

Medicinal Values on *Citrullus lanatus* (Watermelon):

Pharmacological Review

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ABSTRACT

The use of herbal products is of global importance because of their low side effects, accessibility and affordability when compared with conventional medicine. *Citrullus lanatus* (water melon) is popular in indigenous system of folk medicine and it is known to contain bioactive compounds such as cucurbitacin, triterpenes, sterols and alkaloids, vitamins, minerals. Traditionally *Citrullus lanatus* had been reportedly used as purgative and emetic in high dose, vermifuge, demulcent, diuretic and tonic. The seed is used in the treatment of urinary tract infections, bed wetting, dropsy and renal stones, alcohol poisoning, hypertension, diabetic, diarrhoea and gonorrhoea. This review unveils the current experimental research on its biological activities which substantiate its ethno medicinal claims. Biological activities reviewed include; antimicrobial, antioxidant, anti-plasmodial, anti-inflammatory, anti-Prostatic Hyperplasia activity, anti-giardial activity, anti-oxidant, analgesic properties, its effects on the histology of the kidney of adult Wistar rats, antisecretory, antidiabetic, laxative, anti-ulcerogenesis and hepatoprotective activities. In view of its wide pharmacological and biological activities, its traditionally reported therapeutic potential such as, anti-hypertensive, antidiarrhoeal, as well as its in-depth toxicity studies, among others, are yet to be experimented. These should be put into consideration in current researches.

Keywords: *Citrullus lanatus*, traditional medicine, water melon, bioactivity.

INTRODUCTION

It has been reported that infectious diseases account for one-half of all deaths in the tropical countries (WHO, 1977). As a result, people of all continents have long applied poultice and imbibed infusions of indigenous plants dating back to prehistory for health purposes and is still in use today (Sofowora, 1993; Iwu, *et al.* 1983). Plant medicine (phyto-medicine) has been used in healthcare delivery in many parts of Africa and the rest of the world (Elujoba, *et al.*, 2005). Effective health cannot be achieved in Africa, unless orthodox medicine is complemented with traditional medicine (Elujoba, *et al.*, 2005). At least 80% of Africans depend on plant medicine for their healthcare (Sofowora, 1993). Fruits and vegetables

have been recognized as natural sources of various bioactive compounds (Pennington and Fisher, 2010) which could be attributed to their phytoconstituents such as flavonoids, anthocyanins, vitamins C and E, phenolic compounds, dietary fiber, and carotenoids present in fruits and vegetables (González-Aguilar, *et al.*, 2008).

One of such medicinal plant is *Citrullus lanatus*. Although several of its uses in traditional medicine have been documented, many of these claims are yet to be validated by scientific researchers. Therefore, a review of some investigated therapeutic activities of the plant is highlighted in this present article.

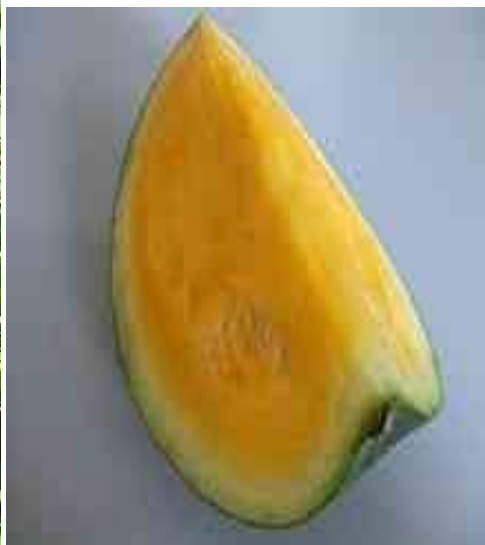
CITRULLUS LANATUS (WATERMELON)



Citrullus Lanatus leaf



Citrullus Lanatus fruit

*Citrullus Lanatus* fruit*Citrullus Lanatus* fruit with yellow flesh

Origin and Botanical Description

Citrullus lanatus (water melon) produces a fruit that is about 93% water, hence the name “water” melon. The “melon” part came from the fact that the fruit is large and round and has a sweet, pulpy flesh. The scientific name of the watermelon is derived from both Greek and Latin roots. The *Citrullus* part comes from a Greek word “citrus” which is a reference to the fruit. The *lanatus* part is Latin, and has the meaning of being woolly, referring to the small hairs on the stems and leaves of the plant (Baker, *et al.*, 2012).

Watermelon is thought to have originated in southern Africa because it is found growing wild throughout the area, and reaches maximum diversity of forms there. It has been cultivated in Africa for over 4,000 years. *Citrullus lanatus* was brought to America by Spanish and quickly became very popular crop (Robinson and Decker, 1997).

Citrullus lanatus is a prostrate or climbing annual plant with several herbaceous, firm and stout stems up to 3 m long. The young parts are densely woolly with yellowish to brownish hairs while the older parts are hairless. The leaves are herbaceous but rigid, becoming rough on both sides; 60–200 mm long and 40–150 mm broad, but usually deeply 3-lobed with the segments again lobed or doubly lobed; the central lobe is much the largest. The leaf stalks are somewhat hairy and up to 150 mm long. The tendrils are rather robust and usually divided in the upper part. Male and female flowers occur on the same plant (monoecious) with the flower stalk up to 40 mm long and hairy. The fruit in the wild form is subglobose, indehiscent and up to 200 mm in diameter; the fruit stalk is up to 50 mm long (van, *et.al*, 2004; Fursa, 1981, Maynard, 2001; Oyolu, 1977).

The fruit is usually globose to oblong or ellipsoid, sometimes ovoid, 5–70 cm long and weighing 0.1–

3.0 kg (0.1–2.5 kg in egusi melon, 1.5–3.0 kg in watermelon), The seeds are obovate to elliptical, flattened, 0.5–1.5 cm × 0.5–1 cm, smooth, yellow to brown or black, rarely white (Jackson, 1990; Laghetti, and Hammer, 2007; Mabblerley, 2008).

Common names

Vernacular names of *Citrullus lanatus* include; Egusi melon and egusi watermelon. Other include; West African watermelon (En). Watermelon, dessert watermelon, Cooking melon, (Rhodes and Zhang, 1999).

Scientific Classification

- ✓ Kingdom- Plantae
- ✓ Phylum- Embryophyta
- ✓ Class- Dicotyledoneae
- ✓ Order: Cucurbitales
- ✓ Family: Cucurbitaceae
- ✓ Genus: *Citrullus*
- ✓ Species: *C. lanatus*

Nutrient composition

Citrullus lanatus contains about 6% sugar and 92% water by weight. As with many other fruits, it is a source of vitamin C. The composition of dried egusi seed without shell per 100 g include: water 5.1 g, energy 2340 kJ (557 kcal), protein 28.3 g, fat 47.4 g, carbohydrate 15.3 g, Calcium 54 mg, Phosphorous 755 mg, iron 7.3 mg, thiamin 0.19 mg, riboflavin 0.15 mg, niacin 3.55 mg and folate 58 µg. The seed being an excellent source of energy and contains no hydrocyanic acid, making it suitable as livestock feed. The seed oil contains glycosides of linoleic, oleic, palmitic and stearic acids. The fruit flesh contains bitter cucurbitacins (Schippers, 2002).

The composition of watermelon per 100 g edible portion (50–70% of the mature fruit) include: water

91.5 g, energy 134 kJ (32 kcal), protein 0.6 g, fat 0.4 g, carbohydrate 7.2 g, Calcium 8 mg, Phosphorous 9 mg, iron 0.17 mg, thiamine 0.08 mg, riboflavin 0.02 mg, niacin 0.2 mg, folate 2 mg and ascorbic acid 9.6 mg (USDA, 2002).

Watermelon is a rich natural source of lycopene, a carotenoid of great interest because of its antioxidant capacity and potential health benefits (Rhodes and Zhang, 1999). Cucurbitaceae plants are known to contain bioactive compounds such as cucurbitacin, triterpenes, sterols and alkaloids (Yuan, *et al.*, 2006).

The amino-acid citrulline had been extracted from watermelon and analyzed (Wada, 1930). Watermelon with red flesh is a significant source of lycopene (Mandel, *et al.*, 2005).

Nutritional values

Every aspect of the fruit of watermelon has nutritional value, including the rind and the seeds. The most common way watermelon is eaten, is the consumption of the pink or yellow flesh, eaten raw, the way it was grown. However, other common ways it is eaten include watermelon rind pickles, deep fried watermelon, watermelon cake, and watermelon lemonade (Wind, 2008).

In southern Africa it has been cultivated since pre-colonial times with other crops such as sorghum and maize. The tender young leaves and fruits are cooked as green vegetables, while the fruit flesh may be cooked as porridge with maize meal. It is also a valuable stock feed, especially in times of drought. The hollowed fruit can be used as a container for cooking or storing berries. The pulp and seeds are prepared in a number of different ways for eating (Globinmed, 2010).

The flat brown seeds have a much higher food value than the flesh and have a nice nutty taste. Significant amounts of vitamin C, minerals, fat, starch and riboflavin have been obtained from them. They can be dried, roasted and eaten as such or ground into flour to make bread. The flour is said to contain saponin and is also used as a detergent. The seed contains a high percentage of oil which is similar to pumpkin seed oil and can be used in cooking (Moldenke and Moldenke, 1952).

In West Africa the seeds are made into pulp and added as thickener to soups. They are also fermented to produce a sweetener locally called 'ogiri' or they are roasted, pounded, wrapped in leaves and then boiled to produce another sweetener called 'igbãlo'. The residue from oil extraction is made into balls that are fried to produce a local snack called 'robo' in Nigeria, or is used as cattle feed. The residue from oil extraction is made into balls that are fried to produce a local snack called 'robo' in Nigeria, or is used as cattle feed (Moldenke and Moldenke, 1952).

Citrullus lanatus seeds are increasingly used for their oil in semi-arid regions and also the use of the

oil in the cosmetic and pharmaceutical industry is increasing. There are also prospects for use of the seeds in the improvement of infant nutrition in view of their high protein and fat content (Maynard, 2001).

Ethnomedicinal relevance

Citrullus lanatus var. *citroide* (Wild melon) has been reportedly used widely in traditional herbal medicine. The fruits of *Citrullus lanatus* is eaten as a febrifuge when fully ripe or even when almost putrid (Grieve and Leyel, 1984). The root is purgative and in high dose it can also serve as emetic (Grieve and Leyel, 1984). The seed is demulcent, pectoral and tonic (Duke and Ayensu 1985). It is sometimes used in the treatment of the urinary tract infections (Grieve and Leyel 1984) as well as bed wetting (Moerman, 1998). The fruit is also diuretic (Grieve and Leyel 1984) and is effective in the treatment of dropsy and renal stones (Chiej, 1984). The seed is also a good vermifuge and has a hypotensive action. Preliminary research indicates that the consumption of watermelon may have antihypertensive effects (USA, 2012). Fatty oil in the seed, as well as aqueous or alcoholic extracts, had been reported to paralyze tapeworms and roundworms (Chopra 1958). The rind of the fruit is prescribed in cases of alcoholic poisoning and diabetes (Duke and Ayensu, 1985). *Citrullus lanatus* is used in Northern Sudan for burns, swellings, rheumatism, gout and as laxative (Schippers and Budd, 1997). The fruits are used as a drastic purgative in Senegal; they are also used to treat diarrhoea and gonorrhoea in Nigeria. Tar is extracted from the seeds and used for the treatment of scabies and for skin tanning (Schippers and Budd, 1997). The seed oil has an anthelmintic action which is better than that of pumpkin seed oil (Jackson, 1990).

BIOACTIVITIES OF CITRULLUS LANATUS

Anti-Inflammatory Activity

In-vivo and in-vitro anti-inflammatory activity of *Citrullus lanatus* seed oil (CLSO) in carrageenan-induced paw edema in rat model and *In-vitro* anti-inflammatory activity was carried out. The potency of the oil compared with standard diclofenac (10 mg/kg) 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(100mg/kg) and diclofenec(10mg/kg) respectively and CLSO at concentration of 100, 250 and 500 mcg/ml showed 42.35%, 68.48% and 78.50% protection of HRBC in hypotonic solution respectively. All the results were compared with standard diclofenac at 50, 100 and 200 mcg/ml which showed 43.74%, 63.93% and 86.73% protection of HRBC in hypotonic solution respectively (Madhavi, *et al.*, 2012).

Antimicrobial activities

The antimicrobial activities of crude chloroform, hexane and ethanol leaves, stem, fruits and seeds extracts from *Citrullus lanatus* var. *citroides* (CL) was carried out against bacteria (*Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Bacillus subtilis* and *Proteus vulgaris*) and fungi (*Aspergillus niger* and *Candida albicans*). Cup-plate diffusion and disc diffusion method were used. Analysis of the data revealed that, the chloroform extract of the fruit exhibited the maximum antibacterial activity. It showed antibacterial activity against *S. aureus*: 36 mm, *B. subtilis*: 38 mm, *E. coli*: 37 mm, *P. vulgaris*: 23 mm and *P. aeruginosa*: 19 mm. Results were compared concurrently to standard drugs; clotrimazole and gentamicin. Based on the current findings, it was concluded that *Citrullus lanatus* var. *citroides* (CL) has antimicrobial activity, which is as potent as standard antimicrobial drugs against the selected microorganisms (Loiy, *et al.*, 2011).

Anti-Prostatic Hyperplasia activity

In order to investigate the effects of methanolic extract of *Citrullus lanatus* seed (MECLS) on experimentally induced benign prostatic hyperplasia, twenty adult male Wistar rats weighing about 135-180g were randomly divided into four groups of five animals each. Group I, which served as normal control (NC) was given corn oil as placebo 1g/kg BW; Group II, served as Hormone treated control (HTC), Groups III, and IV which served as hormone and extract treated (HTEC) received continuous dosage of 300µg and 80µg of testosterone (T) and estradiol (E2) respectively on alternate days for three weeks subcutaneously in the inguinal region while the extract treated received an additional 2g/kg BW (low dose) and 4g/kg BW (high dose) of extract orally for 4 weeks after the successful induction of prostate enlargement. Immediately after induction some animals were randomly selected and sacrificed for gross inspection of prostate enlargement and sperm count evaluation, these procedures were repeated again after four weeks of extract treatment. Portion of the prostate were taken and processed routinely for paraffin embedding and stained with H&E. From results of the study hormone treatment did not affect the body weight of the animals; however it caused a significant decrease in the weight of the testes and rendered all the rats azoospermic. In addition, treatment with extracts caused a significant decrease in the enlarged prostate, seminal vesicle and testes sizes in a dose related manner ($P < 0.05$) compared to the hormone treated control. Histological examination of prostate revealed that the methanolic extract caused significant changes in its histo-architecture. The extracts further caused

a dose dependent reduction in the prostate weight. PSA level was significantly lowered in both HTEC at low and high doses ($P < 0.05$) in dose dependent manner. 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 prostatic hyperplasia (Adesanya, *et al.*, 2011).

Antigiardial activity

An *in vitro* anti-giardial activity of *Citrullus lanatus* fruits, petroleum ether, ethyl acetate, butanol crude extracts as well as Cucurbitacin E and Cucurbitacin L 2-O-β-glucoside pure isolated compounds from *C. lanatus* var. *citroides* was carried out. Cucurbitacin E and Cucurbitacin L 2-O-β-glucoside were revealed to have strong potent anti-giardial activity against *Giardia lamblia* *in vitro* with $IC_{50} = 2$ and 5 ng/ml after 5 days respectively. The ethylacetate extract was the best among all examined extracts followed by petroleum ether and butanol with IC_{50} 0.1, 0.2 and 0.5 µg/ml respectively. The results of this suggest that all the crude extracts and isolated compounds were active against *G. lamblia*, hence the author concluded that *C. lanatus* var. *citroides* may be recommended as new source for the treatment of giardiasis (Loiy, *et al.*, 2011).

Compositional Studies of *Citrullus lanatus* Seed

Proximate, amino acid and mineral composition of *Citrullus lanatus* (egusi melon) flour were determined using standard analytical procedures. The proximate composition analysis of egusi melon showed that the seed contained the following; moisture (4.6±0.3), ash (3.7±0.1), ether extract (45.7±0.1), crude protein (23.4±0.2), crude fibre (12.0±0.1) and total carbohydrate (10.6±0.2). The result of the amino acid analysis showed that egusi melon seed contained good quantities (g/100g protein) of arginine (9.0), isoleucine (4.8), leucine (4.2), and phenylalanine (3.2) which are essential amino acids as well as glutamic acid (16.9) and aspartic acid (16.3). The mineral analysis (mg/100g) of the flour included: Na (13.0±0.2), K (96.1±0.4), Ca (28.2±0.2), Mg (31.4±0.2), Mn (1.7±0.1), Cu (0.4±0.1), Zn (1.2±0.1), Fe (1.3±0.2), and P (125.3±3.1). With this nutrient profile, egusi melon compares favorably with the known protein rich foods such as soybean, cowpeas, pigeon peas and pumpkin (Godwin, *et al.*, 2008).

Histological studies on the Kidney of Adult Wistar Rats

Citrullus lanatus aqueous extract was administered to Wistar rats as follows: Group A: 1.5ml/kg,

Group B: 3ml/kg, Group C: 6ml/kg and Group O: Control (Water). The aqueous extract of *Citrullus lanatus* was given once a day to the animals for 27 consecutive days. The results revealed that the kidney histology of all animals that received the aqueous extract of *Citrullus lanatus* were normal when compared with the control group. Group B (3ml/kg) showed significant ($P<0.05$) difference in weight gain when compared with the control. However the author recommended that more research on this area should be carried out using Electron microscope, where the organelles of the cell can be studied in details (Oyewo, *et al.*, 2012).

Antioxidant, anti-inflammatory and analgesic potential

The antioxidant, anti-inflammatory and analgesic potential of *Citrullus lanatus* seed extract in rodent model was carried out. The seeds were extracted using solvents of increasing polarity. The free radical scavenging activity of all extracts was measured by DPPH and H_2O_2 methods. The methanolic extract of the *Citrullus lanatus* seeds was further evaluated for its *in vivo* anti-inflammatory activity using carrageenan induced rat paw edema and analgesic activity by tail flick and tail immersion methods. The methanolic extract of the seeds (MECL) showed highest antioxidant activity. 200mg/kg of MECL showed significant ($p<0.05$) anti-inflammatory and analgesic activity as compared to diclofenac sodium and morphine respectively. The author suggested that the methanolic extract of seeds of *Citrullus lanatus* has good antioxidant, anti-inflammatory and analgesic potential and may be used as a future food medicine (Gill, *et al.*, 2010).

Effects on rat Uterine Contractility

In other to determine the effects of watermelon extract and citrulline on the myometrium and to investigate their mechanism of actions, the extracts of watermelon flesh and rind and l-citrulline (64 $\mu\text{mol/L}$) were evaluated on 3 types of contractile activity; spontaneous, those elicited by potassium chloride (KCl) depolarization, or oxytocin (10 nmol/L) application in isolated rat uterus. Inhibitors of nitric oxide (NO) and its mechanisms of action, N ω -Nitro-L-arginine methyl ester hydrochloride (l-NAME, 100 $\mu\text{mol/L}$), LY83583 (1 $\mu\text{mol/L}$), and tetraethylammonium chloride (5 mmol/L), as well as Calcium signaling pathways, were determined. Both flesh and rind extracts significantly decreased the force produced by all 3 mechanisms, in a dose-dependent manner. The extracts could also significantly decrease the force under conditions of sustained high Ca levels (depolarization and agonist) and when the force was produced only by sarcoplasmic reticulum (SR) Ca release. l-citrulline produced the same effects on force as watermelon extracts. With submaximal doses of extract, the

additive effects of l-citrulline were found. The inhibitory effects of extracts and l-citrulline were reversed upon the addition of NO inhibitors, and pretreatment of tissues with these inhibitors prevented the actions of both extracts and l-citrulline. Thus, these data show that watermelon and citrulline are potent tocolytics, decreasing the force produced by calcium entry and SR release and arising by different pathways, including oxytocin stimulation. Their major mechanism was suggested to stimulate the NO-cyclic guanosine monophosphate (cGMP) relaxant pathway (Phukphon, *et al.*, 2012).

Antisecretory Effects

The effects of the juice of *Citrullus lanatus* was evaluated on gastric acid secretion and pH in Indomethacin-induced ulceration in male albino rats. The experiment was divided into two studies. Under each study, four groups of rats were pre-treated with distilled water (control), 25% watermelon, 50% watermelon and 100% watermelon juice respectively for 30 days. 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 ($P<0.05$). The results suggest that *Citrullus lanatus* (watermelon) juice has a significant gastroprotective effect in Indomethacin-induced gastric ulceration (Francis, *et al.*, 2013).

Anti-diabetic activity

The anti-diabetic potential of watermelon (*Citrullus vulgaris* Schrad) was evaluated *in vivo*. ICR mice were fed experimental diet containing none, 10% watermelon flesh powder (WM-P) or 1% watermelon rind ethanol extract (WM-E). At the end of 4 weeks, mice were administrated with streptozotocin (40 mg/kg, *i.p.*) for 5 consecutive days to induce diabetes. Supplementation with WM-E significantly decreased blood glucose level and increased serum insulin levels. Feeding of WM-P also induced moderate changes but those were not statistically significant. Immunohistochemical analysis showed watermelon that effectively protected pancreatic cells death, which suggest that watermelon has a beneficial effect on diabetes (Jiyun, *et al.*, 2011).

Laxative activity

The possible laxative effect of aqueous fruit pulp extract of *Citrullus lanatus* in albino's Wistar rats was carried out. Rats were divided in 5 groups of 6 animals each, first group served as control, second group served as standard (sodium picosulfate) while group 3, 4 and 5 were treated with fruit pulp aqueous fruit pulp extract of *Citrullus lanatus* at doses of 250, 500 and 1000

mg/kg body weight (b.w.), per os respectively. The laxative activity was determined based on the weight of the faeces matter. The effects of the aqueous fruit pulp extract of *Citrullus lanatus* and reference standard on the gastro intestinal motility rate were also evaluated. 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 (Swapnil, *et al.*, 2011).

Anti-ulcerogenic property

The anti-ulcerogenic property of crude methanolic extract of *Citrullus lanatus* seeds in two different ulcer models in albino Wistar rats was evaluated. 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 50mg/kg) and Omeperazole (20 mg/kg body weight) that have shown protection index of 64.47% and 70.59% in PL and WS model respectively. Furthermore, *Citrullus lanatus* showed significantly decreased the gastric volume (53.55%), free acid (53.02%), and total acid (36.53%) in case of pyloric ligation model. The ulcer protective effect of *Citrullus lanatus* may be due to its anti-secretory along with its cytoprotective (Alok, *et al.*, 2012).

Hepatoprotective activity

The hepatoprotective effect *Citrullus lanatus* seed oil of was carried out in carbon tetrachloride induced hepatotoxicity in rats by estimated serum hepatic enzyme levels and hisopathological study of liver tissues. *Citrullus lanatus* seed oil ; CLSO (125mg) and CLSO(250mg) were administered orally for 10 days in rats and compared with standard silymarin (100 mg/kg) orally. The results showed significant decrease in serum ALT, AST and ALP levels treated groups which were increased due to CCl₄ induced liver damage are comparable with standard drug. Histopathological study of liver tissue unraveled the hepatoprotective activity of *Citrullus lanatus* seed oil (Madhavi, *et al.*, 2012).

CONCLUSION

This review had shown that *Citrullus lanatus* possesses numerous bioactivities from natural source which is of better advantage than conventional therapies. Thus, in-depth research is hereby recommended in other areas left to be investigated.

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