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A brief review on pharmaceutical uses of *Nelumbo nucifera*

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Abstract

Nelumbo nucifera is placed in *Nelumbonaceae* family and has several vernacular names like Indian lotus, Chinese water lily, etc. It is an aquatic as well as perennial plant. It has wide geographical distribution and relatively a great biological diversity. Scientists through their researches or pharmacological studies revealed that *N.nucifera* possesses several activities like antioxidant activity, anticancer property, antiviral, antipyretic, anti-ischemic, as astringent, hepatoprotective, hypoglycemic, anti-fungal, anti-bacterial, anti-inflammatory, immunomodulatory, and diuretic activities. It also has antifertility, anti-analgesic properties and as well as does gastrointestinal regulation. Lotus's bioactive constituents are mainly alkaloids and flavonoids. This review is to combine pharmaceutical information on *Nelumbo nucifera*. It also discusses the physiological benefits of the plant.

Keywords: Lotus, medicinal, *Nelumbo nucifera*, pharmaceutical

Introduction

Nelumbo nucifera is commonly known by names like lotus and sacred lotus. It is an aquatic perennial herb and belongs to family *Nelumbonaceae* ^[1, 2]. The roots of the plant remain anchored within the muddy base of the water bodies. The leaves are 60cm large in diameter and float atop the surface of the water.

N.nucifera lotus is found all through Asia, Australia, while, *N.lutea*, the water chinquapin, is present in eastern and southern North America ^[3]. *N.nucifera* is an aquatic plant species, which requires a lot of space and full sunlight to flourish. It is commonly called as Kamala or Padma in India. Lotus has thick, creeping, and yellow rhizomes and the fruits are green in colour. Leaves are usually large and of both kind, aerial and floating. These are 20-90 cm in diameter and form a short tip, non-wettable and petiole.

The sepals along with petals and stamens are arranged spirally ^[4]. This plant is not only luxurious and ornamental but it is also a great source of herbal medicine having strong astringent and cooling properties. Lotus also has religious importance in South East Asia, where the seeds and its leaves are also eaten. Therefore it is named as sacred lotus ^[5].

In Asia, Oceania, and America, lotus seeds and the by-products of their processing are broadly consumed. It has a high amount of physically active substances ^[6]. *N.nucifera* contains polyphenols, and therefore shows anti-oxidant activity which is beneficial in various health aspects ^[7, 8]. Lotus seeds are usually sold in China in shelled and dry form. These are rich in alkaloids such as neferine etc. These are sometimes also sold as a raw snack ^[9]. This plant has some special features such as the capability to regulate the flower's temperature under a limited range ^[10]. Its seeds exhibit long viability duration ^[11]. Moreover, its leaves have self-cleaning activity.

Taxonomic Classification ^[12]

Kingdom: Plantae – Plants;

Sub Kingdom: Tracheobionta – Vascular Plants;

Super Division: Spermatophyta – Seed Plants;

Division: Magnoliophyta – Flowering Plants;

Class: Magnoliopsida; Subclass: Magnoliidae;

Superorder: Proteanae;

Order: Proteales;

Family: Nelumbonaceae– Lotus Family;

Genus: *Nelumbo* Adans – Lotus;

Species: *Nelumbo nucifera* Gaen. – Sacred lotus.

Chemical Constituents

Rhizomes

31.2% starch is present in the fresh rhizome and it has no taste and odour. Lotus starch was proved to be superior so it is used in tablets preparation. It has been shown that 50% of alcohol is needed for maximum isolation of constituents [13]. The extract of methanol of rhizome possesses betulinic acid – a steroidal triterpenoid [14]. Fresh rhizome comprises of 0.41% sucrose, 83.8% water, 1.56% of reducing sugar, 9.25% starch, 0.11% fat and 0.06% calcium etc. The oxalate content is seen to be 84.3mg /100mg in the rhizome [15].

Fruits and Seeds

N.nucifera seeds are rich in protein, starch, asparagine, tannin, and fats. Plumule and cotyledons of lotus seeds contain a large amount of Glutathione [16]. The germination rate of stored seeds is said to be closely related to the amount of reduced glutathione [16, 12]. Generally, seeds of the lotus are rich in amino acids, minerals, proteins, and unsaturated fatty acids [17]. *N.nucifera* contain a variety of minerals like potassium(28.5%), magnesium(9.20%), chromium(0.0042%), copper(0.00463%), sodium(1.00%), calcium(22.10%), manganese(0.356%), zinc(0.0840%) and iron(0.1990%). The important secondary metabolites which are present in lotus seeds are nuciferine, dauricine, liensinine, lotusine, pronuciferine, roemerine, arnepavine, and neferine [18, 19, 20, 21, 22, 23, 24, 25]. Procyanidin was also extracted from lotus seedpod [26]. It has also rich compounds like isoliensinine, dimethylcorypalline, flavonoids like (rutin, galuteolin, hyperine) and some other microelements like zinc, magnesium, iron, and calcium(Zn, Mg, Fe, Ca) [9]. Lotus seeds also comprise of glucose, beta-sitosterol, and palmitic acid [27]. Carbohydrates, essential amino acids, vitamins, phosphorous, are also present in a great amount in lotus seeds [28].

Leaves

Leaves have a rich amount of alkaloids. This has been shown by liquid chromatography. Major components are nuciferine and pronuciferine. This was seen in the analysis of non-phenolic fractions of the extract of leaf [12]. Dehydroemerine, anonaine, dehydronuciferine, remerine, neferine, roemerine were extracted from petioles and leaves [29, 30, 31, 32, 33]. Leaves contain flavonoids like leucoanthocyanidin and quercetin [22, 34]. Some other flavonoids like hyperoside, catechin, and astragalin are also present [23, 35].

Flower

Many flavonoids have been reported in stamens of lotus which include Kaempferol, nelumboroside A and nelumboroside B. It also consists of isorhamnetin, glycosides and as well as non-flavonoids which include arbutin, adenine, myo-inositol, in stamen extract [36, 37, 38].

Pharmaceutical Uses

Many pharmacological or pharmaceutical studies scientifically screened *N.nucifera* and have proven its antioxidant activity, antidiarrheal, hypoglycemic, antiviral, hepatoprotective activity, aphrodisiac, immunomodulatory, antipyretic activity, anticancer, psychopharmacological, anti-inflammatory activity, anti-ischemic activity, anti-fertility, anti-proliferative activity, anti-arrhythmic activity, diuretic activity, anti-fibrosis, aphrodisiac activity, aldose reductase inhibitory activity, cardiovascular activity, antibacterial, anti-obesity, hypocholesterolemic activity, antiplatelet and lipolytic activity [18]. Many other Modern Pharmacological

studies also proved lotus seeds have sedative and other properties.

Rhizomes

Rhizomes of lotus and its extracts are reported to have Psychopharmacological, hypoglycemic, anti-diabetic and antioxidant activities [19, 20, 21, 22, 23, 24, 25, 39]. Rhizome knot's extracts have been proven to have antioxidant property than the whole rhizome [40].

Seeds

A seed of lotus is used as a tonic for spleen or as spleen tonic and powder of seeds is used to treat cough [41, 42]. Zipe seeds plumule is used for high fevers with restlessness. Seeds also possess anti-proliferative activity, antidepressant, and anti-fibrosis [43, 42, 44]. Seeds also have antiviral and anti-inflammatory activities [45, 46, 47].

Leaves

Nelumbo nucifera leaves are used as antidiarrheal and for hemorrhoids [48, 49]. Lotus leaves also showed antiobesity and hypocholesterolemic activity [50, 51, 52]. Leaf extracts of lotus have hypolipidemic activity and analgesic activity [53, 54, 55]. From blossoms, liquor of lotus is made and it is effective in reducing oxidative stress [49].

Flowers

N.nucifera flowers, its floral parts, and extracts of the parts are also used for treating diseases like weakness, male sexual disorders, cancer, consolidation of kidney function, hypertension syphilis, body heat imbalance, for stopping bleeding, in case of eliminating the stagnated blood [56]. Flowers extracts have been reported to possess free scavenging capacity, vasodilating effects, aphrodisiac, and antioxidant activity [57, 58, 59].

1. Antioxidant activity

When there is an increase in the accumulation of free radicals in the human body, then it can damage the cells and tissues through strong oxidation. As age increases, free radical scavenging ability of body decreases though affects the body's normal metabolism and its functions and therefore leads to chronic diseases or the aging reactions, which can cause several health problems [60]. Hence, lotus plant is of great importance in the identification of potent radical scavenger which can remove the increased free radicals from the body, particularly which we obtain from daily food. Lotus seeds contain huge amounts of unsaturated fatty acids, therefore which increases their longevity due to which they are very popular. It also constitutes a significant amount of glutathione and ascorbic acid and also as well as several physiologically active substances which maintain life processes and activities. These active substances remain as such for or remain unchanged for many years and may contribute to metabolic processes [61]. Extract of epicarp of lotus seeds is a non-toxic antioxidant. It can successfully do the inhibition of differentiation of precursor fat cells. Additionally, the extract of epicarp also helps in delaying lipid oxidation in pork and also used as natural sausage antioxidant additive [62]. The maximum scavenging rate for water-soluble polysaccharides of the aqueous solution of lotus seed on OH radicals was studied to be 29% [63]. SOD generally affects the scavenging of free radicals and maintain the reactive oxygen metabolism's balance, delays organ aging and protects the film structure [64, 65]. Alcohol extract of lotus

seeds improves peroxidize activity in kidney and rat liver, improves SOD and reduces the amount of thiobarbituric acid reactive compounds ^[66]. *Nelumbo nucifera* seed's hydroalcoholic extract (HANN) was inquired for its antioxidant potency which is used in vivo and in vitro models. Lotus seeds consist of several phytochemicals such as polyphenolics, saponins, carbohydrates and alkaloids which supports the antioxidant property of HANN ^[67]. The antioxidant effect of (Yunyupju) which is a Korean traditional lotus liquor was studied by Lee *et al.*, 2005, in which he said that Yunyupju was made from lotus leaves and blossom. The antioxidant effects reached a peak (of about 80% inhibition) at more than the concentration of 25mg of liquor. These effects are dose-dependent. The liquor also exhibited important DPPH scavenging activities ^[68]. DPPH is 2,2-diphenyl-1-picrylhydrazyl which is a free radical assay ^[69].

2. Antifertility activity

The effect of lotus plant on the male reproductive system, its functions and fertility were studied out by Chauhan *et al.* and almost 50% of the ethanolic extract of the seeds was given orally to the male rats at doses of 50, 100, 200mg/rat per day for about 60 days. Therefore the fertility was decreased as a result when this treatment was done and the results were about 100% in *N.nucifera* treated rats. It also declined the testosterone level of serum. Hence, the lotus seed's ethanolic extract showed antispermatic effect in male rats ^[70]. Lotus extract also possesses anti-estrogenic nature without affecting the normal physiology of female rats. It was studied by Anju Mutreja *et al.* (2008) ^[71]. In 1996, Malaya Gupta *et al.* demonstrated the effect of extract of petroleum ether from seeds of lotus on mature male rats and immature female rats. As a result, the study indicated that the steroidogenesis was supposed in both the testis and ovary of male and female rats respectively ^[72].

3. Immunomodulatory activity

Singh Virendra Kumar *et al.* (2011) studied that the hydroalcoholic extracts of seeds and rhizomes possess immunomodulatory activity. It was reported that the extracts show a stimulating effect on the defense system by regulating the immunological parameters. The lotus plant parts also have enough therapeutical benefits in case of immunomodulation ^[73]. Lotus seeds help in various biological activities and additionally, contain a variety of active factors and glycoproteins which activate the human NK, T, and B cells, inducing cytokines and the compliment, hence enhancing the immunity ^[74]. *N.nucifera* seed extract's immunomodulatory activity was estimated using many in vivo models which included the differential and total leukocyte count (DLC and TLC), neutrophil adhesion test, nitrobluephagocytic response, delayed type hypersensitivity reaction (DTH) and phagocytic response ^[46]. The effect of ethyl alcohol extracts of lotus in (PBMC) i.e, primary human peripheral blood mononuclear cells was studied by Liu *et al.*; 2004. The effect was stimulated by PHA (Phytohemagglutinin which is a specific mitogen for T lymphocytes) which inhibited the cytokines production and cell proliferation ^[75].

4. Analgesic activity

Vikrama Chakravarthy P *et al.* (2009) studied the analgesic effect of white and red lotus seeds on Albino rats. 6 groups were divided which constituted 48 adult Sprague Dawley rats. After the experiment, the results revealed that both kinds of lotus seed extracts possess analgesic effect. The more

pronounced activity was shown by the higher dose group with 600mg/kg of white lotus seeds. The analgesic effect can also be evaluated by inhibiting the production of cyclooxygenase of prostaglandin ^[76].

5. Anti-Parkinsonian activity

Nelumbo nucifera's methanolic seed extract was subdivided with chloroform and was studied by M. Vishnu Vardhan Reddy *et al.* (2014) for its anticataleptic and antioxidant effects in haloperidol - Induced catalepsy rat model through measuring many biochemical and behavioral parameters ^[77].

6. Anti-Obesity and hypolipidemic activity

Nelumbo nucifera's ethanolic extract has shown an inhibitory effect on adipogenesis and reported a beneficial effect in reduction of adipose tissue weights, modulating serum leptin level in rats with a high-fat diet. It also ameliorated the blood lipid profile ^[45]. Antiobesity efficacy of active constituents extracted from lotus leaves through stimulated lipolysis in mice adipose tissue was studied by Ohkoshi *et al.*, 2007. Flavonoids like catechin, astragalin, quercetin, hyperoside, and isoquercitrin showed lipolytic activity in visceral adipose tissue ^[50].

7. Antiviral activity

Kuo *et al.* 2005 studied the inhibitory effects of ethanolic extracts of lotus seeds in herpes simplex type 1 (HSV-1). 100 mg/ml of ethanolic extract suppressed HSV-1 replication (IC₅₀ for replication, 50.0 mg/ml) ^[47]. Kashiwada *et al.*; 2005 extracted (-)-1(5)-norcoclaurine, quercetin 3-O-beta-D-glucuronide, and (+)-1(R)-coclaurine from lotus leaves. The two latter compounds show therapeutic activity against HIV with EC₅₀, 2mg/ml, therefore it was less potent ^[23].

8. Neuropharmacological activity

N.nucifera Gaertner seed's neuropharmacological activities were shown in rats and mice. The extracts effect on phenobarbitone sodium motor coordination activity, anxiolytic activity, induced sleeping time and sleep latency, locomotor activity, cerebral activator activity was examined. In a dose-dependent manner, the extract also showed significant depression in common behavioral tests ^[78].

9. Psychopharmacological activity

Neferine which is present in lotus seed embryo may have anti-depressant activity. This was evaluated by its anti-mobility effects on mice in a forced swimming test 94. Neferine is a direct hydroxytryptamine (S-HT) 1 A receptor agonist and it may do the inhibition of S-HT reuptake or may do the activation of S-HT metabolism. Its effect can be compared with imipramine and maprotiline ^[79].

10. Antidiarrheal and Antidermatophytic activity

Lotus seed oil's antidiarrheal activity was examined and it vigorously inhibited the strains such as *Escherichia coli*, *Shigella sp.*, *Pseudomonas sp.*, *Salmonella sp.*, *Staphylococcus aureus* and *Klebsiella* by disk diffusion method. The inhibitory effect of lotus seed oil was used against dermatophytes like *Trichophyton mentagrophytes*, *Malassezia furfur* and *Trichophyton rubrum* with the 25mg/ml of extract concentration ^[80].

11. Hepatoprotective activity

Extracts of ethanol from lotus seeds are seen to have hepatoprotective effects against cytotoxicity caused by carbon

tetrachloride and production of serum enzymes. The extract is used for protection against cytotoxic and genotoxic effects of aflatoxin B1 ^[69].

12. Hypoglycemic activity

The experiment of hypoglycemic activity of inorganic constituents in lotus seeds on Streptozotocin-induced diabetes in rats was studied by Sivasankari *et al.* The trace elements present in ash of seed is seen to play an indirect or direct role in the secretion of Insulin or works in a synergetic manner to control normoglycemia ^[81]. A methanolic extract of rhizome was taken which amazingly decreased the blood sugar level of normal, Streptozotocin-induced and glucose - fed hyperglycaemic diabetic rats when compared with other control animals. This was to demonstrate the oral hypoglycaemic effect of lotus ^[82]. From the lotus rhizome's nodes, tryptophan (an antidiabetic constituent) has been extracted by analysis of spectroscopic evidence ^[83].

13. Reduction of Pulmonary Fibrosis

Bleomycin-induced pulmonary fibrosis in mice can be reduced by the Isoliesinine which is isolated from seeds. The protective effect also reduced the effect of inflammatory mediators ^[84]. The inhibitory effect of neferine on amiodarone-induced pulmonary fibrosis was studied by Niu *et al.*; 2013. The effect was due to its potential for anti-inflammation ^[85].

14. Gastrointestinal activity

Probiotics are such a class of bacteria that helps in the regulation of the gastrointestinal tract of humans and also promotes absorption and digestion. Lotus seeds are seen to have a role in the promotion of probiotics proliferation. Lotus seed starch's effect on proliferation of bifidobacteria is same as of isomaltooligosaccharide ^[86]. Functional dyspepsia, diarrhea, constipation, and other gastrointestinal disorders come under absorption disorders and gastrointestinal motility. Development of dietary supplements has taken place, meanwhile, new dairy products are made like milk or fermented seeds of lotus. It can set gastrointestinal motility ^[87]. Lotus seed fermented milk can also manage the intestinal flora, enhances intestinal immune function and protects the gastrointestinal mucosal barrier ^[88].

15. Antibacterial activity

Polyphenols of lotus seeds are complex phenolic secondary metabolites. These have powerful inhibitory effects on bacteria and microorganisms. These are the same as that of tea polyphenols ^[89].

16. Anti-inflammatory activity

Tissue inflammation is harmful and it can cause tissue injury and lead to diseases like atopic dermatitis, rheumatoid arthritis, and asthma ^[90]. Pieces of evidence have been found which say that cytokines released by T cells such as IL-10, IL-4 in reaction to antigen stimulation play a part in lung inflammation and asthma ^[91]. Triterpenoid betulinic acid is extracted from lotus rhizome and it shows anti-inflammatory activity against edema. Edema is caused by carrageenan and serotonin in the rat paw ^[92].

17. Antipyretic activity

The antipyretic potential of lotus's stalk ethanol extract was studied by Sinha *et al.*; 2000. The extract was applied on normal body temperature and yeast induced pyrexia by using

rat in in vivo model. 200mg/kg dose of extract declines the body temperature for 3 hours after application, while 400mg/kg dose declines the temperature for up to 6 hours ^[93].

18. Other activities

Lotus seeds possess various other activities like anti - ischaemic activities, antiarrhythmic ^[94], anticancer ^[95, 96, 97, 98], antiaging activity ^[99, 100], antiproliferative, Atherosclerosis ^[101, 102], and treatment for erectile dysfunction ^[103, 104, 105].

Conclusion

The plant, *Nelumbo nucifera*, has gained much popularity due to its nutritional, medicinal and historical importance. Many bioactive compounds are present such as flavonoids, antioxidants, alkaloids, etc. Many pharmacological studies have defined that the plant has antioxidant property, anti-inflammatory, antidiarrheal, immunomodulatory, antibacterial, aphrodisiac, lipolytic, anticancer, hepatoprotective, antifertility, psychopharmacological, diuretic, antipyretic, antiplatelet and cardiovascular activities. Lotus plant consists of a variety of chemical constituents. So lotus plant is of great pharmaceutical importance. It can efficiently be used to combat different human disease conditions. In addition, there is also a need to conserve this plant which is a treasure because of the habitat of the lotus plant is being polluted and threatened. So the lotus is of great significance to mankind.

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