PHARMACOGNOSTIC AND PHARMACOLOGICAL PROFILE OF *LAGENARIA SICERARIA* (MOLINA) STANDLEY: A REVIEW

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Summary

Many herbal plants are used in various medical systems for the treatment and management of various diseases. The plant *Lagenaria siceraria* has been used in different system of traditional medication for the treatment of diseases and ailments of human beings. The plant contains various phytochemical constituents like, triterpenoid, cucurbitacins, flavones, vitamin B, C-glycosides beta glycosides and fair source of ascorbic acid in fruits. It has been reported that the fruits have cardioprotective activity. The leaves of this plant possess antioxidant activity. The plant has been studied for their various pharmacological activities like, antioxidant, cardioprotective, diuretic, immunomodulatory effects, hepato protective, lipid peroxidation and anti-inflammatory activity. The plant is cultivated in different parts of India on a small scale at present. However, systemic information on different aspects of this species is not available. In this review, an attempt has been made to present this information.

Key words: Lagenaria siceraria, cardioprotective activity, phytochemical constituents.

Introduction

The traditional Indian medicinal system mentions herbal remedies for the treatment of various diseases. There exists a plethora of knowledge and information and benefits of herbal drugs in our ancient literature of Ayurvedic and Unani medicine.[8] Herbal medicines are promising choice over modern synthetic drugs. They show minimum/no side effects and are considered to be safe. According to the WHO survey, 80% of the populations living in the developing

countries rely most on traditional medicines for their primary health care needs. Exploration of the chemical constituents of the plants and pharmacological screening may provide us the basis for developing the leads for development of novel agents.[6,8] Therefore laboratories around the world are engaged in screening of plants for biological activities with therapeutic potential. Pharmacognosy is a reliable tool, by which complete information of the crude drug can be obtained. *Lagenaria siceraria* (Molina) Standley [Family: Cucurbitaceae], commonly known as Bottle guard, an excellent fruit in the nature having composition of all the essential constituents that are required for normal and good health of humans.[10-12] The plant enjoys the reputation of being one of the earliest plant to be domesticated on the earth. *L.siceraria* cures pain, ulcers, fever, asthma and other bronchial disorders. Its fruit is traditionally used for its cardioprotective, cardiotonic, general tonic and aphrodisiac properties. The seed oil is applied in headach. Lagenin- a novel ribosome inactivating protein has been isolated from the lyophilized water extract of seeds which is known to possess immunosuppressive, antitumour, antiviral, antiproliferative and anti-HIV activities.

Taxonomical Classification:[10-12,]

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Cucurbitales
Family: Cucurbitaceae
Genus: Lagenaria
Species: *L. siceraria*
Part used: Fruit, root, leaves and seed oil

CULTIVATION AND COLLECTION:

The cultivated form of *L. siceraria* is considered to be of African and Asian origin. *L. siceraria*, popular vegetable, grown almost all the year round, particularly in frost free areas. It can be cultivate in all kinds of soil, but thrives best in heavily manured loams. It required warm humid climate or plenty of watering when grown during dry weather. Seeds may be sown in nursery beds and seedlings transplanted when they have put forth 2-3 leaves. They may be also sown directly, 4-5 seeds together, in mannured bed or pits 5-6ft. apart; the strongest among the seedlings is retained, while others are removed and transplanted. Seedling transplantation is where an early crop is desired, generally two crop raised in India; the summer crop is sown from

the middle of October to the middle of March and the later crop, from the beginning of March to the Middle of July. Round fruit types are usually sown for the early crop and bottle–shaped types for the second crop. Vines are allowed to trail on the ground or trained over walls.

MACROSCOPY:

Lagenaria is a large pubescent, climbing or tailing herb with stout 5-angled stems and bifid tendrils. Leaves are long, petioled, 3-5 lobed, 10-40 cm wide, slightly hairy on both sides. Fruits are large, up to 1.8 m long, fruit bottle shaped with a hard shell- like epicarp when ripe; numerous seeds, long, white, smooth, 1.6- 2.0 cm long. Flowers, white, large, solitary. Petals are ovate, 3-4 cm long. Calyx is green, mottled gray or white, usually club-shaped or ovoid or depressed-globose, as thick as it is long. [4,10-12,17]

MICROSCOPY

Transverse section of *Lagenaria siceraria* leaf showed following features: Upper epidermis consists of elongated parenchymatous cells, covered by cuticle. It shows few stomata, which are of anisocytic type. Lower epidermis contains elongated wavy walled parenchymatous cells, covered by cuticle. Number of covering and collapsed trichomes are present, while very few glandular trichomes are also present. Palisade cells are present at upper and lower epidermis. It shows hexagonal to polygonal, large, thin walled colourless cells, and may be water storing. Mesophyll is made up of 3-4 layered chloroplast containing, compactly arranged, oval to circular cells. It is interrupted by vascular bundles of various sizes. Vascular bundles are surrounded by 2-3 layered sclerenchyma. They are conjoint, collateral and closed. Xylem is placed towards upper epidermis and phloem towards lower epidermis. [4,10-12,17]

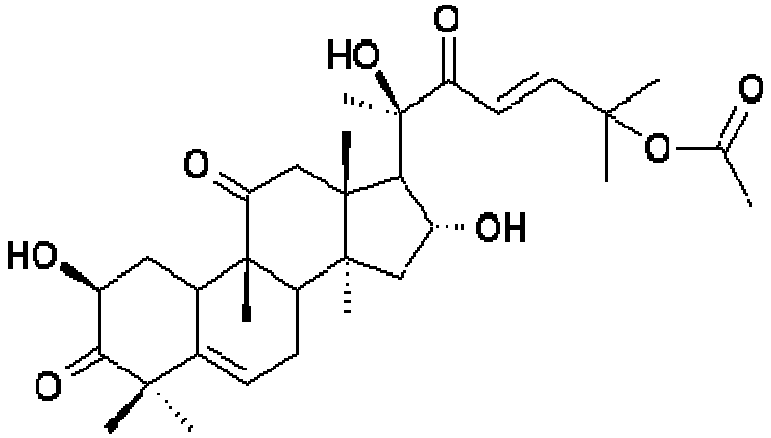
PHYTOCHEMISTRY[10-13,17]

Fruits: The amino acid composition of the fruit is as follows: leucines 0.8; phenylalanine 0.9; valine 0.3; tyrosine 0.4; alanine 0.5; threonine 0.2; glutamic acid 0.3; serine 0.6; aspartic acid 1.9; cystine 0.6; cysteine 0.3; arginine 0.4 and proline 0.3mg/g. The fruit is a good source of B vitamins and a fair source of ascorbic acid. Bitter fruits yield 0.013% of solid foam containing cucurbitacins B, D, G and H, mainly cucurbatacin B; these bitter principles are present in the fruit as aglycones. Phytochemical screening of the fruit revealed two steroids: fucosterols and campesterol.

Leaves: Leaves contain cucurbitacin B.

Roots: Roots contain cucurbitacins B, D, and E.

cucurbitacin B



Seeds: Seeds are reported to contain saponin. The oil obtained from the seed kernels is clear and pale yellow. Kernels from ripe seeds give 45% of oil with the following characteristics: iodine value,126.5; free fatty acids,0.54%; and unsaponified matter, 0.67%. The components of free fatty acids are: linoleic acids, 64.0; oleic, 18.2; and saturated fatty acids, 17.8%. Seeds are reported to contain Lagenin.

PHARMACOLOGY:

Diuretic activity

Study of the juice extract and methanol extract of *Lagenaria siceraria* showed significant diuretic potential, comparable to that of furosemide. Ghule,et al[7,8].(2007) evaluated *Lagenaria siceraria* for its diuretic activity in albino rats. The rats treated with vaccum dried *Lagenaria siceraria* juice extracted (LSJE) and *Lagenaria siceraria* methanol extract (LSME) (100-200 mg/kg; p.o.) showed higher urine volume when compared to the respective control. Dose–response studies showed the maximal activity at 200 mg/kg, p.o. by LSME and LSJE. The excretion of sodium, potassium and chloride has also been significantly increased. The elevated diuretic potential of LSFE and LSME was statistically comparable to that of the standard diuretic agent furosemide (20 mg/kg; i.p.). The result obtained in the study indicate that LSJE and LSME act as effective hyper natremic , hyperchloremic and hyper kalemic diuretics (increased Na+ ,K+ and Cl- excretion volume).

Antioxidant activity

Results showed that fresh fruit extract exhibited higher DPPH (2, 2-diphenyl-1,1-picryl hydrazyl) radical scavenging activity than other samples. Both fresh and dried fruits may give relatively similar antioxidant effects. In DPPH radical scavenging assay, the antioxidants react with the stable free radical DPPH and convert it to 1,1-diphenyl-2-picryl hydrazine with decoloration. The scavenging effects of extract increased with their concentrations to similar extents. The ethanol extract of *Lagenaria siceraria* showed strong H_2O_2 scavenging activity.[8]

Cardioprotective activity

M.Hassanpour Fard et al[3]. (2008) investigated the Cardio protective activity of *Lagenaria siceraria* (LS) fruit powder against doxorubicin induced cardio toxicity in rats. Male wister rats (250-300 g) were randomly divided into three groups. Group 1 was control (gum acacia 2%), Group 2- doxorubicin (10 mg kg-1), and Group 3- doxorubicin with LS (200 mg kg-1 for 18 days). *Lagenaria siceraria* (LS) administration significantly decreased QT ($p<0.01$) and ST ($p<0.05$) while non significant increased in heart rate, significant decreased in serum creatinekinase-MB isoenzyme, aspartate aminotransferase ($p<0.001$) and lactate dehydrogenase($p<0.05$) as compared to Doxorubicin group. While, there was significant increase in the level of glutathione ($p<0.05$) and non significant increased in superoxide dismutase, there was lipid per oxidation ($p<0.01$) was inhibited as compared to Doxorubicin group. Histopathological study of *Lagenaria siceraria* (LS) treated group showed protection against myocardial toxicity induced by Doxorubicin.

Immunomodulatory effects

Study of the methanolic extracts of the fruit of LS showed significant dose-dependant delayed hypersensitivity reaction in rats with increase in white cell and lymphocyte count. Results suggest a promising immunomodulatory activity. Rana A.C.et al. (2008) has been studied the immunomodulatory effect of n-butanol soluble and ethyl acetate soluble fractions of successive Methanolic extract of Lagenaria siceraria fruits in rats. Oral administration of the fractions at doses 100, 200 and 500 mg/kg significantly inhibited delayed type hypersensitivity reaction in rats. Delayed type hypersensitivity response was induced in rats by the method of Doherty. Groups of six rats per treatment were immunized by injecting 20 El of Sheep red blood cells suspension (5x109 SRBC/ml) subcutaneously into right hind foot pad. Seven days later they were challenged by injecting 20 El of Sheep red blood cells suspension (5x109 SRBC/ml) intradermally into the left hind foot pad. The day of immunization was referred to as day 0. Blood samples were collected from all the animals separately by retro orbital puncture on day +7 (before challenge) for primary antibody titre and on day +14 for secondary antibody titre. Antibody levels were determined by the method described by Shinde et al. Serum (25 El) of each rat was taken in microtitre plates. To serial two –fold dilutions of pooled serum (made in 25 E l normal saline) was added 25 El of 1% v/v Sheep red blood cells suspension in normal saline. The microtitre plates were kept at room temperature for 1 hour and then observed for haemagglutination (until control wells showed unequivocally negative pattern). The value of the highest serum dilution showing haemagglutination was taken as the antibody titre. The extracts were fed orally once daily, starting with 7 days prior to sensitization till the challenge (-7,-6,-5,-4,-3,-2,- 1,0,+1,+2,+3,+4,+5,+6,+7). n-butanol and ethyl acetate soluble fractions of successive methanolic extract of Lagenaria siceraria fruits dose dependently and significantly inhibited Sheep red blood cells induced delayed type hypersensitivity reaction response as indicated by decrease in foot pad thickness of rats compared to control group . Both the fractions, significantly increased haemagglutination antibody titre in dose dependent fashion , Both the fractions, significantly increased total WBC, neutrophil and lymphocyte counts, while insignificant change were observed in monocyte, eosinophil and basophil counts. A dose-dependent increase in both primary and secondary antibody titre was observed. The results suggest that test fractions possess promising immunomodulatory activity.[15]

Antihyperlipidemic activities

Study of fruit extract of *L.siceraria* significantly reduced the total cholesterol, LDL and triglycerides and suggests a potential household remedy for hyperlipidemia[19]. Study of methanolic extract of *L.siceraria* demonstrated an antihyperlipidemic potential with significant elevation of HDL cholesterol. Results also provided a valid scientific basis for consumption for the treatment of coronary heart diseases in India.

Anthelmintic activity:

In a study using Pheretima posthuma as test worms, the methanol and benzene extracts significantly demonstrated paralysis and death of worms, compared to a standard of piperazine. Results confirm the traditional use of the seeds of the plant as an antihelmintic.

Anti-Inflammatory activities

B.V. Ghule et al[2] (2006) investigated anti-inflammatory effects of Lagenaria siceraria (Molina) Stand. Fruit juice extract (LSFJE) in rats and mice. LSFJE was studied for its analgesic effect on acetic acid-induced writhing and formalin pain tests in mice. The anti-inflammatory effects were investigated employing the acute inflammatory models, i.e. ethyl phenylpropionate-induced ear edema, carrageenin- and arachidonic acid-induced hind paw edema, and also the albumin-induced paw edema in rats.

Hepato protective activity

Shirwaikar A et al.[5](1996) reported hepatoprotective activity was assessed by examining the influence of the ethanolic extract of Lagenaria siceraria (EELS) (in doses 100 and 200 mg/kg) on hepatotoxicity induced by administration of CCl4 (30% in liquid paraffin). Sylamarin (100 mg/ kg, po) was use as standard. Blood was collected from retroorbital plexus under light ether anesthesia on 15th day for analysis of level of serum glutamate oxaloacetate transminase (SGOT), serum glutamate pyruvate transminase (SGPT), alkaline phosphatase (ALP). Acid phosphatase (ACP) and bilirubin. Histopathalogy of the hepatic cell was carried by using hematoxylin-eosin dye to stain the cells of rats sacrificed under light ether anesthesia. Protein content, lipid per oxidation, superoxide dismutase, and glutathione peroxidase was determined by homogenizing the remaining hepatic tissue in 0.1 M PBS (ph 7.4). Administration of the ethanolic extract of Legenaria siceraria fruit (EELS) orally to different groups of rats reduced the level of SGOT, SGPT, ALP, ACP enzymes, all fractions were tested, in a dose of 250 mg/kg showed significant activity, with the petroleum ether fraction exhibiting comparatively higher activity and this was attribute to fucosterol and camp sterol isolated from the petroleum ether fraction.

Hyperthyroidism, Hyperglycemia and Lipid Peroxidation

Yamini Dixit et al.[16](2008) reported the study of Lagenaria siceraria Peel Extract in the Regulation of Hyperthyroidism, Hyperglycemia and Lipid Peroxidation in Mice. In an in-vitro study the quenching potential of the peel extract (5-100 µg/ml) on the 1, 1-diphenyl-2-picrylhydrazyl (DPPH)- dependent free radicals was examined. Antioxidative potential was also studied in carbon tetrachloride (CCl4) - and hydrogen peroxide (H2O2)-induced lipid

peroxidation (LPO) in liver tissues. In another experiment, an in-vivo study was performed considering three different concentrations of the test peel extract to select its most effective and safe dose for the regulation of hepatic lipid peroxidation (LPO), thyroid function and glucose metabolism. Out of 50, 100 and 200 mg/kg of the peel extract, 100 mg/kg was found to be the most effective and safe concentration, as it could inhibit the levels of serum thyroxine (T4), triiodothyronine (T3) and glucose as well as hepatic Lipid Peroxidation (LPO). Considering this dose, finally the antithyroidal, antiperoxidative and glucose inhibitory potential of the peel extract were tested in T4-induced hyperthyroid animals. After 21 days of treatment, a decrease in the concentrations of serum thyroid hormones, glucose as well as in hepatic lipid peroxidation (LPO) with a parallel increase in antioxidants such as superoxide dismutase (SOD), catalase (CAT) and glutathione (GSH) indicated the efficacy of the test peel in the amelioration of hyperthyroidism, hyperglycemia and hepatic lipid peroxidation.

MEDICINAL USES

The pulp around the seed is emetic and purgative. A poultice of the crushed leaves has been applied to the head to treat headaches. The flowers are an antidote to poison. The stem bark and the rind of the fruit are diuretic. The fruit is antilithic, diuretic, emetic and refrigerant. The juice of the fruit is used in the treatment of stomach acidity, indigestion and ulcers. The seed is vermifuge. A poultice of the boiled seeds has been used in the treatment of boils. Extracts of the plant have shown antibiotic activity. In many parts of China 3 grams per day of this species (the report does not say what part of the plant) has been used as a single treatment for diabetes mellitus.

Conclusion

Medicinal plants play an important role in the lives of rural people, particularly in remote parts of developing countries with few health facilities. The present review reveals that Lagenaria siceraria is utilized for the treatment of various diseases. In the present review I have congregated information pertaining to botanical, phytochemical, pharmacological studies. The plant has been studied for their various pharmacological activities like antioxidant, antihyperglycemic, antihyperlipidemic, cardio protective, immunomodulatory effects, hepato protective, hyperglycemia and lipid peroxidation, analgesic and anti-Inflammatory, diuretic activity studies have also been studied. The fruits of this plant possess cardio-protective activity.

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