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Research Article

ASSESSMENT OF EFFECTS OF EXTRACT FROM ROOTS AND LEAVESOF *CITRULLUS LANATUS*, (THUNB)

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Abstract

Citrullus lanatus Thunb (Family: Cucurbitaceae) is a medicinal plant widely used traditionally in the treatment ofvarious 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 ofvitamins, amino acids, proteins, minerals and fat. The plant has been extensively studied by various scientistand researchers for its pharmacological activities and therapeutic approaches such as antibacterial, antifungal,antimicrobial, antiulcer, antioxidant, anti-inflammatory, gastroprotective, analgesic, laxative, antigiardial,hepatoprotective, against prostetic hyperplasia and atherosclerosis. The present review is an effort to providedetailed information of its uses, chemical composition, pharmacological activities of extract and its isolatedcompounds and safety profile of *Citrullus lanatus* for further research.

Introduction

Cucurbitaceae is the largest family containing 120genera and approximately 825 species typicallydistributed in the tropical countries poorlyrepresented in the temperate regions. The vegetablecrops of family Cucurbitaceae are importanthorticultural crop, mostly grown for its sweet and juicyfruit in warm climates all over the world.Cucurbitaceae are important source of food likepumpkin (*Cucurbita pepo)*, melon (*Cucumis melo),* cucumber (*Cucumis sativa),* water melon (*Citrulluslanatus), Lag enaria siceraria* (bottle gourd)*, andLuffa cylindrica (*sponge gourd). The *Citrullus lanatus*L) is one of the most popular species with high watercontent as high as 92% of the total weight 1. Theplant is traditionally used for centuries in thetreatment of various health aliments. It is animportant medicinal plant in the Ayurveda and Indiantraditional system of medicine 2. The plant is rich inflavonoids, alkaloids, saponins, glycoside, tanninsand phenols. Its nutritive values are also useful to thehuman health. The plant has been extensivelystudied by various scientist and researchers for itspharmacological activities and therapeuticapproaches such as antibacterial, antifungal,antimicrobial, antiulcer, antioxidant, antiinflammatory,gastroprotective, analgesic, laxative,antigiardial, hepatoprotective and against prosthetichyperplasia and atherosclerosis. Fruit is used incooling, strengthening, aphrodisiac and astringent tothe bowels, indigestible, expectorant, diuretic, andstomachic, blood purifier. It also allays thirst, curesbiliousness, good for sore eyes, scabies and itchesand as brain tonic to the brain 1. The present reviewfocus on phytochemical, pharmacognostic,pharmacological and toxicity updates of this plant.

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

Morphological characters:

Citrullus lanatus is a prostrate or climbing annualwith several herbaceous, rather firm and stout stemsup to 3 m long; the young parts are densely woollywith yellowish to brownish hairs while the older partsbecome hairless. The leaves are simple, alternate on long petioles, cordate with seven shallow lobes andvariously serrated margins, very hairy on the abaxial surface, acute,deep green, and about 7 – 15 cm indiameter. Tendrils are simple and spiral.

Male andfemale flowers grow on the same plant. Male flowersare found in clusters and appear before the femaleflowers. Both have yellow petals, five in number, andsepals, also five in number and greenish in color.Occasional hermaphrodite flowers are produced. Thefruits are globular with shallow grooves, about 14 –20 cm long. The skin is greenish yellow. The flesh isalmost white/light yellow, sweet, delicately flavoured,juicy, a pepo. The seeds are small, light brown andsmooth, between 0.4 and 1.1cm long and 0.2 – 0.3cm wide 3.

Traditional claims:

Citrullus lanatus (Thunb) is used as anthelmintic,anticancer, antibacterial, demulcent and diureticbeing used in the treatment of dropsy and renalstones 4. The rind of fruit is prescribed in case ofalcoholic poisoning and diabetes. The root ispurgative and in large doses emetic. The seed isdemulcent, diuretic, pectoral and tonic. It issometimes used in treatment of bed wetting. Seedsare also vermifuge and have hypotensive action.Fatty oils in the seeds as well as in aqueous andalcoholic extracts paralyze tapeworms androundworms. In Northern Sudan, it is often used forburns, swellings, rheumatism, gout and as laxative 5.Fruits of this plant are eaten as febrifuge when fullyripe or when almost putrid. It is also used in case ofenergy source, cleanses and purifies kidney andbladder, prevent erectile dysfunction and used totreat hepatomegaly and jaundice 6, 7.

Chemical Constituents:

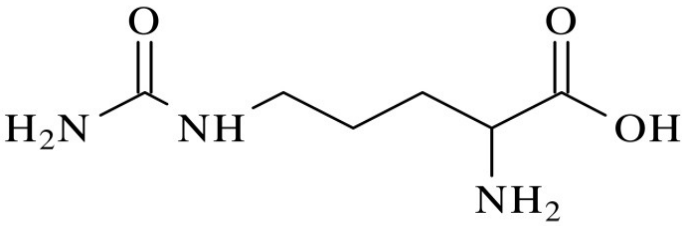
Citrullus lanatus seed contains phytochemicalconstituents like alkaloids, flavanoids, tannins, aminoacids, carbohydrates, cardioglycosides, terpenoids,steroids, carotenoids, oils and fats 5. The amino acidcitrulline was first extracted from watermelon andanalyzed. The nutritional quality of watermelonshows that it is very rich in vitamins A 3%, differentvitamins from vitamin B complex like Thiamine (Vit.B1), Riboflavin (Vit. B2), Niacin (Vit. B3), Pantothenicacid (B5), vitamin B6 and Folate (Vit. B9) whichranges between 1-3%, Vitamin C 14%. The mineralcomposition is Calcium 1%, Iron 2%, Magnesium 3%,Phosphorus 2%, Potassium 2% and Zinc 1%. Alongwith it, it also contains highly unsaturated fatty acidsand oils. It is also rich in essential amino acids likearginine, glutamine and aspartic acid 8.

Pharmacology:

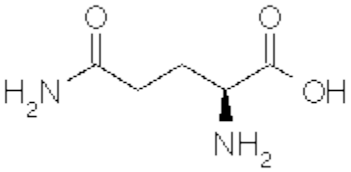
Antibacterial activity and antifungal activity:

Crude extract of watermelon seeds using hotwater, cold water, methanol and ethanol showed theantimicrobial activity using the standard disc diffusionassay method against *Staphylococcus aureus,Pseudomonas aeruginosa*, *Escherichia coli,Klebsiella pneumoniae* and *Bacillus cereus*. All theseed extracts showed evidence of antibacterialproperties 9.In another study, crude extract of *citrulluscolocynthis, citrullus lanatus* and *citrullus vulgaris*were very effective against bacteria and some fungalstrains.the ethanolic extract was found more effectivethan respective aqueous and chloroform extract. Thezone of inhibition was found maximum in E-coli andminimum in *Staphylococcus aureu.* Fungal zone ofinhibition was found more in *Candida albicans* andless in *Trichosporon Begelii* 10.

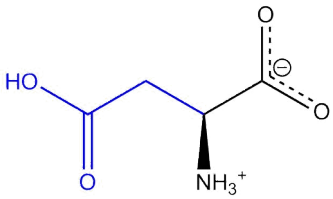
(a-Citrulline, b-Glutamine and C-Aspartic acid)



(a)Citrulline



(b)Glutamine



(C) Aspartic acid

Antimicrobial activity:

The antimicrobial effects of chloroform of *Citrulluslanatus* extracts against the studied bacteria suggestthat, different parts of plant possess remarkabletherapeutic action that can support the traditionalusage of this plant in the treatment of bacterial andfungal diseases such as gastrointestinal infection,diarrhea, respiratory and skin diseases. Theseantimicrobial activities are likely due to the presenceof secondary metabolites like tannins and flavonoids,alkaloids, saponins, terpenes and steroids in plant.The high potency of *Citrullus lanatus* against thesemicrobes could provide an example of prospectingfor new compounds 6. In another study, antimicrobialefficacy of *Citrullus lanatus* and other citrullus plantswere evaluated against gram negative, positive andsome fungal strains including *E-coli, Klebsiellapneumonia, Pseudomonas aeruginosa, Bacillussubtilis* and *Bacillus pumilus* some fungal *Candidaalbicans, Aspergillus niger, Penicillium chrysogenum*using agar well diffusion method at concentration 100mg/mL. In this, almost all species of plants werefound to have activity on at least two microbial strains7. Determination of antimicrobial activity of methanolextract of *Citrullus lanatus* seed was carried outagainst 10 bacterial species (Staphylococcus aureus,Klebsiella pneumoniae, Bacillus subtilis, Escherichiacoli, Salmonella typhi, Enterococcus faecalis, Vibriocholerae, Shigella dysenteriae, Proteus mirabilis,Pseudomonas aeruginosa) and 5 fungal species(Aspergillus flavus, Aspergillus niger, Penicilliumnotatum, Trichophyton mentagrophytes, Candidaalbicans). Inhibition zones formed by the extract werecompared with the standards: Streptomycin andAmphotericin B. The methanolic seed extract at aconcentration of 1000 µg/ml was effective againstbacteria: Vibrio cholerae (7 mm), Proteus mirabilis (7mm), Shigella dysenteriae (7 mm), Staphylococcusaureus (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), Penicilliumnotatum (11 mm), *Candida albicans* (9 mm). Theresults of Citrullus lanatus seed extract demonstratedantimicrobial activity against the organisms tested 11.

Antiulcerative activity:

Methanolic extract of *Citrullus lanatus* (MECL)seeds showed maximum antioxidant potential andwas evaluated for its anti-ulcerogenic activity byPyloric Ligated (PL) and Water Immersion Stress(WIS) induced ulcer models in rat. Gastric volumeand free and total acidity were measured in PL modelwhereas; ulcerative index was measured in both themodels at 100, 200 and 300 mg/kg doses of MECL.Rats treated with MECL (300 mg/kg) showedsignificant decrease in the gastric volume, free acidityand total acidity in case of PL model and showedsignificant percentage inhibition of ulcer as indicatedby decrease in ulcerative index in both the models.The extract of *Citrullus lanatus* seeds possessesgood antioxidant and anti-ulcer activity 12. In anotherstudy, the presence of secondary metabolites suchas flavonoids, tannins, saponins, terpenoids claimedto present in the most members of the Cucurbitaceaefamily. Proximate and metal content analysis of theseeds provides information that the consumption ofthe seeds of *Citrullus lanatus* is safe. This study alsoprovides preliminary data for the first time that theseeds of *Citrullus lanatus* possesses significant antiulceractivity in animal model. The anti-ulcer activityis probably due to the presence of bioactivecompounds like flavanoids, saponin and tannins.Further studies are required to confirm the exactmechanism underlining the ulcer healing andprotecting property of the extract and to identify the ,chemical constituents responsible for it 13. Theantiulcer activity of crude methanolic extract of*Citrullus lanatus* seeds in two different ulcer modelsin albino Wistar rats was also studied. The extract at300 mg/kg body weight, once daily orally for 7 dayshas a significant effect in pyloric ligation (PL, 4 hligation) and in water immersion (WS, 25 0C 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 50mg/kg) and Omeperazole (20 mg/kg body weight) ,that have shown protection index of 64.47% and70.59% in PL and WS model respectively 14.

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, Ferricreducing power activity, Hyderogen peroxide(H2O2)scavenging activity and Nitric Oxide(NO) scavengingactivity. The total Phenolic contents and Flavanoidcontents were estimated taking Gallic Acid andQuercetin calibration curve

respectably. In this study,it was found that all the extracts possess In-vitro antioxidantactivities. But the order of possessingactivities were n-hexane>ethanol>chloroform extractsof *Citrullus lanatus* seeds 15.

Anti-inflammatory activity:

Citrullus lanatus seed oil is extracted with nhexaneand tested for in-vivo and in-vitro anti-inflammatory activity. The oil was screened for *in-vivo*anti-inflammatory activity by Carrageenan-inducedpaw edema in rat model and *In-vitro* anti-inflammatory activity by human red blood cellmembrane stabilization method. The potency of theoil was compared with standard Diclofenac (10mg/kg). The oil showed significant reduction ofedema in Carrageenan induced Rat Paw EdemaModel maximum at 3 hr (percentage reduction in pawvolume 44.44%, 55.56% and 63.11% for CLSO (50mg/kg), CLSO (100 mg/kg) and diclofenec (10 mg/kg) respectably and CLSO at concentration of100, 250 and 500 mcg/ml showed 42.35%, 68.48%and 78.50% protection of human red blood cellmembrane in hypotonic solution respectably 16. Inanother study, mouse model with ear edema inducedby xylene and the rat model with paw edema orgranuloma by carrageenan or cotton pellet were usedfor anti-inflammatory effect of the *Citrullus lanatus*aqueous extract. Effects of the extract on analgesiawas tested respectively by measuring the latency ofmice licking hind foot from hot plates and by countingthe times of body twisting in response to acetic acid.The extract significantly inhibited the ear edema,granuloma hyperplasia and paw edema. Itsignificantly lifted pain threshold on mouse hot-plateresponses and reduced their writhing time 17.

Gastroprotective Activity:

Gastroprotective potential of *Citrullus lanatus* fruitpulp aqueous extract (CLE) on pyloric ligation andindomethacin induced ulcer model in wistar albino rats was evaluated. In indomethacin induced ulcermodel, CLE was administered in the doses of 250mg/kg, 500 mg/kg & 1000 mg/kg body weight orallyfor five days for three times in a day after theinduction of ulcer. The extent of healing wasdetermined via reduction in ulcer index and alterationin various biochemical parameters in gastric mucosa.In pyloric ligation model, CLE resulted in significantincrease in pH, enzymic antioxidants i.e. Superoxidedismutase & Catalase, with a significant decrease

involume of gastric juice, free and total acidity, protein& carbohydrate concentration and Lipid peroxidaselevels. The presence of the flavonoids andpolyphenols may be responsible for thegastroprotective effect of CLE 18.

Activity against prosthetic hyperplasia:

Administration of MECLS for one month reducedthe prostate size significantly (P< 0.05), both at highand low dose, but could not restore the initial size ofshrunken testes and severe oligospermia caused bythe hormones. The histological studies clearlyestablish MECLS as a potential candidate inmanagement of androgen dependent conditions likebenign prostate hyperplasia 8.

Laxative Activity:

The laxative activity was determined based on theweight of the fecal matter. The effects of the aqueousfruit pulp extract of *Citrullus lanatus* and referencestandard on the gastro intestinal motility rate werealso evaluated. Phytochemicals screening of theextract revealed the presence of flavonoids, tannins,polyphenols, sterols and polyterpenes. The aqueousfruit pulp extract of *Citrullus lanatus* administeredorally at three different doses produced significantlaxative activity and reduced loperamide inducedconstipation in dose dependant manner. The effect ofthe extract at 500 and 1000 mg/kg (p.o.) was similarto that of reference drug sodium picosulfate (5 mg/kg,p.o). The same doses of the extract (500 and 1000mg/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 theaqueous fruit pulp extract of *Citrullus lanatus* has asignificant laxative activity 19.

Antigiardial Activity:

Antigiardial activities of *Citrullus lanatus* var.citroides (wild watermelon) fruits, petroleum ether,ethyl acetate, butanol crude extracts as well asCucurbitacin E and Cucurbitacin L 2-O-β-glucosidepure isolated compounds from *Citrullus lanatus* var.citroides was investigated. In this study, CucurbitacinE and Cucurbitacin L 2-O-β-glucoside were revealedto have strong potent antigiardial activity againstGiardia lamlia in vitro with IC50= 2 and 5 ng/ml after5 days respectively. The ethyleacetate extract wasthe best among all examined extracts followed bypetroleum ether and butanol with IC50 0.1, 0.2 and0.5 µg/ml respectively. The results suggested that allthe crude

extracts and isolated compounds wereactive against G. lamblia, hence *Citrullus lanatus* var.citroides may be recommended as new source forthe treatment of giardiasis 20.

Anti-hepatotoxic activity:

In the study, the ability of watermelon juice toprotectagainst CCl4-induced hepatotoxicity andoxidative stress was investigated. It has beenhypothesised that one of the principal causes ofCCl4-induced liver injury is formation of lipidperoxides by free radical derivatives of CCl4. Thetrichloromethyl radical produced by carbontetrachloride leads to liver damage by alkylatingcellular proteins and other macromolecules with asimultaneous attack on polyunsaturated fatty acids toproduce lipid peroxides (Lipid peroxidation, a ROSmediatedmechanism, has been implicated in thepathogenesis of various liver injuries and subsequentliver fibrogenesis in experimental animals.Hepatocellular necrosis leads to elevations of serumAST and ALT activities and an increased incidenceand severity of histopathological hepatic lesions inrats 21.

Anti-atherosclerotic activity:

Administration of *C. lanatus* 'sentinel' extractattenuated atherosclerosis in both arch and thoracicregions of aortas in mice. Aortic arch and thoracicaortic regions represent different developmentalorigins of aortic smooth muscle cells and reduction ofatherosclerosis in these two distinct aortic regionsprovides strong evidence of a role for C. lanatus'sentinel' extract. There is evidence that the maincomponent of C. lanatus, citrulline, has a beneficialeffect on atherosclerosis and aortic vascularremodeling. Citrulline administration improvedendothelium-dependent vasorelaxation anddecreased aortic medial thickening It is possible thatcitrulline in C. lanatus 'sentinel' extract maycontribute to reducing atherosclerosis 22.

Anti-secretary activity:

The effects of the juice of *Citrullus lanatus*(watermelon) was evaluated on gastric acid secretionand pH in Indomethacin-induced ulceration in malealbino 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 wassignificantly 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 platemethod was evaluated. The AECL produced asignificant analgesic activity in a dose dependentmanner. All the doses of AECL (250, 500 and1000mg/kg) had shown a good analgesic activity.The reaction time obtained for these three dosesafter 90 minutes of drug administration was found outto be 5.15 mins, 8.92 mins and 10.82 minsrespectively which was comparable to Diclofenacsodium (5 mg/kg) that showed the reaction time of12.36 mins 24.

Safety and toxicity profile:

Acute toxicity of *Citrullus lanatus* extracts werestudied in rodents. The n-hexane extract of *Citrulluslanatus* seed oil (CLSO) using acute toxic classmethod was evaluated as described in OECDguidelines no. 423. The *Citrullus lanatus* seed oil wasfound safe upto a dose of 2,000 mg/kg body weight[16]. The toxicity study of aqueous extract of rootsand leaves was also evaluated on mice. No micedied during the observation period so maximumtolerance experiment was carried out according toGLP 2003 by state food and drug administration.Twenty mice were given orally single maximum doseof 43.5 g/kg at two time points (7 am and 5 pm) butno mice died in period of 7 days [17]. The ethanolicextract of *Citrullus lanatus* was also found to show nomortality up to the maximum dose level of 2000mg/kg body weight of the extract after administeredorally 25.

Conclusion

Citrullus lanatus (Thunb.) has been indicated inthe treatment of various health ailments by traditionaland Ayurvedic system of medicine. The researchcarried out till now have confirmed pharmacologicalpotential of *Citrullus lanatus* and is found to be safe.Further research is necessary to reveal its detailedmolecular mechanism behind these pharmacologicalactivities.

Conflict of Interests

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

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