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Review

A mini review of phytoconstituents and pharmacological activities of *Citrullus lanatus* (Thunb.)

Aymen Owais Ghauri[a*], Umbreen Farrukh[c], Nudrat Fatima[c], Sana Khalid[b], Sanober Kamal[c], Iqbal Azhar[b]

[a*] Department of Pharmacognosy, Faculty of Pharmacy, Jinnah University for Women, Karachi.
[b] Department of Molecular Neuroscience, Faculty of Medicine, University of Toyama,2630 Sugitani, Toyama, 930-0194, Japan.
[c] Department of Pharmacognosy, Dow College of Pharmacy, Dow University of Health Sciences

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Correspondence:
Aymen.owais@juw.edu.pk

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Abstract

Citrullus lanatus (Thunb.), is a globally utilized fruit during hot summer season. When a plant is explored for medicinally important phytoconstituents then other parts of the plant are also screened. This review provides knowledge about phytoconsituents and pharmacological activities of *C. lanatus* fruit, juice, leaf, rind and seeds. The plant has nutritional and medicinal value due to phenolic compounds and flavonids present in fruit and juice. The seeds are essential due to its fatty acid content. The major phytoconstituents reported include Lycopene, β Carotene, Cucurbutacin E, Citrulline, Arginine, β ionone, citral and ascorbic acid. Xanthophylls are also reported in some varieties. Some researchers have conducted toxicological studies on *C. lanatus* seeds and found it safe for long term use. Others have reported antioxidant, anti-inflammatory and anticancer properties. It also possesses antibacterial, antiulcer and antispasmodic activities. Citrulline, arginine and phenolic play role in dilation of vessels. Much research work is carried out on *C. lanatus* seeds as compared to other parts of the plant.

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Introduction: *Citrullus lanatus* (Thunb.), a member of the family Cucurbitaceae, is widely grown globally bearing more than one thousand varieties. Different varieties are grown in Far East, Middle East, South Asia, Central Asia, Europe, Tropical Africa, Central and South America and Australia [1]. The red to pink pulp is an edible portion of fruit though its rind is also cooked somewhere. There is variation of phytoconstutuents in different parts of berry (pepo) i.e., pulp, rind, skin, seeds. The leaves of the plant are also tested for different chemical constituents and confirmed the presence of valuable phytoconstituents. In Pakistan it is grown in the interior areas of Province Punjab and Sindh. In terms of production, Punjab ranks first, Balochistan second, Sindh third and fourth KPK having share of 55.87%, 21.29%, 10.29% and 11.84% respectively [2, 3]. In this review we will discuss the phytoconstituents present in different parts of the plant and mention the pharmacological activities reported in literature. The parts are shown in Figure1.

Leaves of *Citrullus lanatus:* The leaves of *Citrullus lanatus* are simple, alternate, dark green to dull green in color depending upon the habitat and variety with deeply divided lamina into several lobes with a prominent central midrib.

Fruit of *Citrullus lanatus:* The shape, size and color of watermelon fruit which is botanically called "Pepo" varies greatly. The color ranges from light green to dark green some with stripes and others plane, shape is sometimes round, sometimes oval and usually oblong. The inner flesh is usually red but yellow pulp is also found. Rind is hard having more weight than fleshy pulp and is used for cooking food and sometimes fed to animals [4]

Seeds of *Citrullus lanatus:* The seeds of watermelon are dark brown to black hard cover and cream to white internal flat kernel which is oval in shape. The seed kernel is extremely nutritious with high amount of minerals and vitamins. Different snacks and sauces are prepared using seed kernel. Seed oil is rich in fatty acids is reported to treat kidney stones, skin and urinary tract infections [5, 6].

Materials and methods: The objective of our search was to collect updated knowledge about the phytoconstituents present in different parts of the *Citrullus lanatus* plant and reported pharmacological activities of leaves, fruit, rind and seeds. For this purpose, we searched different databases like MEDLINE, AMED, Google Scholar, Research Gate, PubMed, Elsevier etc using words like *Citrullus lanatus* and Watermelon along with Phytoconstituents, Pharmacological activities, medicinal properties.

The respective research and review articles were found and thoroughly reviewed to collect information related to phytochemistry and pharmacological screening of different parts of *Citrullus lanatus* plant. The gathered knowledge was then compiled and written as per format.

Review of phytoconstituents and pharmacological activities: After thorough literature search it was found that a number of medicinally important phytoconstituents are present in leaves, fruit pulp, rind and seeds of *Citrullus lanatus.* Following is the summarized data of phytoconstituents explored by different researchers in authentic literature.

Leaves: Alebiosu et al through Thin-layer Chromatographic Studies and UV Analysis reported that leaves of C. lanatus contain important secondary metabolites like alkaloids, flavonoids, saponins, tannins, carbohydrates, phenols and glycosides while the absence of anthraquinones was reported [7]. Leaves of *C. lanatus* possess analgesic and anti-inflammatory activities. These are also antimicrobial and used for the treatment of diseases like malaria and gonorrhea [7]. In recent research watermelon leaf extract was tested on experimental animal model of obesity and diabetes and the researchers suggests leaf extract of *C. lanatus* for the management of Diabetes mellitus [8].

Rind: Siti Suhaila et al (2018) revealed that peels of watermelon contain alkaloids, flavonoids, saponins, tannins, phenolic compounds and terpenoids. Peels were reported to possess highly significant antimicrobial activity against *S. epidermidis* and *T. mentagrophytes.* The researchers claimed that this activity is due to the alkaloids and terpenoids present in peel of *C. lanatus* [9].

In a comparative study it was found that C. lanatus rind possesses highest quantity of caretenoid

Results of the investigation reveal that *Citrullus lanatus* rind was superior to *Citrullus lanatus* Pulp, seed. *Citrullus lanatus* pulp,seed and rind were low in their pro-vitamin A (carotenoid) though that of the rind was higher compared with other parts of the fruit. More so, vitamin C (ascorbic acid) content of the rind and seed were significantly ($p<0.05$) lower compared with the pulp [2].

Seeds: Some researchers have reported the presence of alkaloids, tannins, saponins, flavonoids, and phenols. They have also reported vitamin B1, B2, B3, B6 and B12 in watermelon seeds. Seed extract exhibited significant antimicrobial activity against fifteen different bacterial strains out of which only *Lactobacillus* sp, *Necropsobacter rosorum*, *Neisseria sicca*, *Neiserria subflava*, *Pseudomonas oryzyhabitans* showed positive results at higher concentrations while *Proteus mirabilis, Bacillus cereus, Staphylococcus aureus, Escherichia coli, Tsukamurella hongkongensis, Staphylococcus petrasii, Dietziamaris, Klebsiella pneumoniae, Advenella incenata*, and *Serriatia marcescens* showed no activity in all concentrations [10]. Others have investigated phytoconstituents in *C. lanata* seeds through LC ESI-MS/MS and HPLC and reported presence of stigmasterol, quinic acid, malic acid, epicatechin, caffeic acid, rutin, *p*-coumaric acid, quercetin, ferulic acid, scopoletin, apigenin, and kaempferol. These constituents resulted in pharmacological activities like antiperistalsis, antidiarrheal and antisecretory [11].

Seed Oil: Enemor et al (2019) evaluated nutrient composition of *C. lanatus* seeds and found that watermelon seeds contain fat, carbohydrate and protein in 22.77%, 13.99 % and 8.9% respectively. The total ash content was found to be 0.96% and moisture content up to 48.7%. These researchers also conducted amino acid profile and found that seeds contain phenyl alanine, arginine, valine, glutamate and serine amino acids in abundance. Further vitamin A and C as well as minerals like iron, magnesium, sodium and potassium were also reported in these seeds [12]. *C. lanatus* seed oil was quantified through GC-MS for fatty acids and revealed linoleic, oleic, stearic and palmitic acids in 51.4%, 36.7%, 6.3% and 5.6% respectively. This seed oil is non-irritating and is beneficial for hydrating and moisturizing the skin therefore it is used

in dermal cosmetic products [6]. Robert et al (2012) worked on different varieties of *C. lanatus* seed oil using TD-NMR. These researchers found that variety *C. lanatus* var. *egosi* has highest seed oil content i.e 35.6% followed by varieties *C. lanatus* var. *lanatus* 23.2% and *C. lanatus* var. *citroides* 22.6% [13].

Pulp: The pulp of watermelon is the most attractive part of red color popular in summer season. The phytoconstituents reported in pulp are lycopene (caretenoide), pro vitamin A (β Carotene), cucurbutacine E (Triterpene), citrulline and L-arginine (Amino acids). Further plenty of beneficial vitamins (A, B complex and C) and minerals (magnesium, potassium, calcium, phosphorus, iron [14-15]. The characteristic aroma of C. lanatus fruit is due to fatty acids which are medium and short chained, geranial, beta ionone and neral [16].

The reported activities of watermelon flesh include antioxidant and antimicrobial but similar researchers compared different parts of watermelon and concluded that rind and seeds have more significant antioxidant and antimicrobial activities then pulp [17].

The phytoconstituents like lycopene and beta carotene are already proven to treat cancer and cardiao vascular problems [18]. Some other researchers have reported several other pharmacological activities like analgesic, anti-inflammatory [19], antiulcer activity [20], hepatoprotective activity and laxative activity [15].

Conclusion

Citrullus lanatus (Thunb.) commonly known as watermelon, an indigenous fruit of Pakistan, has significant therapeutic potential due to variety of phytoconstituents including phenolic compounds, vitamins, minerals etc. present in different parts like leaves, fruit, rind and seeds. The plant could be utilized in preparation of phytomedicine and organic cosmaceuticals in future in addition to its nutritional benefits.

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Table. 1. Important Phytoconstituents with structures

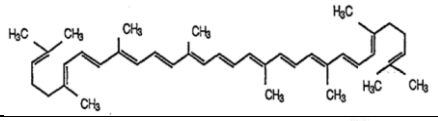
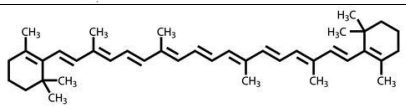
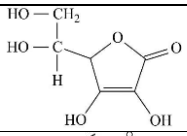
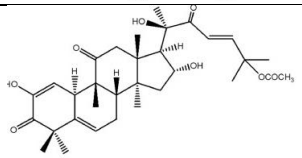
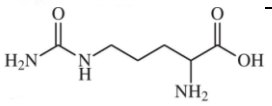
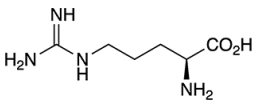
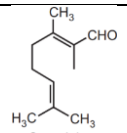
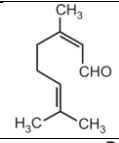
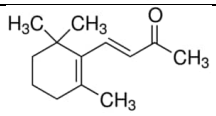
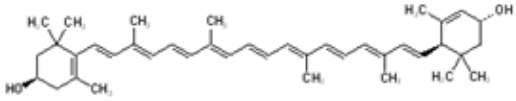
Constituent	Structure	Medicinal Importance	Reference
Lycopene		Antioxidant Anticancer Anti-inflammatory	[21]
β Carotene		Prevention of Cardiovascular Disease Lung Cancer	[22]
Ascorbic Acid		Scurvy, prevents heart disease, stroke, diabetes and cancer	[23]
cucurbutacin E		Antitumor Antiinflammatory Arthrosclerosis Blood Circulation promoter Antidiabetic	[24]
Citrulline		Protecting Cardiovascular Disease Antidiabetic	[25, 26]
L-arginine		Strengthening immune system Protecting Cardiovascular Disease	[27, 28]
Geranial (Citral a)		Antiinflammatory Anticancer Antimicrobial Antioxidant Anti-diabetic	[29, 30, 31]
Neral (Citral b)		Antiinflammatory Anticancer Antioxidant	[30, 31]
β ionone		Anti-inflammatory Cancer-preventing Antibacterial Antifungal Antileishmanial	[32]
Xanthophylls		Antiinflammatory Antioxidant	[33]

Table. 2. Important Pharmacological properties investigated *in vitro* or *in vivo.*

Pharmacological activity	Protocol	Reference
Antibacterial Property	*C. lanatus* seed extract was tested against *Staphylococcus sp., Escherichia coli, Proteus sp., Klebsiella sp.* and *Pseudomonas aeruginosa*. Cold Methanol extracts exhibited highest antibacterial effects *Staphylococcus sp.* While against *P. aeruginosa* hot methanol and chloroform extract showed significant antibacterial effect. The saponins present in extract were assumed to be responsible for antibacterial effect.	[34]
Anticancer Property	*C. lanatus* rind extracted was tested for anticancer activity against seven human cell lines. Further there was also investigation about phytoconstituents through UPLC/T-TOF-MS/MS techniques which showed 45 bioactive compounds including flavonoids, glycosides and phenolic compounds. The test extract reduced cell proliferation via increasing the caspase-3 activity and BAX/BCL-2 ratio.	[35]
Anti-Diabetic Property	The study was performed on male Wistar Alloxan induced diabetic rats. The rats were given *C. lanatus* seed extract as test drug, Glibenclamide as standard drug and vehicle as control for 28 days. Lipids and Glucose levels in blood were estimated through Randox diagnostic Kits. There was significant decrease in blood glucose level, cholesterol and triglycerides at the end of the study. This research suggests that *C. lanatus* seed extract could be used for normalizing blood glucose levels and lipid profiles for diabetic patients.	[36]
Anti-Hypertensive Property	The research study was performed on obese persons who were given watermelon rind, seeds and flesh along with a control group. The secondary bioactive components citrulline, arginine and phenolic compounds were tested in plasma using UHPLC-MS technique for 24 hours and endothelial function was examined through FMD technique for seven hours. The result suggests that these components play role in dilation of vessels.	[37]
Anti-inflammatory	Anti-inflammatory activity was explored for *C. lanatus* seed oil through carrageenan-induced paw edema in albino rats in vivo and human red blood cell membrane stabilization method in vitro. Diclofenac was used as standard drug. Significant anti-inflammatory activity was exhibited by both methods.	[19]
Antioxidant Property	C. lanatus seeds extracted in Ethanol, chloroform and n-Hexane were tested for anti-oxidant activity through DPPH radicalscavenging, Ferric reducing power, H_2O_2 and Nitric Oxide scavenging activities in vitro. All the samples possessed antioxidant activity with highest in n-Hexane and lowest in chloroform extracts.	[38]
Antispasmodic Property	In this research work *C. lanatus* seeds were evaluated for antispasmodic and bronchodilator activity on isolated rabbit jejunum, trachea, and urinary bladder. The result exhibited that the flavonoids of *C. lanata* seeds disturb the target genes which regulates Calcium level in cytosol thus act as calcium channel blocker thus produce relaxation of smooth muscles. This activity suggests the test compound as a good candidate for the treatment for asthma and diarrhea.	[11]
Benign prostatic hyperplasia	This research study was performed on Wistar rats in which Benign prostatic hyperplasia was induced and then different groups were treated with rind aqueous extract, ethanolic extract and juice of *C. lanatus* for three weeks. One group was kept as control i.e., BPH was induced but no drug was given. At the end of the study the animals were sacrificed and tested for prostate gland measurement, oxidative stress and histopathology. It was evident from results that prostate size was enlarged in control group while the activities. of Superoxide dismutase, Catalase and Gluthatione peroxidase were higher in test groups. The Malondialdehyde concentrations were found lower in test groups as compared to control. The results indicate that *C. lanatus* rind and juice could provide a good alternative treatment for Benign prostatic hyperplasia.	[39]
Gastric Antacid and Anti-Ulcer Property	1. The research study was performed on Wistar albino rats in which gastric ulcer lesions were induced through Indomethacin and pyloric ligation model. aqueous fruit pulp concentrate of *Citrullus lanatus* citroides was administered in two different doses for five days. 2. A significant decrease in ulcer indices was found in both models. The gastroprotective model exhibited increased pH and decrease in gastric juice volume and total acidity. The researchers suggest that main phyto constituents responsible for this effect may be flavonoids and polyphenols.	[40]
Neuroprotective Property	The study was performed in Wistar albino rats to explore the neuro protective effect of *C. lanatus* seed extracts on bilateral common carotid artery occlusion (BCCAO) induced cognitive impairment and oxidative stress. The result indicated that test compound i.e., *C. lanatus* seed extract treated cognitive impairment and oxidative stress damage successfully.	[41]
Toxicological Studies	In this research study ethanolic extract of *C. lanatus* seeds was tested for Acute oral toxicity with 2g/kg body weight dose in laboratory rats. Further 28 days the extract was orally given to different groups in 250, 500 and 1000 g/kg body weight doses. At the end of study period the animals were sacrificed, and haematological and histopathological parameters were checked along with body weight and biochemical markers. No mortality was recorded in acute toxicological study. The extract was found safe upto 1000mg/kg dose in sub-chronic toxicity test. Vital organs of treated animals were also found safe which proves the safety of *C. lanata* seed extract.	[42]

Fig.1. Different parts of *Citrullus lanatus* (1a Leaf; 1b Fruit; 1c Pulp; 1d Rind; 1e Seeds)