



REVIEW ARTICLE

Nelumbo nucifera Gaertn.: A comprehensive review of its pharmacological potency, ethnomedicinal applications and bioactive compounds

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Abstract

Nelumbo nucifera Gaertn., also called “Padma or Kamala” in Hindi, is a species of attractive, edible, aquatic plant, recognised for its ecological and medicinal value. The following review integrates the details of pharmacological properties, ethnomedicinal uses and bioactivity compounds of *N. nucifera*, in view of the therapeutic potential. A thorough review of the literature based on different scientific databases, such as PubMed, Scopus and Science Direct, was carried out, which included the studies that were published since 2000 and up to 2025. The essential pharmacological processes were detected via a systematic review. *Nelumbo nucifera* has a large spectrum of bioactive components, such as tannins, alkaloids and flavonoids, which have antiviral, anti-inflammatory and antioxidant properties. Traditionally *N. nucifera* has been used in the treatment of digestive disorders, respiratory disorders and infertility. Modern studies endorse its effectiveness in diabetes mellitus, cardiovascular diseases and neurodegenerative diseases. *Nelumbo nucifera* has potential use as a useful therapeutic agent in traditional and modern medicine. Therefore, it is necessary to conduct further, mechanistic research to clarify the active compounds and their synergistic interactions so that novel uses can be developed in clinical practice.

Keywords: antioxidant activity; anti-inflammatory effects; ethnobotany; hypoglycemic effects; *Nelumbo nucifera*; neuroprotection; traditional medicine

Introduction

Plants have a wonderful capacity to biosynthesise a broad spectrum includes primary as well as secondary metabolites, the latter of which are significant organic substances with significant medicinal potential (1). Plant-derived products have various positive bioactive properties and medicinal effects, which make them generally safe to consumed. A survey provided by the Food and Agriculture Organisation states that about 25 % of the synthetic drugs were made using medicinal plants and about 70–80 % of the world population uses herbal medicines to prevent and treat illnesses, especially in developing nations (2). The International Union for Conservation of Nature and the World Wildlife Fund estimate 50000 to 80000 species of flowering plants used medicinally in the world, with India, China, Sri Lanka and Thailand accounting for the largest portions of the nation's contribution (20 %, 18.9 %, 16.6 % and 15.5 %, respectively). In the United States, the percentage is 11.8 and more or less three-quarters of commonly prescribed drugs in the U.S. are plant-based (3).

The sacred lotus (*Nelumbo nucifera* Gaertn.) has morphological and physiological peculiarities of adaptation to wet conditions, including a rhizomatous form of growth, peltate leaves and smelly flowers. The plant can control the temperature of its flowers, as the homeothermic organisms do and has a unique air

circulation system in its leaf and stem system, which underscores its evolutionary uniqueness (4). The several parts of the plant can be consumed, which include leaves, roots, seeds and rhizomes as a source of delicious meals with nutritional value. Here, the major attention will be on the seeds and rhizomes, which comprise high amounts of dietary fibre, vitamins, minerals and essential amino acids, increasing the nutritional value of lotus as a functional food (5).

Nutritionally, the lotus plant's leaves, roots, seeds and rhizomes are consumed not just for their palatable taste but also for their health benefits. The focus here is primarily on the seeds and rhizomes, which are high in dietary fiber, vitamins, minerals and essential amino acids, enhancing the nutritional profile of lotus as a functional food (6).

Nelumbo nucifera has abundant leaves, seeds, flowers and rhizomes that contain alkaloids, flavonoids, polyphenols and terpenoids that exhibit strong antibacterial, anti-inflammatory and antioxidant properties. This in turn has made the plant a popular topic of research in phytochemistry and pharmacology (7). Consequently, the plant has garnered extensive research interest in phytochemistry and pharmacology (8). *Nelumbo nucifera* has a traditional history of use in the treatment of ulcers, as well as fever, cholera and diarrhea, among others. The biological activity of *N. nucifera* has been gradually studied in the last 20 years, with studies

investigating therapeutic use of hydroalcoholic extract of its seeds (9). and epicarp studies have demonstrated its efficacy in anti-diabetic (10), anti-inflammatory (11), sleep improvement (12), muscle wasting (13) and UV protection (14). Different biologically active components have been determined in diverse parts of the lotus plant, such as procyanidins in seed pods, anthocyanins and flavanols in flowers, fatty acids and flavonoids in stamens and organic acids, flavonoids, essential oils and alkaloids in leaves (15).

Materials and Methods

Article eligibility criteria

The search strategy involved the use of a combination of terms, such as *N. nucifera*, phytochemistry, ethnobotanical applications and pharmacology. The appropriate literature was searched in different scientific databases, which includes Google Scholar, Medline, PubMed and Scopus. Articles published in the English language between the years 2000 and 2025 were filtered to limit the review. Abstracts and titles of the articles retrieved were filtered in terms of their relevance to the focus of the study.

Software and technique used

Various databases such as Webbook, ChemSpider and PubMed were used in this study to determine the chemical structure of the phytoconstituents found in *N. nucifera*. The identified structures have been represented visually with the use of ChemDraw (version 12.0.2). Besides, the VOSviewer program (version 1.6.18) was utilised to draw a map of the world that participates in *N. nucifera* research.

Worldwide research and collaborations on *Nelumbo nucifera*

The information about the world research on *N. nucifera* was obtained using Scopus, which led to a list of studies that demonstrates the number of projects and publications of different nations over the past three years (2018–2025). The results indicate that since 2014, more than 10 research papers have been published annually. China had the highest number of publications (351), followed by India (104), Thailand (65), South Korea (64), Japan (38),

the United States (31), Pakistan (29), and Taiwan (27), as shown in Fig. 1.

Collaborative research involving scientists from countries such as China, India, Thailand, South Korea, Japan, Taiwan, Pakistan, Vietnam, Germany, the United Kingdom and Canada are evident from the marked circles on the map in Fig. 2. The analysis reveals a substantial increase in publications over the last 5 years, underscoring the growing global interest in the medicinal significance of this plant.

Morphology of *Nelumbo nucifera*

There are various species in the family Nymphaeaceae and one of them is *N. nucifera* which is member of genus *Nelumbo* and order Proteales. The plant, also called the Indian lotus, water lily, or Chinese lily (16), is a recurrent water plant, has large leaves, a nodal root system, a fleshy yellow rhizome and single, fragrant and white and reddish-pink flowers. The flowers are hermaphroditic with a lovely smell. The plant gives birth to one seed that is contained in the rigid and brownish pericarp of its aggregate fruit and the seeds are released by bending them towards the water. The roots have a foundation in the pond or riverbed and the leaves are on the surface of the water, as shown in Fig. 3. The long petioles contain small hairy areas and have prickles, which ensure buoyancy in water environments, as the tuber has air holes along its length (17).

Geographical distribution

Commonly known as the holy lotus, *N. nucifera* has a wide range of distribution that includes China, India, Sri Lanka, Iran, Australia and Japan. Lotus is found in wet places such as river floods and stagnant rivers. Its seeds and leaves are widely eaten in Southeast Asia (18). The plant species *N. nucifera* is common in tropical and subtropical regions of Asia, including China, Thailand, Nepal, India and many other Asian countries (19). Some European Union countries too have been introduced to the species and these include Romania and Hungary (Fig. 4).

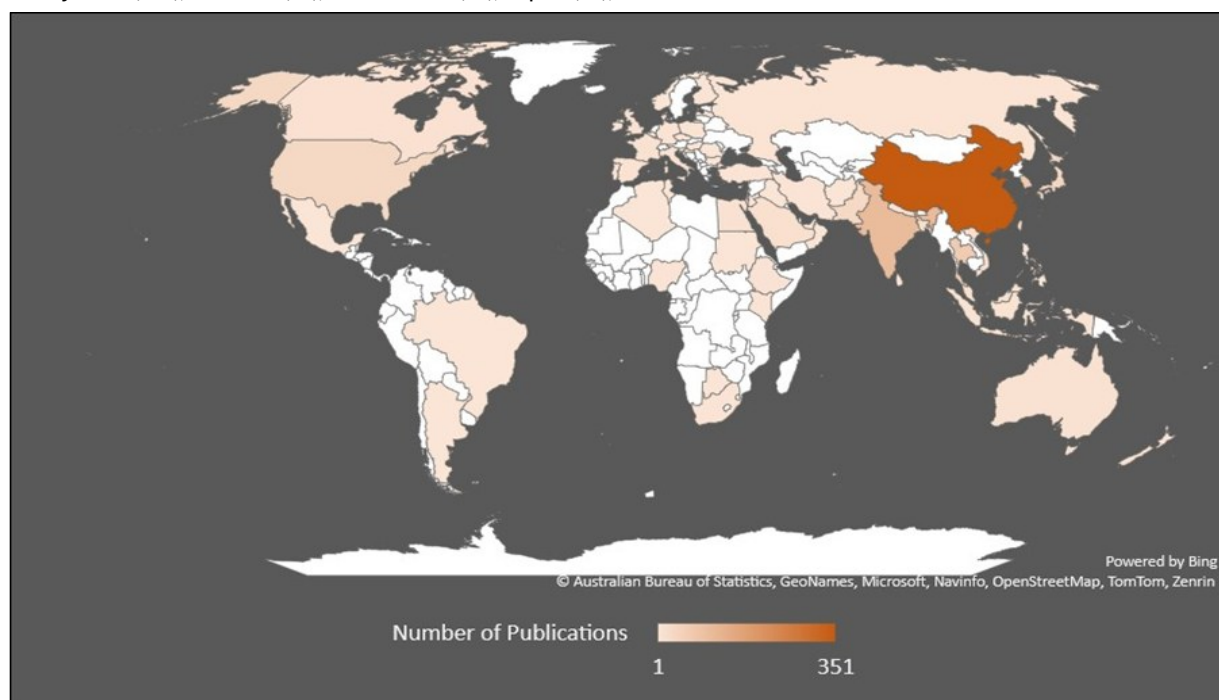


Fig. 1. Spatial distribution map highlighting research papers published worldwide on *Nelumbo nucifera*. A spatial technique was used to generate a map from microsoft excel and open source web platform [Source: Created using Bing Maps (Microsoft)].

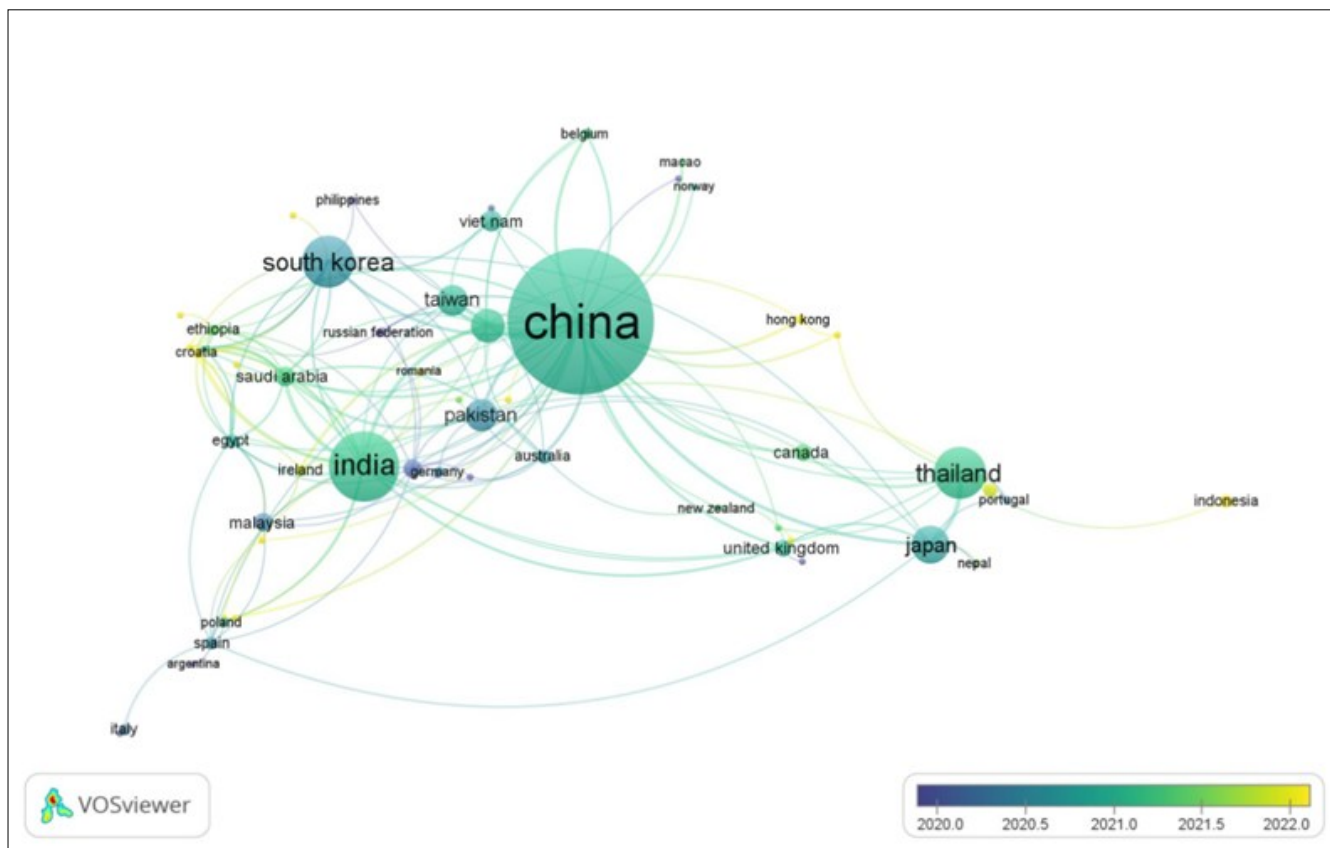


Fig. 2. Network visualisation of collaborative studies conducted worldwide for *Nelumbo nucifera* using VOSviewer (version 1.6.18).



Fig. 3. Representation of the morphology of *Nelumbo nucifera*. A: leaf; B: flower; C: seeds; D: rhizomes.

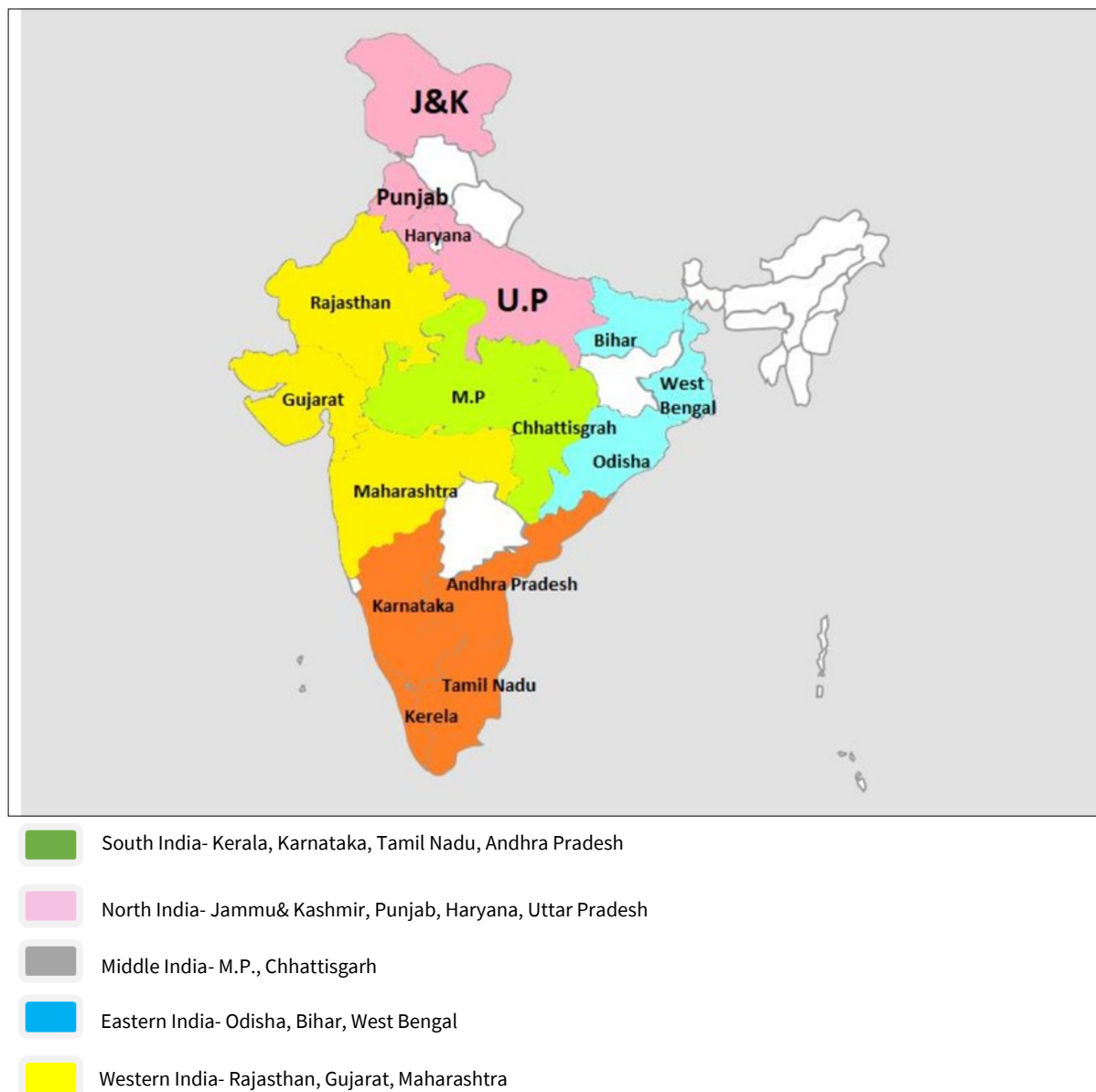


Fig. 4. *Nelumbo nucifera* location in India using map chart (<https://www.mapchart.net/>).

Phytochemistry of *Nelumbo nucifera*

Nelumbo nucifera extracts contain a diverse range of secondary metabolites, comprising phenols, flavonoids, terpenoids, sterols, cardiac glycosides, tannins, coumarins, alkaloids and quinones, as summarised in Table 1. Primary metabolites, such as carbohydrates, proteins and lipids, are also present in these extracts (46, 47).

Nelumbo nucifera contains polyphenols, which show antioxidant properties and have a positive effect on many health dimensions (48), as depicted in Fig. 5. In China, lotus seeds are generally sold in their dried form, typically with the shell intact. These seeds are rich in alkaloids, particularly neferine, which has been quantified at approximately 0.16 mg/g in lotus seed extract using HPLC analysis (49), as well as other phytochemicals that are found in various parts of plants. The embryos are rich in nuciferine, pronuciferine, lotusine, rutin, hyperin and demethylcoclaurine. Stamen contains a large amount of different chemicals such as linalool, luteolin-glucoside, dehydmonaine, anonaine, arnepavine, kaempferol-3-O-D-glucuronide, asimiloin, demethylcoclaurine and lirinidine. It is known that the flower contains quercetin, luteolin, luteolin-glucoside, kaempferol, kaempferol-3-O-glucoside and isoquercitrin (50). In addition to these constituents, the seeds also

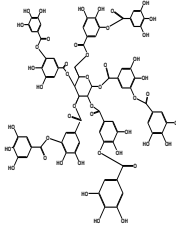
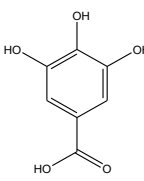
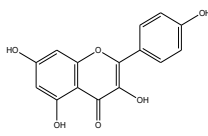
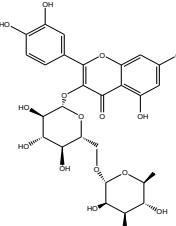
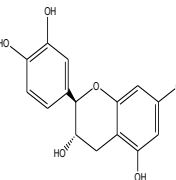
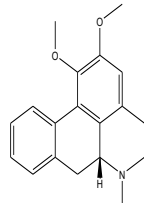
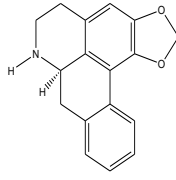
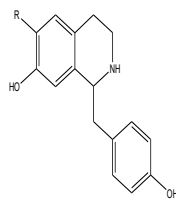
contain gluconic acid, malic acid, acetic acid, succinic acid, dauricine, nuciferine, roemerine, lotusine, N-normuciferine and the leaves contain roemerine and nor-nuciferine (51).

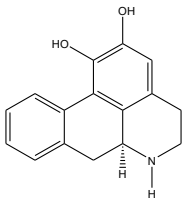
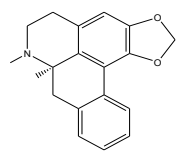
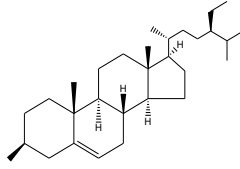
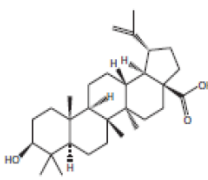
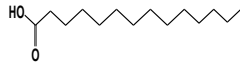
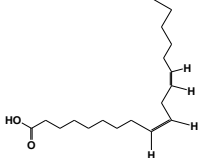
Nutritional profile of *Nelumbo nucifera*

All of the bioactive compounds in the nutritional profile of *N. nucifera* comprise carbohydrates, vitamins, minerals and other bioactive compounds that promote cardiovascular health, weight management and anti-aging effects because of antioxidant properties. This presents the importance of the lotus plant and its seeds and flowers not only as a source of nutritious meals but also as an asset in medicine in most cultures.

Lotus seeds contain 61–62 % carbohydrates, 16–21 % protein, 2.4–3 % crude fat and 5–9 % humidity (fresh weight basis) (52). They also contain vital minerals like magnesium, potassium and phosphorus. Lotus seeds have health benefits due to nitrogenous compounds such as alkaloids and flavonoids whose properties make them anti-inflammatory (53). Lotus rhizomes contain a lot of fiber, which facilitates digestion and health of the gut, besides being low in fat and cholesterol, hence a healthy choice of food. Also, these rhizomes contain vitamin C, potassium and other important nutrients (54).

Table 1. Phytoconstituents of *Nelumbo nucifera* and their therapeutic effects

Compounds	Common name	IUPAC	Molecular weight	Parts of plant	Structure	Previously Documented bioactivities	References
Phenols	Tannic acid	[2,3-dihydroxy-5-[[[(2R,3R,4S,5R,6S)-3,4,5,6-tetrakis[[3,4-dihydroxy-5-(3,4,5-trihydroxybenzoyl)oxybenzoyl]oxy]oxan-2-yl]methoxycarbonyl]phenyl]3,4,5-trihydroxybenzoate	1701.2	Stamen and petals		Aldose-Reductase-Inhibitor, Allergenic, Antibacterial, Anticariogenic, Anticolic, Anticolic	(15, 20, 21)
	Gallic acid	3,4,5-trihydroxybenzoic acid	170.12	Fruit and seed		Analgesic, Antibacterial, Antiflu, AntiHIV, Anti-inflammatory, Antioxidant, Antitumor, Antiviral, Hepatoprotective	(22–25)
“Flavonoids”	Kaempferol	3,5,7-trihydroxy-2-(4-hydroxyphenyl)chromen-4-one	286.24	Flowers And rhizomes		Anticancer, Antibacterial, Antifertility, Anti-inflammatory, Antioxidant	(26–28)
	Rutin	2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-[[[(2R,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxymethyl]oxan-2-yl]oxychromen-4-one	610.5	Leaf		Antiaaggregant, Antibacterial, Anticancer, Antidementia, Antidiabetic, Antierhythmic, AntitumorAntiviral, Cytoprotective, PAF-Inhibitor	(29–33)
	catechin	“(2R,3S)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-2H-chromene-3,5,7-triol”	290.276	Leaf		Anti-HIV, Antioxidant, Hepatoprotective, Neuroprotective	(34, 35)
	Nuciferine	“(6aR)-1,2-dimethoxy-6-methyl-5,6,6a,7-tetrahydro-4H-dibenzo[de,g]quinolone”	295.4	Fruit and seed		Antispasmodic Hepatoprotective, Immunomodulatory	(33, 34, 36)
“Alkaloids”	“Anonaine”	“(12R)-3,5-dioxo-11-azapentacyclo[10.7.1.0.2,6.0.8,20.0.14,19]icosa-1(20),2(6),7,14,16,18-hexaene”	265.31	Fruit and seed		Antibacterial, Antiseptic, Fungicide, Hypotensive, Insecticide, Pesticide	(37)
	“coclaurine”	“(1S)-1-[(4-hydroxyphenyl)methyl]-6-methoxy-1,2,3,4-tetrahydroisoquinolin-7-ol	285.34	Fruit and seed		Antiaaggregant, Antioxidant, Cytotoxic, Depressant, Hypothermic	(36)

"Asimilobine"	(6aR)-1-methoxy-5,6,6a,7-tetrahydro-4H-dibenzo[de,g]quinolin-2-ol	267.32	Fruit and seed		Anti-malarial, Antimutagenic, Antihistaminic, antioxidant, Antiperoxidant	(38, 39)
"Roemerine"	(12R)-11-methyl-3,5-dioxo-11-azapentacyclo[10.7.1.0 ^{2,6} .0 ^{8,20} .1 ^{4,19}]icosa-1(20),2(6),7,14,16,18-hexaene	279.3	Fruit and seed		Antidiarrheal, Haemorrhoids, Antibesity, Hypcholesterolaemia activity	(27, 40)
"Steroids"	β -Sitosterol	414.7	Flowers And rhizomes		Immunomodulatory, antimicrobial and anti-inflammatory, cancer-preventive, anti-fertility, antinociceptive	(39, 41)
"Terpenoids"	Betulinic acid	456.7	Flowers And rhizomes		Antibacterial, Anticancer, Antiedemic, AntiHIV, Anti-inflammatory, Antimalarial, Antiplasmodial	(42, 43)
Fatty acid	Palmitic acid	256.42	Rhizomes		Hemolytic, Antiallopecic, 5-Alpha-Reductase-Inhibitor, Antioxidant	(41, 44)
	Linoleic acid	280.4	Rhizomes		Alopecia, Anti-Acne, Antiandrogenic and antianaphylactic, Antiarthritic and Antihistaminic, Anti-inflammatory,	(43-45)

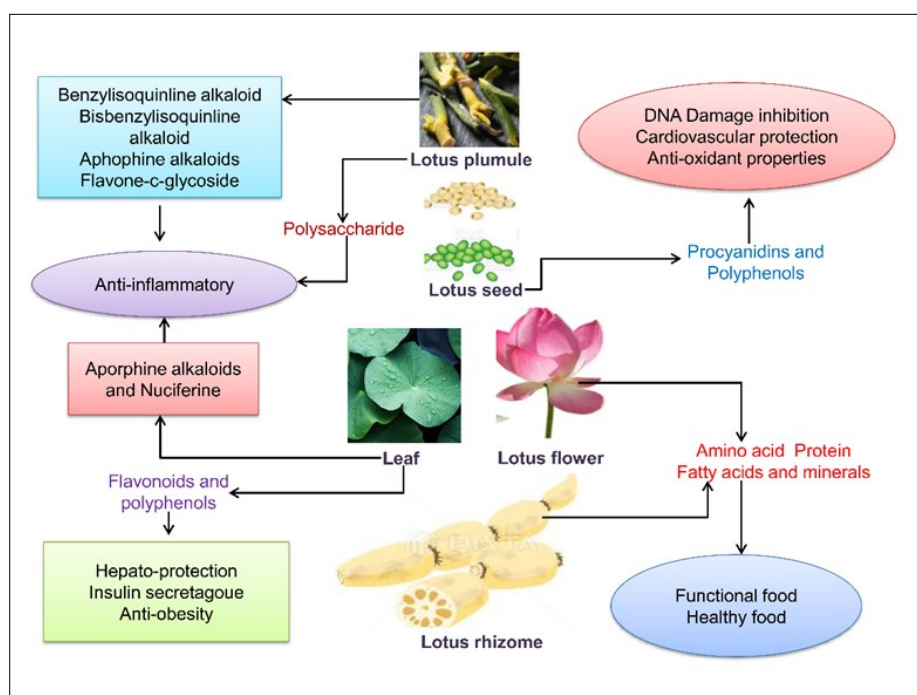


Fig. 5. Bioactive compounds of *Nelumbo nucifera* plant parts and their uses.

Even though the rhizomes of lotus are not as widely consumed as seeds and leaves, yet they are also nutritionally and medically valuable. Historically, the phytochemical composition of lotus leaves and flowers has been applied in a variety of medical practices because of their versatility (55). The culinary use of the lotus rhizome has been applied in stir-fries as well as snacks. Traditionally, it has been served in ritual foods, but nowadays, whole-grain seeds are starting to be added to common foods, such as soups, desserts, savoury dishes and others (56).

Traditional use of *Nelumbo nucifera*

Numerous chronic health issues have been treated with lotus plants, including tissue inflammation, leucorrhea, leprosy, dermatopathy, palpitations, insomnia, enteritis, indigestion, cancer, excessive menstrual bleeding and bad breath. *Nelumbo nucifera* is also used as food in Asia (57).

In traditional medicine, it is the seed pods that are valued in their capacity to be hemostatic. Traditional Chinese medicine uses lotus seed embryos to cure insomnia, cardiovascular diseases, neurological disorders and high fever (15, 52). The leaves are applicable in the therapy of hematuria, metrorrhagia and epistaxis. The perianth and the stamen are also prepared into herbal teas that have soothing and therapeutic effects. Traditionally, all the components of *N. nucifera* have been used in some form in therapeutic applications. The rhizomes are especially characterised by the cholagogue, diuretic and nourishing effects, so they are effective in treating hemorrhoids, colitis and dyspeptic disorders (58). The stem is a diuretic and an anthelmintic in Ayurvedic medicine, which treats nervous lethargy, leprosy, skin disorders and nausea. The applications of the leaves include hyperlipidemia, hemorrhagia, metrorrhagia, hematemesia and epistaxis (59), which are shown in Fig. 6 and summarised in Table 2.

Clinical applications

Nelumbo nucifera has long been an important component in traditional Chinese herbal medicine and has gained official recognition in the Chinese Pharmacopoeia due to its biological activities. The plant is frequently used in the formulation of bioactive herbs, such as Tangzhiqing tablets, which target hyperlipidemia and Sishen Wan and Shenling Baizhu San, which are effective in treating inflammatory bowel disease. Nuciferine, a key medicinal compound isolated from *N. nucifera*, exhibits various beneficial effects, including antioxidant properties that help combat oxidative stress, anti-HIV activity that inhibits viral replication and anti-obesity effects that may aid in weight management. Recent studies have highlighted the efficacy of isoliensinine from *N. nucifera* in inhibiting the SARS-CoV-2 3CLPro enzyme, achieving an IC₅₀ value of 29.93 µM, which indicates significant inhibition of enzyme activity. Previous researches investigated the potential of bisbenzylisoquinoline derivatives for developing antiviral agents in opposition to SARS-CoV-2, focusing on the inhibition of the 3CLPro enzyme, which is critical for viral replication (16). In healthcare, various formulations such as lipid-lowering decoctions, Honghe powder, leaf decoctions, lipid-lowering capsules and Qingjian capsules are employed according to traditional practices to avoid and cure diseases such as atherosclerosis, hyperlipidemia and coronary heart disease.

Pharmacological activity

Antioxidant activity

Damage to cells and tissues is associated with the human body's production of free radicals, contributing to various health complications and the aging process. A decline in the body's ability to eliminate these free radicals can impact metabolic and physiological functions, resulting in aging-related reactions and the pathophysiology of chronic illnesses. This oxidative stress poses significant health risks (60), as illustrated in Fig. 7. "When reactive oxygen and nitrogen species (ROS, RNS) are developed in excess of antioxidants' ability to neutralise them, this is known as oxidative stress. This imbalance increases pro-oxidative activity, which can damage cellular components. Conditions associated with oxidative stress include neurodegenerative diseases, kidney disorders, respiratory issues, aging, cancer and metabolic conditions such as diabetes, heart disease and obesity. The production of free radicals, such as hydroxyl radicals, superoxide anions, nitric oxide, hydrogen peroxide (H₂O₂) and peroxynitrite (ONO₂), is closely associated with oxidative stress (61).

In earlier research, the leaves of *N. nucifera* were used to extract fifteen different chemicals (19). Researchers assessed the antioxidant efficiency of these compounds using ferric reducing power (FRAP) assays and radical scavenging assays with 2,2-azinobis (3-ethyl-benzothiazoline-6-sulfonic acid) and 2,2-diphenyl-1-picrylhydrazyl (DPPH). The epicarp of lotus seed extract has been identified as an effective antioxidant, capable of preventing the development of fat cell precursors and functioning as a natural antioxidant in food items, such as delaying lipid oxidation in pork (60). Lotus seed alcohol extract enhances superoxide dismutase (SOD) levels, reduces reactive thiobarbituric acid (TBARS) and increases peroxide activity in rat liver and kidney tissues (61). The observed dose-dependent rise in catalase (CAT) and SOD levels, along with the decrease in TBARS, highlights the potent antioxidant activity of *N. nucifera* extracts. *In vitro* studies suggest that phenolics, alkaloids and saponins presence in these extracts contributes to their free radical scavenging and antioxidant effects (62).

In seedlings treated with stress, the activity of ascorbate peroxidase was greater than that of control seedlings, while CAT and monodehydroascorbate reductase activities showed no significant difference. Notably, leaf stalk extracts demonstrated potential fever-reducing properties (63). Another study revealed that *N. nucifera* stamen extract has the potential to be a high antioxidant flavonoid component with anti-aging potential to postpone the chronological aging of yeast by acting at the levels of enzyme regulation and gene expression (sir2 and sod2), which reduces oxidative stress and maintains central metabolism as illustrated in Fig. 8 (18).

Immunity

In earlier research investigated the impact of lotus ethyl alcohol extracts on inhibiting cell growth and cytokine production in blood mononuclear cells (PBMCs) that were activated by phytohemagglutinin (PHA) (64). The main focus of this research was to understand how these extracts influence T lymphocytes, which contributes in the development of systemic lupus erythematosus (SLE). This research revealed that (S) arnepavine plays a role in preventing lymph node enlargement and increasing the survival rate of MRL/MpJ lpr/lpr mice. This positive impact was linked to its ability to reduce splenocyte growth suppressor genes associated with interleukin 2 (IL 2), interleukin 4, interleukin 10 and interferon γ (IFN

Table 2. *Nelumbo nucifera*-related patents and their purported qualities (WIPO, n.d.)

Utilization	primary composition	Attributes	Patent Number
cosmetics	<i>N. nucifera</i> extract	As a perfume	KR1020100049342
Cosmetics	Callus extract	Excellent whitening effect	EP3437632
Herbal medicines	<i>N. nucifera</i> extract	Immunotropic and antioxidant activity	RU0002496508
Herbal medicines	<i>N. nucifera</i> extract	The agent possessing anxiolytic and antidepressive action	RU0002497538
As a drink	All parts of the lotus, including leaf, root, stalk and flower	Tea pack	KR1020040050198
Herbal medicine	Leaf extract	Preventing and treating metabolic diseases, hyperlipidemia or fatty liver	KR1020110096194
Herbal medicine	Lotus seed powder	Reduces the desire to smoke and purify the body from harmful substances	WO2011099894
Herbal medicines	<i>N. nucifera</i> extract	Preventing and treating hangovers is provided to reduce the concentration of alcohol and acetaldehyde in blood	KR1020050104036
Cosmetics	<i>N. nucifera</i> extract	Inhibit elastase and control fibronectin, preventing and improving skin sagging and decreasing elasticity	KR1020060034007
Pharmaceutical composition	seed extract	For the protection of brain nerve cells	WO2013129772
Herbal medicine.	Stamen extract	Antioxidant activity	KR1020040072146
Herbal medicine	<i>N. nucifera</i> extract	Improving blood lipid	KR1020190096478
Pharmaceutical composition	Seed extract	To prevent and treat metabolic disorder	KR1020140070901
Herbal medicine	Stamen	To prevent or treat hyper lipidemia, total cholesterol level and neutral lipid content in blood should be reduced	KR100703596
Pharmaceutical and cosmetics	Extract of <i>N. nucifera</i>	Having skin whitening, anti-aging and anti-wrinkle effects	KR100828193
Pharmaceutical composition	Extract of rhizomes	Effectively used in the protection of liver cells, the prophylaxis and treatment of liver damage and the inhibition of mutation by a liver carcinogen	KR1020030031729
Herbal medicine	Stamen extract	Preventing and treating diabetic complications	KR1020070056172
Food	Lotus seed extract	Seed red pepper paste	KR1020200118586
Food	Lotus seed extract	Seed soy sauce	KR1020200117739
Beverages	<i>N. nucifera</i> extract	The <i>N. nucifera</i> Gaertn-Lespedeza cuneata mixture has completed the soaking and ageing process	KR1020220010127
Breeding	<i>N. nucifera</i>	Ecological restoration	CN111296218
Herbal medicines	<i>N. nucifera</i> extract	Antibacterial and antifungal	KR1020110105580
Pharmaceutical composition	Seed extract	Healthy functional food products for preventing or treating thrombosis	KR1020190006235
Pharmaceutical composition	<i>N. nucifera</i> extract	For preventing and treating atopic dermatitis	KR1020100028443
Nutraceutical food	Leaf extract	For reducing blood glucose Prevent diabetes	KR1020110111960
Producing Functional pills	Seed extract	Delay of urination and defecation can be overcome	KR101994999
Functional toothpaste	<i>N. nucifera</i> extract	Anti-inflammatory and antibacterial properties and to prevent dental caries	KR1020120053374

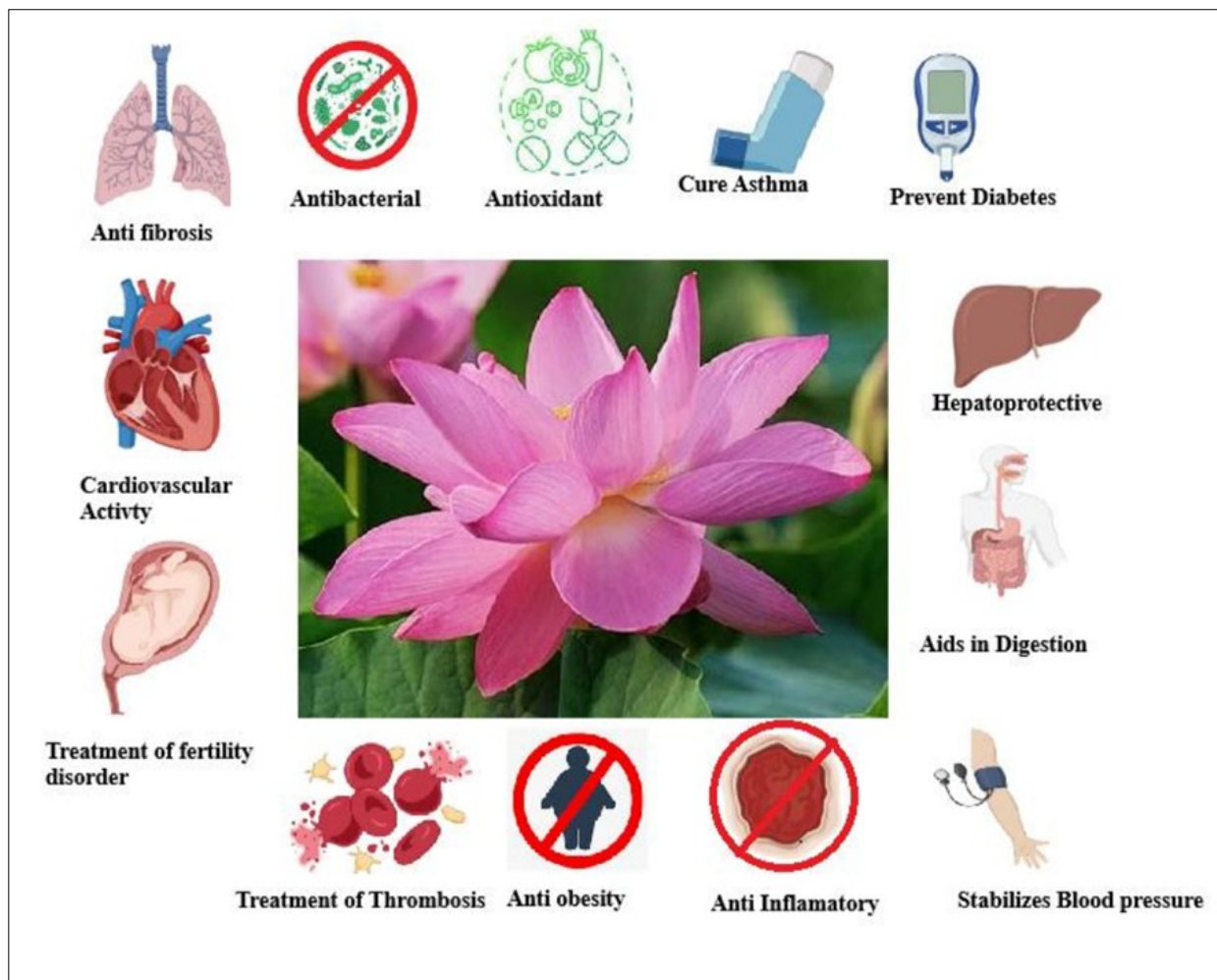


Fig. 6. Traditional uses of *Nelumbo nucifera*.

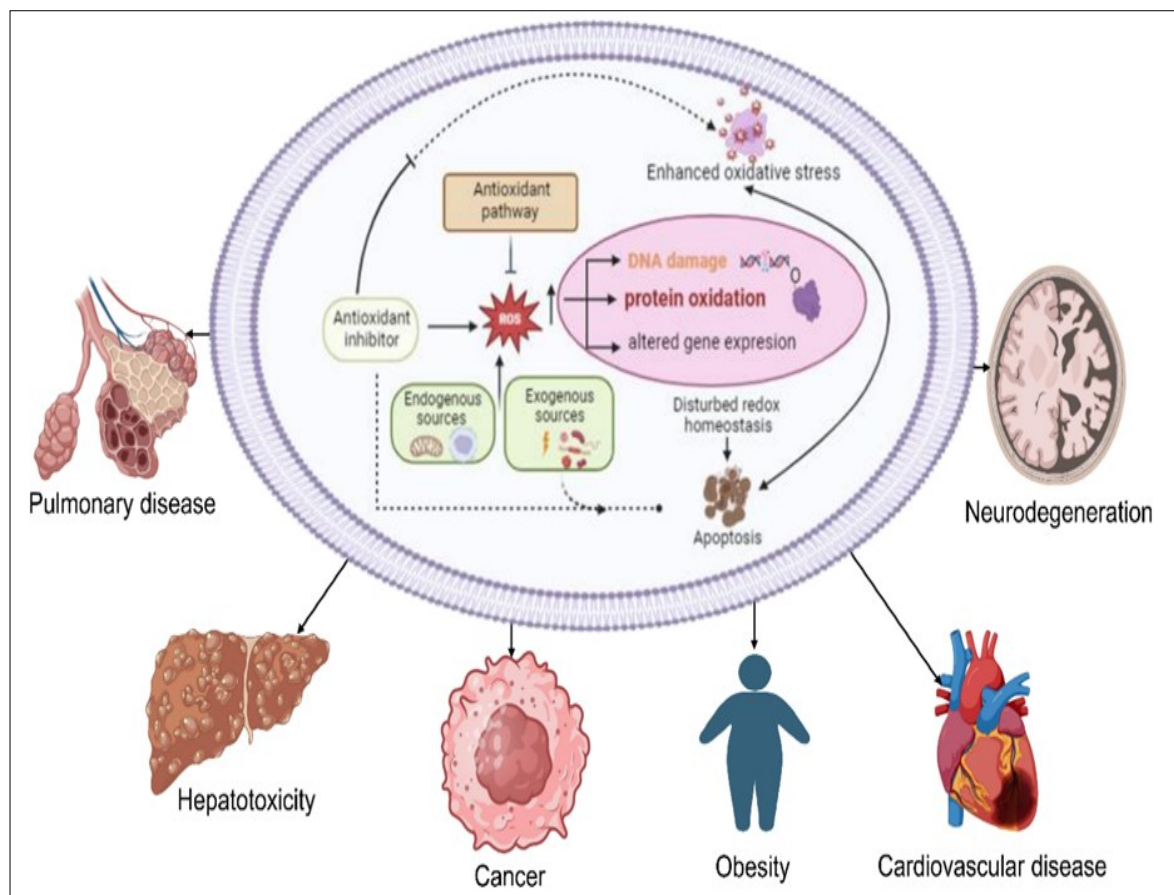


Fig. 7. Oxidative stress results from an imbalance between the generation of reactive oxygen and nitrogen species (ROS, RNS) and the capacity of antioxidants to counteract them. Elevated pro-oxidative activity can damage cellular components.

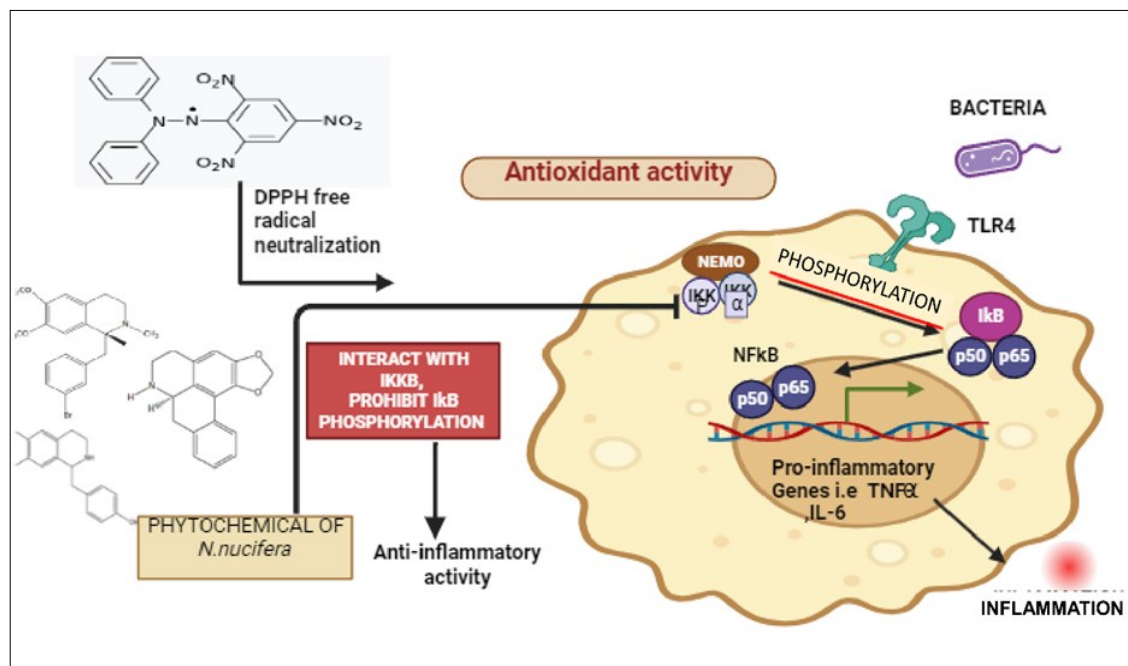


Fig. 8. Antioxidant and anti-inflammatory mechanisms of *Nelumbo nucifera* phytochemicals, showing inhibition of IκB phosphorylation and neutralisation of free radicals.

γ) decrease cell proliferation and accumulation of complexes, lower urinary protein levels and inhibit the production of anti-double-stranded DNA antibodies. Moreover, the study showed that (S) armepavine also restricted IL-2 and IFNγ production in PBMCs (64). These findings recommend that (S) armepavine could assist as a therapy for autoimmune conditions, such as SLE.

Anti-inflammatory activity

A basic immunological reaction, inflammation can cause tissue damage even if it is protective. It is connected to a number of illnesses, like atopic eczema, rheumatoid arthritis and respiratory distress (65). Cytokines released by T cells, such as IL-10 and IL-4, are known to contribute to asthma and lung inflammation. Lotus rhizome extracts, particularly those containing triterpenoids like betulinic acid, exhibit significant anti-inflammatory properties. Research has shown that betulinic acid effectively reduces edema and inflammation (66, 67). Additionally, studies indicate that adding nuciferine to RAW264.7 macrophages significantly diminishes inflammation induced by lipopolysaccharide (LPS) (67). This effect is enhanced by the activation of the peroxisome proliferator-activated receptor (PPAR) pathway, suggesting that nuciferine has therapeutic potential in managing inflammatory conditions. Furthermore, lotus seed pro isolate (LSPI) has been found to modulate inflammatory responses in LPS-stimulated macrophages by inhibiting the initiation of nuclear factor kappa B (NF-κB) and the mitogen-activated protein kinase (MAPK) pathways. These pathways are critical for the regulation of pro-inflammatory gene expression. By reducing intracellular ROS production caused by LPS, LSPI demonstrates promise as a functional food ingredient for managing inflammatory diseases (68). In summary, the anti-inflammatory belongings of *N. nucifera* and its bioactive components highlight their significant potential for therapeutic applications in treating inflammation-related conditions as illustrated in Fig. 9

Treatment for erectile dysfunction

Research has explored the effects of *N. nucifera* on male reproductive health, particularly regarding erectile dysfunction (69). In a previous research observed the impact of a petroleum ether extract from lotus seeds on female albino mice (70). This extract was carried out at a dose of 3 mg/kg and demonstrated anti-fertility effects by disrupting the oestrus cycle, particularly during the metestrus stage. The extract interfered with ovarian steroid synthesis, leading to changes in the oestrus cycle and a significant reduction in uterine mass. These findings indicate that *N. nucifera* extracts may exert notable effects on reproductive functions, warranting further study into their mechanisms of action and potential therapeutic applications in addressing erectile dysfunction and related reproductive health issues.

Restenosis and atherosclerosis

In the recent past, studies have indicated the possible applications of *N. nucifera* extracts in the management of vascular diseases, in particular restenosis and atherosclerosis. Another researchers elicited a considerable decrease in the luminal area and the rate of stenosis of a rat model using an extract prepared of the leaves and roots of *N. nucifera* after four weeks (71). It implies that *N. nucifera* would assist in improving the condition of the vascular health and prevent re-narrowing of blood vessels after interventions. The authors also discovered that extract of lotus leaf markedly repressed the growth and migration of vascular smooth muscle cells (VSMCs) in a rabbit that was induced with atherosclerosis by a high-cholesterol diet (72). The fact that this occurred is a pointer that the active constituents of *N. nucifera* have the potential to reverse the pathophysiological processes of atherosclerosis. A component of angiotensin II-mediated VSMCs increase was also found to be prevented by an active ingredient of lotus, neferine, that also proves the potential benefits of *N. nucifera* extracts in the treatment of vascular disorders (73). Combined with the studies, *N. nucifera* can be said to be a promising therapeutic regimen to prevent and cure restenosis and atherosclerosis and therefore, subsequent research in its pharmacology and applications in cardiovascular health is

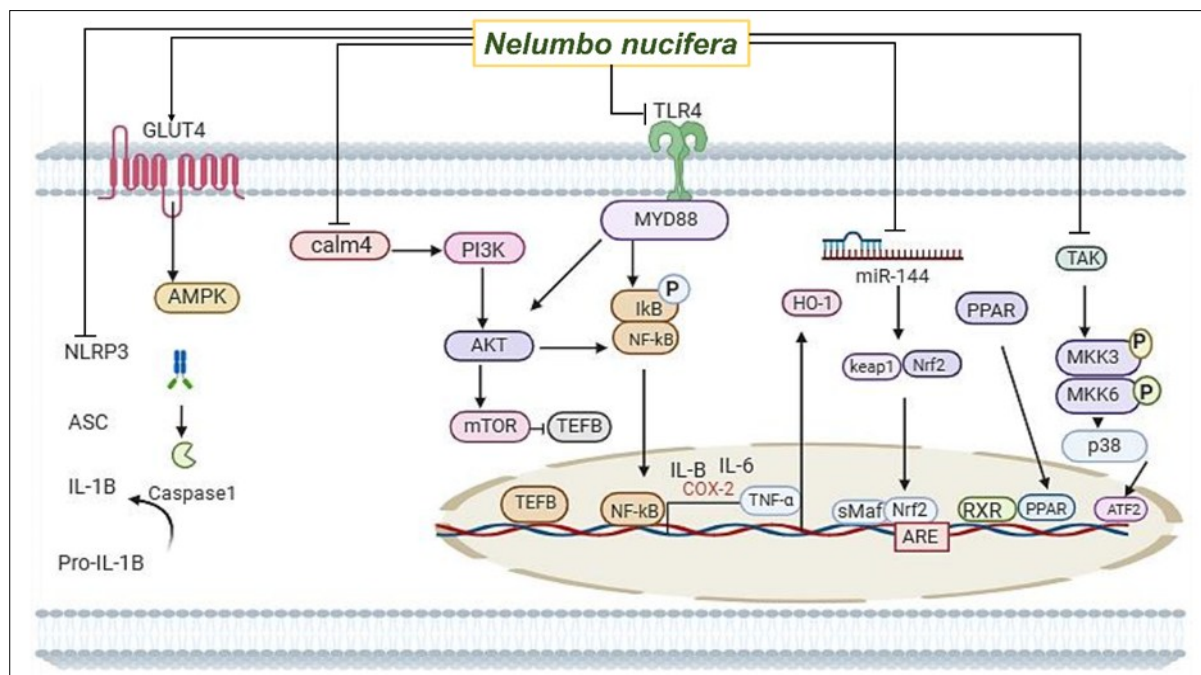


Fig. 9. Mechanisms of the anti-inflammatory effects of *Nelumbo nucifera*.

Note: Fig. 9 illustrates various substances and signalling pathways involved in reducing inflammation. Key proteins targeted by the active compounds in *N. nucifera* include AKT (Protein Kinase B), CALM4 (Calmodulin 4), AMPK (AMP-Activated Protein Kinase) and PPAR (Peroxisome Proliferator-Activated Receptor). The involvement of these pathways is significant in the context of alcohol-induced liver diseases (ALDs) and the effects of neferine on biological systems. Additional proteins such as HO-1 (Heme Oxygenase-1), TFEB (Transcription Factor EB), Nrf2 (Nuclear Factor Erythroid 2-Related Factor 2), MyD88 (Myeloid Differentiation Factor 88), TLR4 (Toll-Like Receptor 4) and NLRP3 (NOD-Like Receptor Pyrin Domain Containing 3) are implicated in these processes. The activation of these pathways leads to the inhibition of pro-inflammatory responses, including the modulation of glucose transporter isoform 4 (GLUT4) and the apoptotic-associated speck-like protein (ASC).

required.

Pulmonary fibrosis prevention

Research has hinted that *N. nucifera* seed extracts are antifibrotic and they can be employed to prevent pulmonary fibrosis. It has been demonstrated that such extracts can regulate fibrotic reactions that can afford protection against the damage of the lung tissue. Specifically, antifibrotic effects of *N. nucifera* seed extracts are justified by the ability to control the oxidative stress and inflammation mechanism (74). The bioactive compounds that exist in the seeds i.e., the alkaloids and polyphenols play roles that help increase the antioxidant defences which in effect reduce the oxidative damage of the lung tissues. Later studies have found that *N. nucifera* seed extracts are able to increase the levels of antioxidant enzymes like SOD and CAT enzymes. The extracts would have the potential to minimise the formation of fibrotic events in the pulmonary tissues by alleviating oxidative stress (75).

Anticancer activity

Research indicates that *N. nucifera* is highly active in cancer cells, particularly neferine, which is an alkaloid extracted out of the plant. Neferine leads to cell death in HepG2 cell line in a dose-dependent relationship (76). The anticancer activities of the *N. nucifera* extracts were further detailed with help of cultured cells of the HepG2 which had effects on mitochondrial membrane potential, intracellular calcium level, cell membrane integrity, apoptotic body development and DNA fragmentation. These findings highlight the potential avenues, based on which *N. nucifera* will be able to exert its anticancer effects by modulating the primary cellular responses, as concerns, to apoptosis and cell death as illustrated in Fig. 10 (77). It was found that 15 compounds in *N. nucifera* have a great ability in reducing the development of numerous cancer cell lines, including

prostate, melanoma, stomach cancer cells and 7-hydroxydehydronuciferine is one of the most notable ones (78), as illustrated in Fig. 10. All 15 compounds isolated from moreover, neferine has also been verified to induce apoptosis in A549 lung carcinoma cells, which would also be an indication of its direct antitumor application moreover, neferine has also been proved to induce apoptosis in A549 lung carcinoma cells, which would also be an indication of its direct antitumor applicatio (79). A DPPH radical scavenging experiment has proven that the antioxidant activity of methanol extracts of *N. nucifera* is extremely good. Besides this, the extracts have also shown anti-inflammatory effect in-vitro on MCF-7 human breast cancer cells. Now, the 9-octadecadienoic acid and 2,2,4-trimethyl -13,15-tetraenyl -cyclohexanol in *N. nucifera* can be applied in the cure of various cancers, with the two compounds mentioned above showing potential as effective anticancer agents against the MCF-7 cell line. *Nelumbo nucifera* can be utilised in the treatment of various cancers, since it has a very high potential to be a viable treatment due to the immense pharmacological studies carried out on the compounds (80).

Hepatoprotective activity

Studies conducted on the hepatoprotective property of *N. nucifera* have shown that it can be used to reduce liver toxicity attributed to different toxins. Appropriate studies have shown that lotus plant extracts and especially plumule extracts, contain high amounts of alkaloids, which are the sources of their protective action against hepatotoxicity (81). One study examined the effectiveness of lotus plum extract in liver damage caused by carbon tetrachloride (CCl₄) as illustrated in Fig. 11. The extract showed hepatoprotective action stimulation of the messenger RNA (mRNA) related to antioxidant enzymes, including CAT and copper/zinc (Cu/Zn) SOD expression (82). This implies that it has a beneficial effect on the antioxidant defence system of the liver and thus the oxidative stress and

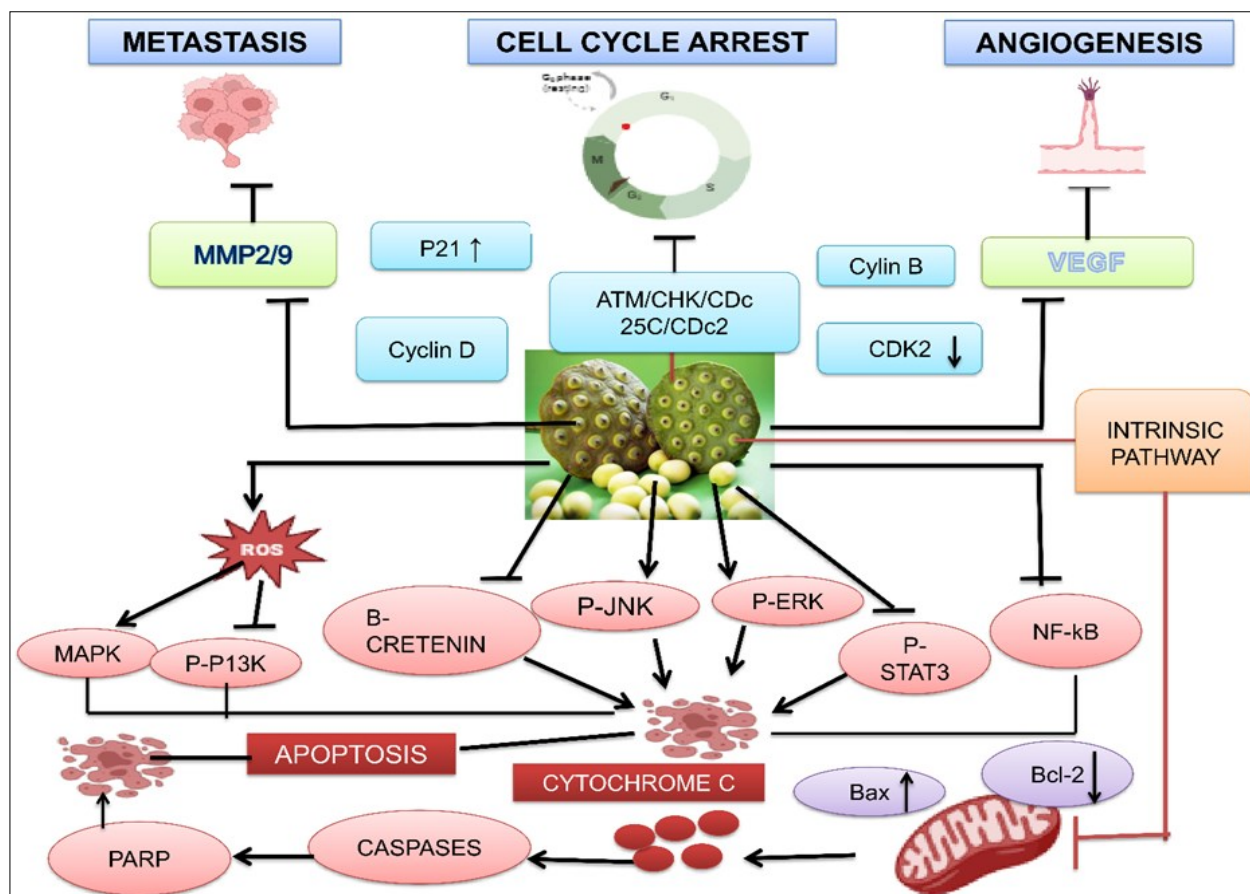


Fig. 10. Schematic representation of the molecular mechanism underlying the anticancer activity of *Nelumbo nucifera*.

inflammation are diminished. Also, a study concentrated on the activity of lotus seed extract on liver inflammation by LPS. These researches showed that compounds of lotus had a potential to decrease the liver damage and inflammation by regulating major pathways of antioxidants and inflammatory processes (83). In further investigations, Previous researchers observed the hepatoprotective properties of an ethanol foliage extract of *N. nucifera*, thus validating its effectiveness in preventing CCL₄-induced liver injury of Sprague-Dawley rats (72). The findings showed that *N. nucifera* extracts had a good antioxidant and hepatoprotective effect, which indicated that *N. nucifera* extracts might be used as an adjunct in the treatment of liver-related disease. The evidence is overall in favour of *N. nucifera* as a hepatoprotective agent and this should undergo more research on its mechanism and its uses in liver health.

Antithrombotic activity

Studies have also shown that *N. nucifera* is antithrombotic and this characteristic might aid in the treatment of disorders associated with excessive blood clotting. According to a previous study, neferine-one of the most potent compounds in lotus seeds-significantly reduces the release of dense granules from platelets stimulated with collagen and thrombin (84). Neferine prevented platelet aggregation induced by U46619, thrombin, and collagen in mouse platelets and suppressed adenosine diphosphate (ADP)-induced aggregation in mouse plasma. Moreover, neferine promoted the disaggregation of already formed platelet aggregates, suggesting that this compound may have potential as an antithrombotic agent. Under electrical stimulation, neferine significantly prolonged the carotid occlusive thrombosis time in rat models. These findings indicate that *N. nucifera* and its active constituents, particularly neferine, may be beneficial in the treatment and prevention of thrombotic disorders.

However, further studies are required to elucidate their mechanisms of action and clinical applications.

Hypoglycemic action

Lotus seeds have been researched and have been found to be hypoglycemic, so they could serve as an alternative treatment for diabetes. Research has shown that the quantity of the mineral in *N. nucifera* seeds, like potassium, chromium, sodium, magnesium, calcium and manganese, is significant in maintaining blood sugar levels (85). These are trace elements, which are important in several biological functions and in insulin secretion, which is involved in keeping the glucose levels of the body at homeostasis. Lotus seed-resistant starch (LSRS) has been reported in the experimental studies to exhibit a considerable decrease in the level of glucose blood of diabetic rat models. The LSRS administration led to a 16 % to 33.6 % decrease in blood glucose with a 25 to 39 % rise in serum insulin level. This indicates that LSRS can increase insulin sensitivity and elevate glucose tolerance; it is a viable intervention in the management of diabetes (86). Moreover, *N. nucifera* powder dietary supplement has been promising in the management of blood glucose in high-fat-diet-induced obese mice. The findings indicated reduced body weight and fat mass and increased tolerance to glucose and suggested that *N. nucifera* could be used as a functional food in glycemic control (87). In conclusion, the hypoglycemic action of *N. nucifera* is a promising area of research on its mechanisms and clinical uses for diabetes and this phenomenon should be explored in future studies.

Analgesic effect

Numerous research have looked into the potential of *N. nucifera* as an analgesic, which suggests its potential to be a natural painkiller (88). The central analgesic response in mice was evaluated using the tail flick test, and the latency period was recorded as the time taken

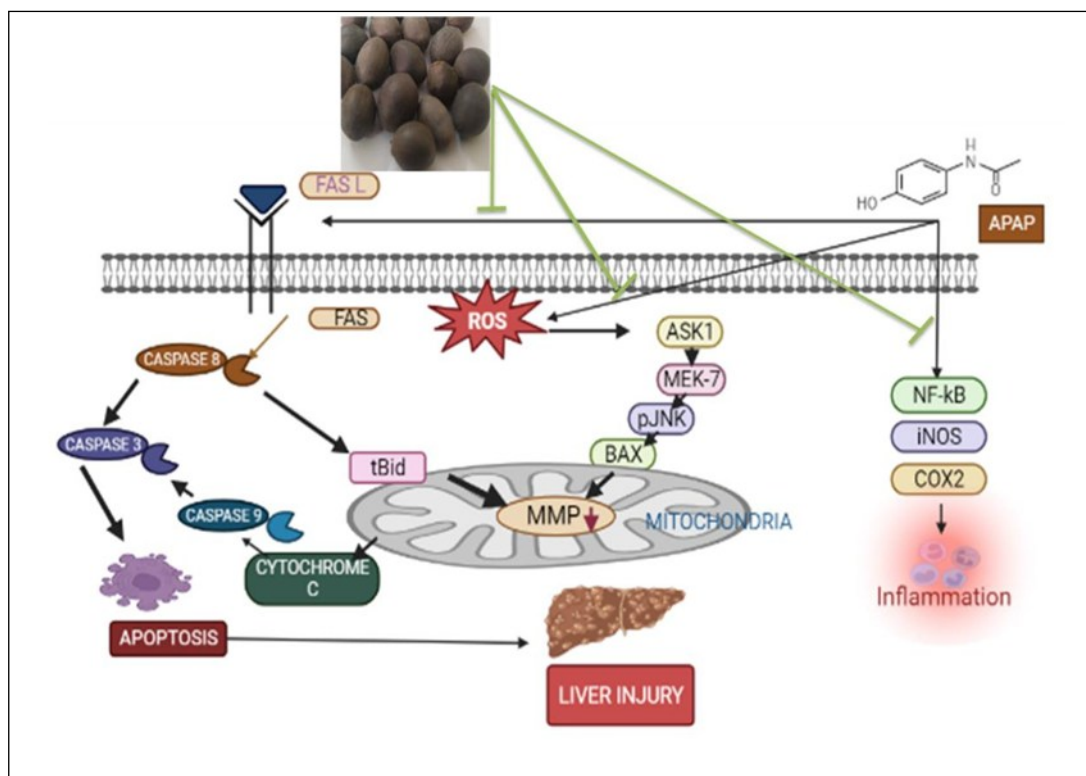


Fig. 11. Protective effects of lotus seed extract (LSE) against acetaminophen (APAP)-induced hepatotoxicity.

Note: The extract mitigates apoptosis, reduces oxidative stress and decreases inflammatory responses, suggesting its potential as a therapeutic strategy for APAP overdose.

for tail withdrawal from the stimulus (89). The total writhes and the proportion of the writhes inhibition were documented in the acetic acid-induced writhing test, which was also utilised to assess the peripheral analgesic effect in the mouse. Findings of the study if *N. nucifera* fruit extract possessed a strong analgesic impact on a mouse model. This effect perhaps could relate to synergistic activity of flavonoids, saponins and tannins on the inhibition of the arachidonic acid pathway. The results showed the *N. nucifera* potential as a natural analgesic option due to its therapeutic role, which should be followed up in other studies on its mechanisms and uses in pain management.

Neuromodulatory activity

Nelumbo nucifera has been researched due to its possible impacts on neurological well-being, especially the alkaloid neferine. Studies have demonstrated that lotus seed extract can reverse the scopolamine-induced memory loss in rats, which implies that it may be used in treating the cognitive functions of the body. This effect relates to the inhibition of acetylcholinesterase (ACHE), a degradation enzyme of acetylcholine, which is an essential part of memory and learning (90). Studies on lotus seed extract have revealed its potential of overcoming the effect of scopolamine-induced amnesia on rats. The results reveal that lotus seed extract alleviates dementia symptoms by suppressing the action of ACHE, as we can see in Fig. 12.

The intraperitoneal administration of higenamine at a 10 mg/kg dose has been shown to have potential in the treatment of ischemic injuries, as it was determined to reduce brain infarct size, mortality and myeloperoxidase (MPO) activity of rats with middle cerebral artery occlusion (MCAO). The effects of these are explained by the fact that heme oxygenase-1 (HO-1) is induced by the PI3K/Akt/Nrf2 signalling pathways, which may be used in the treatment of stroke (91). This also helps to prove the theory that the

neuroprotective properties of lotus alkaloids may be used in clinical practice.

Correspondingly, in mice subjected to forced swimming, neferine and its analogs (liensinine and isoliensinine), administered intraperitoneally at dosages of 25 or 50 mg/kg, exhibited activity against mechanisms involving serotonin, correlating with antidepressant effects. Additionally, neferine has been shown to improve learning and memory in diabetic mice by affecting the NLRP3 inflammasome pathway (92). In animal models, it has also demonstrated substantial protective effects against the onset of Parkinson's disease due to increased dopamine production and tyrosine hydroxylase levels. Key actions of neferine, including its antidepressant-like effects, are believed to be associated with its binding to the 5-hydroxytryptamine 1A (5-HT_{1A}) receptor. It has been suggested that neferine docks with the 5-HT_{1A} receptor through its aromatic rings, highlighting the significance of this interaction for ligand-receptor binding (93).

Intestinal function

The beneficial bacteria that help in digestion, absorption and the regulation of the gastrointestinal tract are called probiotics. Studies indicate that lotus seeds help in the increase of probiotics and these can assist in the improvement of gut health. The gastrointestinal issues, such as functional dyspepsia, diarrhoea, constipation, etc., are typically associated with absorption problems and gut motility issues (79) and triggered the emergence of dietary supplements, as well as novel dairy products, including fermented lotus seed products. The stated developments suggest the possibility of lotus seeds having a beneficial effect on gastrointestinal motility and the health of the gut in general (94). Lotus seed fermented milk can be useful in balancing microbiota of the intestines, enhancing resistance to pathogens and preserving mucosal integrity. In summary, the *N. nucifera* could have important intestinal health-

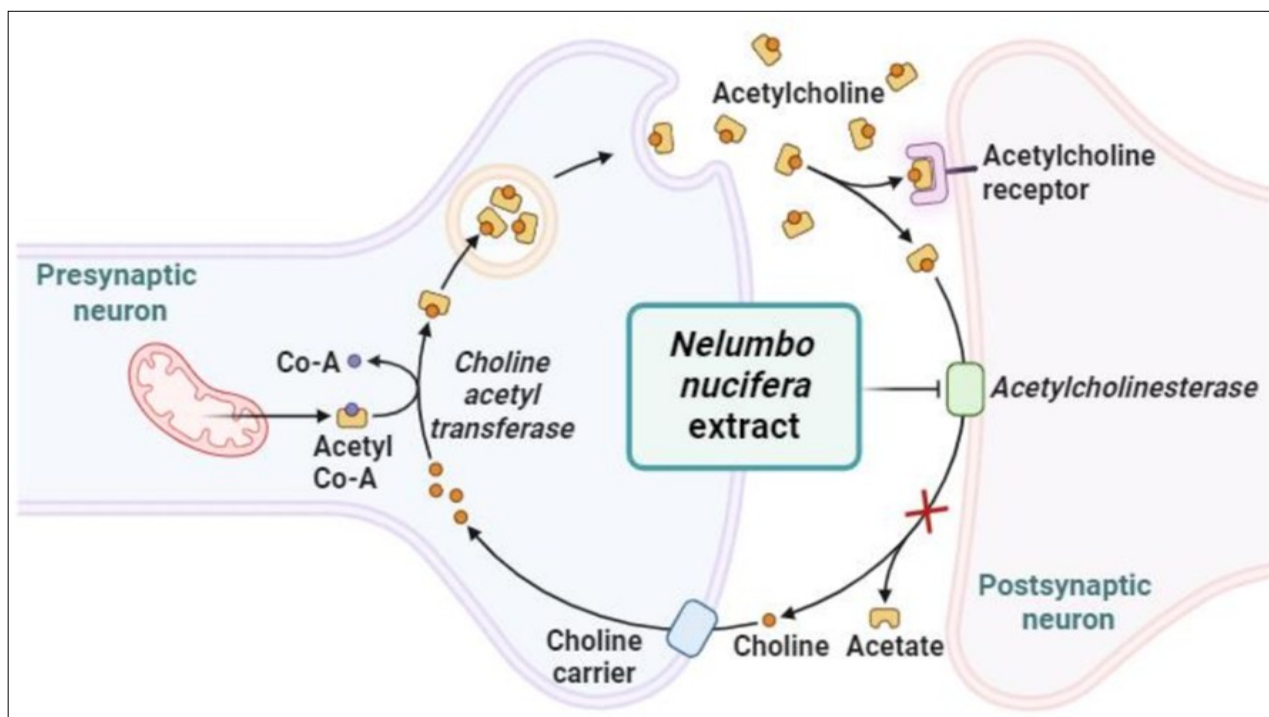


Fig. 12. Schematic diagram of the anti-neurodegenerative activity of *Nelumbo nucifera*.

promoting effects and its potential as a prebiotic functional food is evident.

Antiviral activity

Studies have examined the antiviral effects of *N. nucifera*, especially its effect on viral infection. Previous researchers conducted a study that examined the possibilities of lotus seed extracts in negative effects on the action of herpes simplex virus type 1 (HSV-1) (95). The results suggested that a 100 mg/mL ethanolic extract was revealed to have a significant reducing effect on viral replication, with the IC₅₀ of 50.0 mg/mL indicating the effectiveness of the extract against the HSV-1. Three compounds, namely (-)-1(5)-norcoclaurine, quercetin 3-O-β-D-glucuronide, and (+)-1(R)-coclaurine, were isolated from lotus leaf extracts (96). Although these compounds had some antiviral effect, their activity was lower in comparison to other active constituents and the IC₅₀ value of the compounds was 2 mg/mL to prohibit HIV and so, more studies are necessary to determine other active compounds of *N. Nucifera* (97). The findings indicate the potential of *N. nucifera* as a basis of antiviral compounds and, therefore, there is a need to explore more about its mechanisms and application in treating viral infections.

Diuretic activity

Nelumbo nucifera has been examined concerning its diuretic qualities with promising results as a possible urinary health promoter. The diuretic efficacy of *N. nucifera* rhizomes has been evaluated in albino rats. The methanolic extract of the rhizomes produced substantial diuresis in a dose-dependent manner at 300, 400 and 500 mg/kg, compared with furosemide (20 mg/kg). The extract also significantly enhanced natriuretic and chloruretic activity, indicating its potential role as a urinary health promoter (98, 99). Although the extract in extracting the electrolytes was not as effective as furosemide, which is a common diuretic, it was effective in stimulating the urine production. The results indicate that *N. nucifera* can be utilised as a natural diuretic for its conventional implementation in the fluid retention treatment and urinary health.

Conclusion

Nelumbo nucifera, also referred to as the sacred lotus, is proving to be widely known in terms of its vast health potential and historical importance in traditional medicine. It is appreciated due to the wide series of therapeutic benefits, such as pain relief, anti-inflammatory properties and digestive health aid. Various of these traditional applications have been supported by modern scientific studies and include the antioxidant, antidiabetic, antiobesity and neuroprotective properties of the plant. Although the results are positive, it must be noted that most of the studies are still preliminary. Additional clinical tests on a larger scale should be carried out to prove the safety and efficacy of *N. nucifera*. The standardisation of extracts, ideal drug dosage and drug interactions are some of the critical factors to consider. The solution to these problems will be paramount in the safe implementation of *N. nucifera* in modern medicine. To conclude, *N. nucifera* has an enormous potential in both traditional and contemporary medicine. The scope of its therapeutic operations is a solid basis for future studies, which would contribute to our knowledge on this wonderful plant and its possible use in medical care.

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Authors' contributions

SM contributed to writing original draft, editing and data curation, while YR contributed to writing original draft and conceptualisation. Both authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest: Authors do not have any conflict of interests to declare.

Ethical issues: None

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