced the adrenaline-inducing effect in atrial autonomic neurons of guinea pigs. The dose-effect

Table 8: Antioxidant activity of plant (Ganga *et al*., 2012).

Sacred Lotus Parts	DPPH Radical Scavenging Assay (µmol TE/100g DW)	FRAP Assay µmol TEG/g DW)	ORAC Assay (µmol TE/g DW)
Seed embryo	0.71±0.04c	81.81±1.53c	292.81±7.33d
Flower stalk	0.63±0.04d	22.98±0.39e	214.60±19.31e
Stamen	1.06±0.01b	281.46±4.12a	561.98±16.44b
Old leaf	1.21±0.00a	231.08±1.70b	1001.12±58.33a
Petal	0.86±0.06c	71.65±2.71d	370.49±16.82c
Leaf stalk	0.43±0.01e	15.39±0.38f	119.94±3.26f

Table 9: Roles of Bioactive in different disease (Deng *et al.*, 2022).

Pharmacological Action	Primary Bioactive	Target/Effect
Antioxidant	Flavonoids, alkaloids	Scavenges ROS, boosts antioxidantenzymes
Anti-inflammatory	Neferine, quercetin	↓ TNF-α, IL-6; inhibits NF-κB
Antidiabetic	Alkaloids, flavonoids	↓ Blood glucose, ↑ insulin sensitivity
Anti-obesity	Leaf extract	↓ Lipogenesis, inhibits lipase
Neuroprotective	Neferine, liensinine	↑ Memory, ↓ AChE, anti-amyloid
Hepatoprotective	Polyphenols	↓ Liver enzymes, oxidative damage
Anticancer	Neferine, flavonoids	Apoptosis, anti-proliferative
Cardioprotective	Flavonoids, alkaloids	↓ Lipids, protects myocardium
Antimicrobial	Phenolics, alkaloids	Bacteriostatic and fungistatic effects
Wound Healing	Polyphenols	Regeneration, antioxidant effect

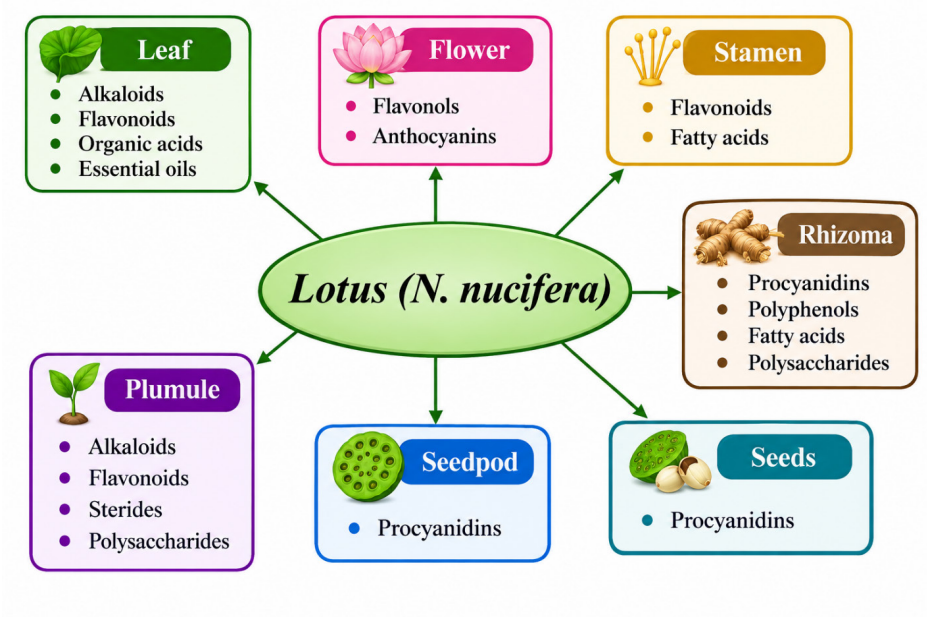


Figure 4: The main constituents in each tissue of lotus (*N. nucifera*).

relationship of isoprenaline was suppressed and altered by neferine at a dosage of 30 μmol/L, just like propranolol. In addition, we looked at how neferine affected the left atrial Ca^{2+} dosage response curve in guinea pigs. The dualistic activity of neferine demonstrated the antagonism of Ca^{2+}, similar to verapamil (Ren *et al.*, 2024). Using Planned Electrical Stimulation (PES) in an open chest setting, the electrophysiological effects of neferine (8 mg/kg, i.v.) on ischemic ventricular tachyarrhythmias were studied in normal and ischemic myocardium five to eight days after an acute myocardial infarction. Neferine was helpful in preventing ventricular tachycardias and abrupt cardiac mortality following myocardial ischemia-induced damage (Huang *et al.*, 2025; Paudel and Panth, 2015).

Antimicrobial Activity

Kills germs and fungi (including *S. aureus* and *E. coli*). Polyphenolic compounds likely damage microbial membranes, leading to this impact (Intui *et al.*, 2023).

Wound Healing and Skin Benefits

The antimicrobial and antioxidant characteristics aid in the healing process and promote tissue regeneration (Mohan *et al.*, 2020).

Charting the future of lotus

The future of climate resistance, medical potential, and socioeconomic effect is being shaped by *Nelumbo nucifera*. Research into the plant's reactions to climate variability has shown important adaptation systems that are vital in a changing environment, shedding light on the plant's survival tactics (Bhat *et al.*, 2023). Investigations on the potential health benefits of *Nelumbo nucifera* are also progressing, bridging traditional uses with contemporary pharmacological advancements. This exploration not only enhances our understanding of its therapeutic capabilities but also opens new avenues for medical applications (Qing *et al.*, 2023). In tandem, the commercial and artistic roles of *Nelumbo nucifera* continue to grow, showcasing

its varied contributions on an international level. All of these things show how useful the plant is and how many other areas it could be used in the future. The dynamic nature of *Nelumbo nucifera*, with its many uses in ecology, medicine, and economics, guarantees that it will remain an important plant species for the foreseeable future (Xiang *et al.*, 2024).

CONCLUSION

The capacity of ethnomedicinal plants to affect multiple disease-related pathways is the basis of their promise as a cure for Alzheimer's Disease (AD). A variety of bioactive chemicals found in these plants have the potential to address important disease targets, including oxidative stress, metal dysregulation, inflammation, cholinergic deficiency, amyloid-beta aggregation, and tau protein hyperphosphorylation. While certain plant extracts have anti-amyloidogenic characteristics that prevent amyloid plaques from forming or aggregating, others have the ability to alter tau phosphorylation, an essential step in the creation of neurofibrillary tangles. The metal-chelating agents and antioxidant chemicals present in ethnomedicines can help reduce oxidative stress and the imbalance of metals that causes AD pathogenesis. To alleviate the neuroinflammation common to Alzheimer's disease, anti-inflammatory drugs can be used, and substances that boost cholinergic transmission can be used to treat the neurotransmitter deficiencies linked to cognitive loss. Because AD is so complicated, however, it is still difficult to turn these basic discoveries into effective treatments (Wang *et al.*, 2024). Ensuring patient safety and efficacy and embracing a comprehensive approach to managing this severe condition requires future research to further explore these pathways and evaluate the therapeutic potential of ethnomedicinal plants through clinical studies. Neurodegenerative disease medication discovery has become a very risky, expensive, and ineffectual process, which has created a lot of problems for the pharmaceutical business (Gul *et al.*, 2025). Consequently, research into non-conventional medication sources, especially those derived from herbs, is gaining momentum. There is a pressing demand for medication alternatives that have few or no negative side effects because synthetic medications are frequently linked to unwanted side effects. Multiple research projects have shown that medicinal herbs may be effective in treating Alzheimer's disease. Patients with memory loss or Alzheimer's can see a marked improvement in their quality of life when medicinal herbs are integrated into their treatment plans. Additional research is necessary to completely comprehend the processes by which these plants alleviate the illness; however, they do show potential. The function and underlying processes of several medicinal herbs in the management of Alzheimer's disease should be explored in future large-scale clinical trials.

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ABBREVIATIONS

AD: Alzheimer's Disease; **AChE:** Acetylcholinesterase; **ALT/AST:** Alanine aminotransferase/Aspartate transaminase; **Bcl-2:** B-cell lymphoma 2; **DPPH:** 1,1-diphenyl-2 picrylhydrazyl; **NLE:** *Nelumbo nucifera* leaves; **ROS:** Reactive Oxygen Species; **TCM:** Traditional Chinese Medicine.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS CONTRIBUTIONS

MK and NSG conceived the review idea. AD and MK analysed the data and drafted the manuscript. NSG provided valuable insights during the manuscript writing process. MK, AD and NSG revised the manuscript. All authors read and approved the final manuscript.

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