



Phytochemical and Pharmacological profile of *Citrullus lanatus* (THUNB)

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ABSTRACT

Citrullus lanatus Thunb (Family: Cucurbitaceae) is a medicinal plant widely used traditionally in the treatment of various disorders in world. The phytochemical evaluation of plant showed presence of carbohydrate, alkaloids, steroids, saponins, glycoside, flavonoids, tannins and phenolic compounds. The plant also showed presence of vitamins, amino acids, proteins, minerals and fat. The plant has been extensively studied by various scientist and researchers for its pharmacological activities and therapeutic approaches such as antibacterial, antifungal, antimicrobial, antiulcer, antioxidant, anti-inflammatory, gastroprotective, analgesic, laxative, antiangiardial, hepatoprotective, against prostetic hyperplasia and atherosclerosis. The present review is an effort to provide detailed information of its uses, chemical composition, pharmacological activities of extract and its isolated compounds and safety profile of *Citrullus lanatus* for further research.

Keywords: *Citrullus lanatus*, Cucurbitaceae, Citrulline, Giardiasis.

INTRODUCTION

Cucurbitaceae is the largest family containing 120 genera and approximately 825 species typically distributed in the tropical countries poorly represented in the temperate regions. The vegetable crops of family Cucurbitaceae are important horticultural crop, mostly grown for its sweet and juicy fruit in warm climates all over the world. Cucurbitaceae are important source of food like pumpkin (*Cucurbita pepo*), melon (*Cucumis melo*), cucumber (*Cucumis sativa*), water melon (*Citrullus lanatus*), *Lag enaria siceraria* (bottle gourd), and

Luffa cylindrica (sponge gourd). The *Citrullus lanatus* L) is one of the most popular species with high water content as high as 92% of the total weight ¹. The plant is traditionally used for centuries in the treatment of various health ailments. It is an important medicinal plant in the Ayurveda and Indian traditional system of medicine ². The plant is rich in flavonoids, alkaloids, saponins, glycoside, tannins and phenols. Its nutritive values are also useful to the human health. The plant has been extensively studied by various scientist and researchers for its pharmacological activities and therapeutic approaches such as antibacterial, antifungal, antimicrobial, antiulcer, antioxidant, anti-inflammatory, gastroprotective, analgesic, laxative, antiangiardial, hepatoprotective and against prosthetic hyperplasia and atherosclerosis. Fruit is used in cooling, strengthening, aphrodisiac and astringent to the bowels, indigestible, expectorant, diuretic, and stomachic, blood purifier. It also allays thirst, cures biliousness, good for sore eyes, scabies and itches and as brain tonic to the brain [1]. The present review focus on phytochemical, pharmacognostic, pharmacological and toxicity updates of this plant.

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Botanical Description:**Taxonomy:**Botanical name: *Citrullus lanatus* (Thunb)

Class: Equisetopsida

Kingdom: Plantae

Genus: Citrullus

Family: Cucurbitaceae

Order: Cucurbitales

Vernacular names:

Common name: Watermelon, Wild Watermelon

Local name: Tarbooz

English: Watermelon

Marathi: Tarbooz, Kalingad

Bengali: Tormuz

Malayalam: Thannimathan

Kanada: Kallagadi

Assamese: Tarmuj

Telugu: Pendalam

Tamil: Kizhangu

Figure-1. *Citrullus lanatus* (Thunb)**Morphological characters:**

Citrullus lanatus is a prostrate or climbing annual with several herbaceous, rather firm and stout stems up to 3 m long; the young parts are densely woolly with yellowish to brownish hairs while the older parts become hairless. The leaves are simple, alternate on long petioles, cordate with seven shallow lobes and variously serrated margins, very hairy on the abaxial surface, acute, deep green, and about 7 – 15 cm in diameter. Tendrils are simple and spiral. Male and female flowers grow on the same plant. Male flowers are found in clusters and appear before the female flowers. Both have yellow petals, five in number, and sepals, also five in number and greenish in color. Occasional hermaphrodite flowers are produced. The fruits are globular with shallow grooves, about 14 – 20 cm long. The skin is greenish yellow. The flesh is almost white/light yellow, sweet, delicately flavoured, juicy, a pepo. The seeds are small, light brown and smooth, between 0.4 and 1.1cm long and 0.2 – 0.3 cm wide ³.

Traditional claims:

Citrullus lanatus (Thunb) is used as anthelmintic, anticancer, antibacterial, demulcent and diuretic being used in the treatment of dropsy and renal stones ⁴. The rind of fruit is prescribed in case of alcoholic poisoning and diabetes. The root is purgative and in large doses emetic. The seed is demulcent, diuretic, pectoral and tonic. It is sometimes used in treatment of bed wetting. Seeds are also vermifuge and have hypotensive action. Fatty oils in the seeds as well as in aqueous and alcoholic extracts paralyze tapeworms and roundworms. In Northern Sudan, it is often used for burns, swellings, rheumatism, gout and as laxative ⁵. Fruits of this plant are eaten as febrifuge when fully ripe or when almost putrid. It is also used in case of energy source, cleanses and purifies kidney and bladder, prevent erectile dysfunction and used to treat hepatomegaly and jaundice ^{6,7}.

Chemical Constituents:

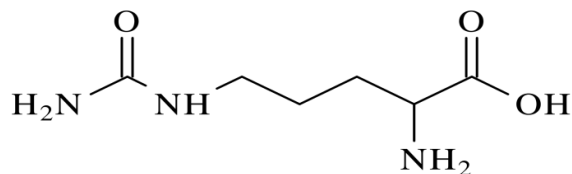
Citrullus lanatus seed contains phytochemical constituents like alkaloids, flavanoids, tannins, amino acids, carbohydrates, cardioglycosides, terpenoids, steroids, carotenoids, oils and fats ⁵. The amino acid citrulline was first extracted from watermelon and analyzed. The nutritional quality of watermelon shows that it is very rich in vitamins A 3%, different vitamins from vitamin B complex like Thiamine (Vit. B1), Riboflavin (Vit. B2), Niacin (Vit. B3), Pantothenic acid (B5), vitamin B6 and Folate (Vit. B9) which ranges between 1-3%, Vitamin C 14%. The mineral composition is Calcium 1%, Iron 2%, Magnesium 3%, Phosphorus 2%, Potassium 2% and Zinc 1%. Along with it, it also contains highly unsaturated fatty acids and oils. It is also rich in essential amino acids like arginine, glutamine and aspartic acid ⁸.

Pharmacology:**Antibacterial activity and antifungal activity:**

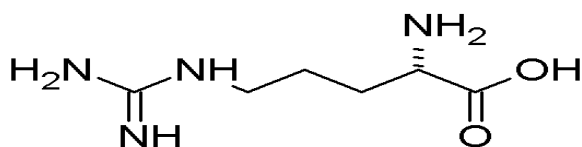
Crude extract of watermelon seeds using hot water, cold water, methanol and ethanol showed the antimicrobial activity using the standard disc diffusion assay method against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae* and *Bacillus cereus*. All the seed extracts showed evidence of antibacterial properties ⁹.

In another study, crude extract of *Citrullus colocynthis*, *Citrullus lanatus* and *Citrullus vulgaris* were very effective against bacteria and some fungal strains. The ethanolic extract was found more effective than respective aqueous and chloroform extract. The zone of inhibition was found maximum in E-coli and minimum in *Staphylococcus aureus*. Fungal zone of inhibition was found more in *Candida albicans* and less in *Trichosporon Begelii* ¹⁰.

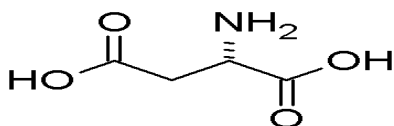
Figure-2. Amino acids in *Citrullus lanatus*
(a-Citrulline, b-Glutamine and C-Aspartic acid)



(a)



(b)



(c)

Antimicrobial activity:

The antimicrobial effects of chloroform of *Citrullus lanatus* extracts against the studied bacteria suggest that, different parts of plant possess remarkable therapeutic action that can support the traditional usage of this plant in the treatment of bacterial and fungal diseases such as gastrointestinal infection, diarrhea, respiratory and skin diseases. These antimicrobial activities are likely due to the presence of secondary metabolites like tannins and flavonoids, alkaloids, saponins, terpenes and steroids in plant. The high potency of *Citrullus lanatus* against these microbes could provide an example of prospecting for new compounds⁶. In another study, antimicrobial efficacy of *Citrullus lanatus* and other citrullus plants were evaluated against gram negative, positive and some fungal strains including *E-coli*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Bacillus subtilis* and *Bacillus pumilus* some fungal *Candida albicans*, *Aspergillus niger*, *Penicillium chrysogenum* using agar well diffusion method at concentration 100 mg/mL. In this, almost all species of plants were found to have activity on at least two microbial strains⁷. Determination of antimicrobial activity of methanol extract of *Citrullus lanatus* seed was carried out against 10 bacterial species (*Staphylococcus aureus*, *Klebsiella pneumoniae*, *Bacillus subtilis*, *Escherichia coli*, *Salmonella typhi*, *Enterococcus faecalis*, *Vibrio cholerae*, *Shigella dysenteriae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*) and 5 fungal species (*Aspergillus flavus*, *Aspergillus niger*, *Penicillium notatum*, *Trichophyton mentagrophytes*, *Candida albicans*). Inhibition zones formed by the extract were

compared with the standards: Streptomycin and Amphotericin B. The methanolic seed extract at a concentration of 1000 µg/ml was effective against bacteria: *Vibrio cholerae* (7 mm), *Proteus mirabilis* (7 mm), *Shigella dysenteriae* (7 mm), *Staphylococcus aureus* (6 mm), *Escherichia coli* (6 mm), *Enterococcus faecalis* (6 mm), *B. subtilis* (6 mm), *Salmonella typhi* (5 mm) and fungi: *Aspergillus niger* (13 mm), *Aspergillus flavus* (12 mm), *Penicillium notatum* (11 mm), *Candida albicans* (9 mm). The results of *Citrullus lanatus* seed extract demonstrated antimicrobial activity against the organisms tested¹¹.

Antiulcerative activity:

Methanolic extract of *Citrullus lanatus* (MECL) seeds showed maximum antioxidant potential and was evaluated for its anti-ulcerogenic activity by Pyloric Ligated (PL) and Water Immersion Stress (WIS) induced ulcer models in rat. Gastric volume and free and total acidity were measured in PL model whereas; ulcerative index was measured in both the models at 100, 200 and 300 mg/kg doses of MECL. Rats treated with MECL (300 mg/kg) showed significant decrease in the gastric volume, free acidity and total acidity in case of PL model and showed significant percentage inhibition of ulcer as indicated by decrease in ulcerative index in both the models. The extract of *Citrullus lanatus* seeds possesses good antioxidant and anti-ulcer activity¹². In another study, the presence of secondary metabolites such as flavonoids, tannins, saponins, terpenoids claimed to present in the most members of the Cucurbitaceae family. Proximate and metal content analysis of the seeds provides information that the consumption of the seeds of *Citrullus lanatus* is safe. This study also provides preliminary data for the first time that the seeds of *Citrullus lanatus* possesses significant anti-ulcer activity in animal model. The anti-ulcer activity is probably due to the presence of bioactive compounds like flavanoids, saponin and tannins. Further studies are required to confirm the exact mechanism underlining the ulcer healing and protecting property of the extract and to identify the chemical constituents responsible for it¹³. The antiulcer activity of crude methanolic extract of *Citrullus lanatus* seeds in two different ulcer models in albino Wistar rats was also studied. The extract at 300 mg/kg body weight, once daily orally for 7 days has a significant effect in pyloric ligation (PL, 4 h ligation) and in water immersion (WS, 25 °C for 3 h) stress induced ulcer model, as it showed protection index of 57.33% and 63.38% respectively which is comparable to the standard drugs (Ranitidine 50 mg/kg) and Omeperazole (20 mg/kg body weight) that have shown protection index of 64.47% and 70.59% in PL and WS model respectively¹⁴.

Antioxidant activity:

The In-vitro anti-oxidant activity of the n-Hexane, Chloroform and Ethanol extract of *Citrullus lanatus*

seeds were studied using 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity, Ferric reducing power activity, Hydrogen peroxide (H₂O₂) scavenging activity and Nitric Oxide (NO) scavenging activity. The total Phenolic contents and Flavanoid contents were estimated taking Gallic Acid and Quercetin calibration curve respectively. In this study, it was found that all the extracts possess In-vitro antioxidant activities. But the order of possessing activities were n-hexane > ethanol > chloroform extracts of *Citrullus lanatus* seeds [15].

Anti-inflammatory activity:

Citrullus lanatus seed oil is extracted with n-hexane and tested for in-vivo and in-vitro anti-inflammatory activity. The oil was screened for in-vivo anti-inflammatory activity by Carrageenan-induced paw edema in rat model and In-vitro anti-inflammatory activity by human red blood cell membrane stabilization method. The potency of the oil was compared with standard Diclofenac (10 mg/kg). The oil showed significant reduction of edema in Carrageenan induced Rat Paw Edema Model maximum at 3 hr (percentage reduction in paw volume 44.44%, 55.56% and 63.11% for CLSO (50 mg/kg), CLSO (100 mg/kg) and diclofenec (10 mg/kg) respectively and CLSO at concentration of 100, 250 and 500 mcg/ml showed 42.35%, 68.48% and 78.50% protection of human red blood cell membrane in hypotonic solution respectively [16]. In another study, mouse model with ear edema induced by xylene and the rat model with paw edema or granuloma by carrageenan or cotton pellet were used for anti-inflammatory effect of the *Citrullus lanatus* aqueous extract. Effects of the extract on analgesia was tested respectively by measuring the latency of mice licking hind foot from hot plates and by counting the times of body twisting in response to acetic acid. The extract significantly inhibited the ear edema, granuloma hyperplasia and paw edema. It significantly lifted pain threshold on mouse hot-plate responses and reduced their writhing time [17].

Gastroprotective Activity:

Gastroprotective potential of *Citrullus lanatus* fruit pulp aqueous extract (CLE) on pyloric ligation and indomethacin induced ulcer model in wistar albino rats was evaluated. In indomethacin induced ulcer model, CLE was administered in the doses of 250 mg/kg, 500 mg/kg & 1000 mg/kg body weight orally for five days for three times in a day after the induction of ulcer. The extent of healing was determined via reduction in ulcer index and alteration in various biochemical parameters in gastric mucosa. In pyloric ligation model, CLE resulted in significant increase in pH, enzymic antioxidants i.e. Superoxide dismutase & Catalase, with a significant decrease in volume of gastric juice, free and total acidity, protein & carbohydrate concentration and Lipid peroxidase

levels. The presence of the flavonoids and polyphenols may be responsible for the gastroprotective effect of CLE [18].

Activity against prosthetic hyperplasia:

Administration of MECLS for one month reduced the prostate size significantly ($P < 0.05$), both at high and low dose, but could not restore the initial size of shrunken testes and severe oligospermia caused by the hormones. The histological studies clearly establish MECLS as a potential candidate in management of androgen dependent conditions like benign prostate hyperplasia [8].

Laxative Activity:

The laxative activity was determined based on the weight of the fecal matter. The effects of the aqueous fruit pulp extract of *Citrullus lanatus* and reference standard on the gastro intestinal motility rate were also evaluated. Phytochemicals screening of the extract revealed the presence of flavonoids, tannins, polyphenols, sterols and polyterpenes. The aqueous fruit pulp extract of *Citrullus lanatus* administered orally at three different doses produced significant laxative activity and reduced loperamide induced constipation in dose dependant manner. The effect of the extract at 500 and 1000 mg/kg (p.o.) was similar to that of reference drug sodium picosulfate (5 mg/kg, p.o.). The same doses of the extract (500 and 1000 mg/kg, p.o.) produced a significant increase ($p < 0.01$) of intestinal transit in comparison with castor oil (2 ml) ($p < 0.01$). The results showed that the aqueous fruit pulp extract of *Citrullus lanatus* has a significant laxative activity [19].

Antigiardial Activity:

Antigiardial activities of *Citrullus lanatus* var. citroides (wild watermelon) fruits, petroleum ether, ethyl acetate, butanol crude extracts as well as Cucurbitacin E and Cucurbitacin L 2-O- β -glucoside pure isolated compounds from *Citrullus lanatus* var. citroides was investigated. In this study, Cucurbitacin E and Cucurbitacin L 2-O- β -glucoside were revealed to have strong potent anti giardial activity against *Giardia lamblia* in vitro with IC₅₀= 2 and 5 ng/ml after 5 days respectively. The ethyleacetate extract was the best among all examined extracts followed by petroleum ether and butanol with IC₅₀ 0.1, 0.2 and 0.5 μ g/ml respectively. The results suggested that all the crude extracts and isolated compounds were active against *G. lamblia*, hence *Citrullus lanatus* var. citroides may be recommended as new source for the treatment of giardiasis [20].

Anti-hepatotoxic activity:

In the study, the ability of watermelon juice to protect against CCl₄-induced hepatotoxicity and oxidative stress was investigated. It has been hypothesised that one of the principal causes of CCl₄-induced liver injury is formation of lipid

peroxides by free radical derivatives of CCl₄. The trichloromethyl radical produced by carbon tetrachloride leads to liver damage by alkylating cellular proteins and other macromolecules with a simultaneous attack on polyunsaturated fatty acids to produce lipid peroxides (Lipid peroxidation, a ROS-mediated mechanism, has been implicated in the pathogenesis of various liver injuries and subsequent liver fibrogenesis in experimental animals. Hepatocellular necrosis leads to elevations of serum AST and ALT activities and an increased incidence and severity of histopathological hepatic lesions in rats ²¹.

Anti-atherosclerotic activity:

Administration of *C. lanatus* 'sentinel' extract attenuated atherosclerosis in both arch and thoracic regions of aortas in mice. Aortic arch and thoracic aortic regions represent different developmental origins of aortic smooth muscle cells and reduction of atherosclerosis in these two distinct aortic regions provides strong evidence of a role for *C. lanatus* 'sentinel' extract. There is evidence that the main component of *C. lanatus*, citrulline, has a beneficial effect on atherosclerosis and aortic vascular remodeling. Citrulline administration improved endothelium-dependent vasorelaxation and decreased aortic medial thickening. It is possible that citrulline in *C. lanatus* 'sentinel' extract may contribute to reducing atherosclerosis ²².

Anti-secretory activity:

The effects of the juice of *Citrullus lanatus* (watermelon) was evaluated on gastric acid secretion and pH in Indomethacin-induced ulceration in male albino rats. Rats pre-treated with *Citrullus lanatus* juice exhibited significant dose-dependent reduction of gastric lesions formation ($P < 0.05$). Also, ulcerogenesis in the pretreated groups was significantly lower than that observed with the control ($P < 0.05$) ²³.

Analgesic activity:

The analgesic activity of aqueous extract of *Citrullus lanatus* peels (AECL) using Eddy's hot plate method was evaluated. The AECL produced a significant analgesic activity in a dose dependent manner. All the doses of AECL (250, 500 and 1000mg/kg) had shown a good analgesic activity. The reaction time obtained for these three doses after 90 minutes of drug administration was found out to be 5.15 mins, 8.92 mins and 10.82 mins respectively which was comparable to Diclofenac sodium (5 mg/kg) that showed the reaction time of 12.36 mins ²⁴.

Safety and toxicity profile:

Acute toxicity of *Citrullus lanatus* extracts were studied in rodents. The n-hexane extract of *Citrullus lanatus* seed oil (CLSO) using acute toxic class

method was evaluated as described in OECD guidelines no. 423. The *Citrullus lanatus* seed oil was found safe upto a dose of 2,000 mg/kg body weight [16]. The toxicity study of aqueous extract of roots and leaves was also evaluated on mice. No mice died during the observation period so maximum tolerance experiment was carried out according to GLP 2003 by state food and drug administration. Twenty mice were given orally single maximum dose of 43.5 g/kg at two time points (7 am and 5 pm) but no mice died in period of 7 days [17]. The ethanolic extract of *Citrullus lanatus* was also found to show no mortality up to the maximum dose level of 2000 mg/kg body weight of the extract after administered orally ²⁵.

CONCLUSION

Citrullus lanatus (Thunb.) has been indicated in the treatment of various health ailments by traditional and Ayurvedic system of medicine. The research carried out till now have confirmed pharmacological potential of *Citrullus lanatus* and is found to be safe. Further research is necessary to reveal its detailed molecular mechanism behind these pharmacological activities.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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