*Original Research Article*

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## Review of studies published on the medicinal importance of different parts of *Citrullus lanatus* in the last ten years

**[§]Akintunde Olukayode Gbolahan and Thomas Funmilola Clara**

Department of Veterinary Physiology and Biochemistry, College of Veterinary Medicine
Federal University of Agriculture, Abeokuta, Ogun State Nigeria

[§]Corresponding author: Akintunde Olukayode Gbolahan; Email address: akintundeog@funaab.edu.ng

### Abstract

Watermelon (*Citrullus lanatus*), (CL) is an edible fruit of *Cucurbitaceae* family. It is cultivated worldwide for it is nutritive and medicinal values. The records of online scientific publications on CL were accessed using Google, Google Scholar, PubMed, science.gov, Scopus, and Worldwide science as search engines, were collected from January 2010 to April 2021 and analyzed using descriptive statistics. Emphasis was placed on phytochemical, proximate, antioxidant, and pharmacological published articles on different parts of CL during this period. A total of 121 published articles that focused on different parts of CL in the last ten years were retrieved with phytochemicals 17.4% (21), proximate 7.4% (9), antioxidants 6.6% (8), pharmacology 68.6% (83). The pharmacology field was subdivided into antimicrobial 14.9% (18), cardioprotective 10.2% (13), reproduction 9.2% (12), toxicology and hepatoprotective 6.6% (8) each, analgesic, and anti-inflammatory 5.8%, neuroprotective 3.3% (4), anthelmintics (0.8%). Considering publications on different parts of CL, the seed received the highest attention with 42.1% (51) followed by fruits 35.5% (43), rind 18.1% (22), leaf 2.5% (3) while the least was whole fruit 1.7% (2). It was observed in this review on published articles that the CL fruits received the highest level of attention considering the phytochemicals, proximate, and antioxidant components to exhibit good antimicrobial potentials. While the CL leaf received little attention on antimicrobial ability. Also, different parts exhibited cardioprotective, reproduction, toxicology, hepatoprotective, neuroprotective, analgesic, and anti-inflammatory activities, anti-ulcerative efficacy due to phytochemicals, antioxidant, and proximate constituents in different parts of CL. It is worth noting that neuroprotective, hepatoprotective, antidiabetic, and anthelmintics effects of different parts of CL received little attention. While there is still dearth of information on use of different parts of CL on cancer investigations and use. This scientific review on different parts of CL had highlighted knowledge gap that still exists on different parts of CL.

**Keywords:** ***Citrullus lanatus,*** **Watermelon, Phytochemical, Proximate, Antioxidant Pharmacology**
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## INTRODUCTION

In Africa and many parts of the world today, plants have been used to treat different types of ailments and diseases (Messaoudi *et al.,* 2019). It has been observed that infectious diseases are causing about one-half of all deaths in tropical countries (WHO, 2021). People of all continents have long relied on indigenous medicinal plants for health purposes and are still in use till today (Wahid *et. al.,* 2020). Orthodox medicine has been used to complement modern medicine for effective health delivery in Africa (Kolawole *et. al.,* 2016). However, a larger number of Africans depend on plant medicine for their healthcare. Fruits and vegetables have been recognized as natural sources of various bioactive compounds (Pennington and Fisher, 2010) with medicinal importance. One of such medicinal plants is watermelon *(Citrullus lanatus,* CL).

Watermelon is an edible fruit that belongs to the genus *Citrullus* and the family Cucurbitaceae (Zia *et al.,*2021). Watermelon biomass can be categorized into three main components namely flesh, seed, and rind. The flesh contributes approximately 40% of the total weight, the rind and seeds represent approximately 60% of total watermelon fruit with the seeds and rind always discarded this contribute to massive agro-waste (Chakrabarty *et al.,* 2020; Mohamed *et al.,* 2020; Zamuz *et al.,* 2021). It has been noted that half of the watermelon fruit is edible while the other half goes to waste (Zia *et. al.,* 2021).

The watermelon is an ancient fruit that originated from the deserts of Kalahari in Africa (Zamuz *et al.,* 2021). Although today, it grows abundantly almost everywhere in the environment. Watermelon formerly called Tsamma melon was found in the Kalahari Desert. Some of the African slaves who went to the United States brought along the Tsamma melon, and that is how it started growing in Baja in California (Zamuz *et al.,* 2021). Watermelon was being cultivated in the African continent as early as 2000 B.C. Some of the hieroglyphics found in the pyramids of Egypt showed watermelon as a fruit. It was taken to China at the end of the 9th century (Zia *et.al.,* 2021). The Chinese also started cultivating it rapidly, and it soon became a desirable fruit. Today, China is the top producer of watermelon in the entire world. Throughout history, several other Asian countries like Pakistan and India have cultivated watermelon. It is largely found in the northern parts of India. It appears this fruit was largely unknown in other Mediterranean cultures of the time, but they were certainly cultivated in Asia (China in particular) by the end of the 9th century and the word “watermelon" was present in English dictionaries in 1615. Several other Asian regions have cultivated watermelon in ancient history (Kumari and Gupta 2016).

At maturity, watermelon plant grows into long, rambling vines and spread to a diameter of 4 or 6 feet. Watermelon vines are covered with large leaves, light yellow flowers, and juicy fruit. Watermelons are grown in China with the edible seeds (Gill and Leema 2016). They range in size from large and heavy to moderate size and small hybrids. The rind is hard, green, and usually striped. The fruit may be round, oval, or cylindrical, depending on variety, and weigh from 3 to 25kg. The color of the outer cover varies from white through shades of green and may be mottled or striped. The juice color varies from yellow to red but the wine -colored varieties are most popular. The fruit is about 90% water and 8 to 12% sugar (Globinmed 2010).

There are myriads of studies and reviews on the cosmeceutical importance of CL (Zia *et al.,*2021), phytochemical, antioxidants, and pharmacological importance of CL (Khulakpam *et al*., 2015); Shylam *et. al.,* 2010). But there is a need to be specific on medicinal values of different parts in CL. This will reveal the phytochemical, proximate antioxidants, and pharmacological importance of different parts of CL. The aim of this study is to review previous studies and reviews done through scholar published articles on phytochemical, proximate antioxidants, and pharmacological effects of different parts of CL in the last ten years from Jan. 2010 to April 2021. This will highlight the knowledge gap that still exists in studies on different parts of CL in the last ten years on medicinal value of different parts of CL. It also advocates for new frontlines in research on different parts of CL.

### Names used to describe watermelon

Vernacular names/Common name: Watermelon, Wild Watermelon. In Nigeria, it is generally known as watermelon; Local name: Tarbooz Telugu: Pendalam; English: Watermelon Malayalam; Thannimathan Marathi: Tarbooz, Kalingad Bengali: Tormuz Canada: Kallagadi Assamese: Tarmuj (Globinmed 2010).

SCIENTIFIC CLASSIFICATION

Kingdom: Plantae; Order: *Cucurbitales*; Family: *Cucurbitaceae*; Genus: *Citrullus*; Species *Citrullus lanatus* (Globinmed, 2010).

**Search methodology**

This review was based on a database search using the following search engines Google, Google Scholar, PubMed, science.gov, Scopus, Ebsconhost, and Worldwide science, in no particular order, to access online journals. The keywords used were" watermelon", *"citrullus lanatus"*, proximate, antioxidant, phytochemical, pharmacological with greater considerations to different parts of CL involved. All publications from Jan 2010 up to April 2021 were collated and analyzed. Theses, proceedings, unpublished projects, and abstracts were excluded from this search. The authors appreciate reviews and studies on CL before January 2010 but they were not included in this analysis.

All publications by different authors were broadly classified based on studies and reviews on different parts of CL in research areas or fields like phytochemicals, proximate, antioxidants, and pharmacology. The field of pharmacology was further subdivided into antimicrobial; hepato-protective; anti-ulcerogenic; anti-diabetic; reproduction; toxicology; analgesic and anti-inflammatory activities. All data generated were presented in pictorial (pie and bar charts) and linear graphs using Microsoft Excel (Version 2013) with descriptive statistics.

Figure1: Whole Watermelon fruit

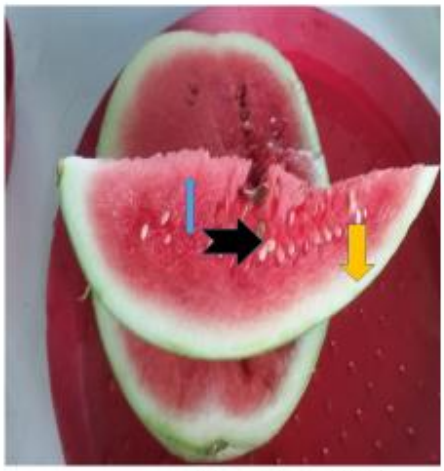
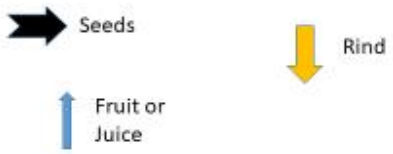
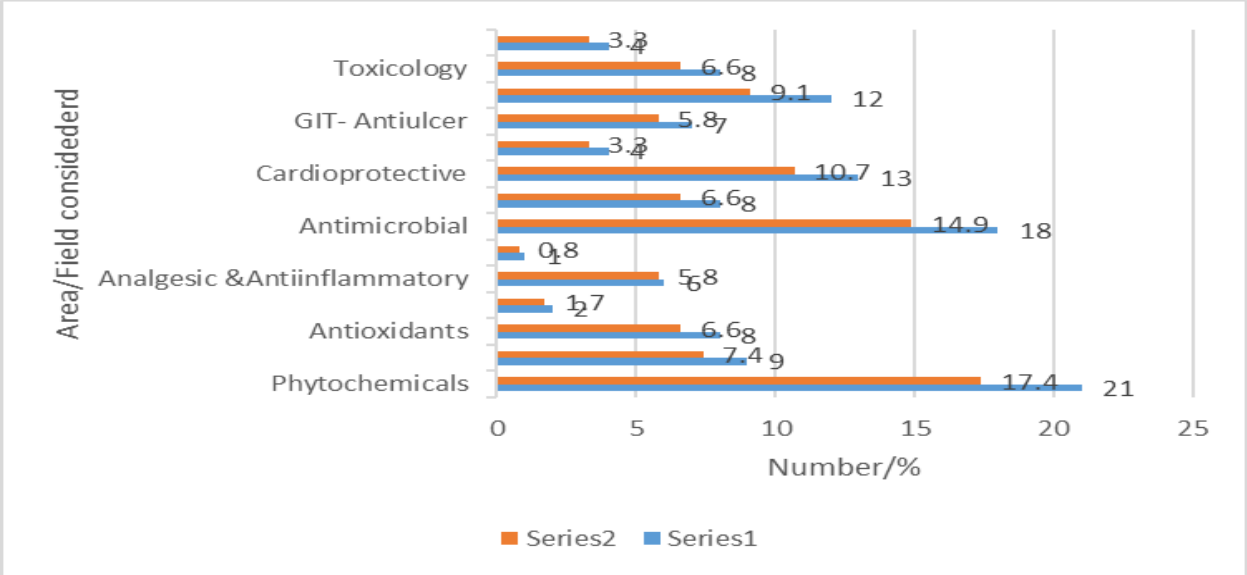


Figure 2: Sliced Watermelon fruit



**Published findings on watermelon from January 2010- April 2021.**

A total of hundred and twenty-one (121) published scholarly articles were found using a combination of selected search engines. It was generally discovered in all the publications considered that phytochemicals 17.4% (21) received the highest attention others were antimicrobial 14.9% (18), cardio-protective 10.7% (13) , reproduction 9.1% (12), proximate 7.4% (9), antioxidant, hepato-protective, toxicology 7.4% (8) each, anti-ulcerative 5.8% (7), analgesic and anti-inflammatory 5.8% (6), ethno-pharmacology and neuroprotective 3.3% (4) each, antidiabetics 1.7% (2), while the least percentage and number of publications was from anthelmintics 0.8% (1) of the total publications considered, (Figure 3).




Bar/Series1 = Number of published articles on CL considered in the area or field. Bar/Series 2 = Percentage of published articles on CL considered in the area or field.

Figure 3: Column graph of Number/ percentage of review articles published in different fields on different parts of *Citrullus lanatus* in last ten years.

The publications on medicinal values of different parts of CL were rated on the pharmacological activities utilizing the knowledge from phytochemicals, proximate, and antioxidants. The articles considered for pharmacology were 68.6% but 83 in number compared to total publications under consideration. This was subdivided into antimicrobials 21.7% (18) the highest in all the published articles considered for pharmacology. Others were cardio-protective 15.7% (13), reproduction 14.5% (12), hepatoprotective and toxicology 10.3% (8) each, anti-ulcerative 8.4% (7), analgesic and anti-inflammatory 5.8% (6), neuroprotective and ethno-pharmacology 3.3% (4) each while the least was anthelmintics 1.2% (1), see Figure 4.

Considering publications on different parts of CL generally the seeds received the highest attention 42.1% (51) Others were fruits 35.5% (43), rind 18.1% (22), leaf 2.5% (3) and the least of was whole fruits 1.7% (2), see figure 5.

It was observed that in reviewing articles published on different parts of CL that have to do with the pharmacological activities which were 76 in number, the seed received the highest attention 47.0% (35), followed by fruits 30.1% (22), rinds 21.7% (18), and least by leaf 1.2%) (1), see figure 6.

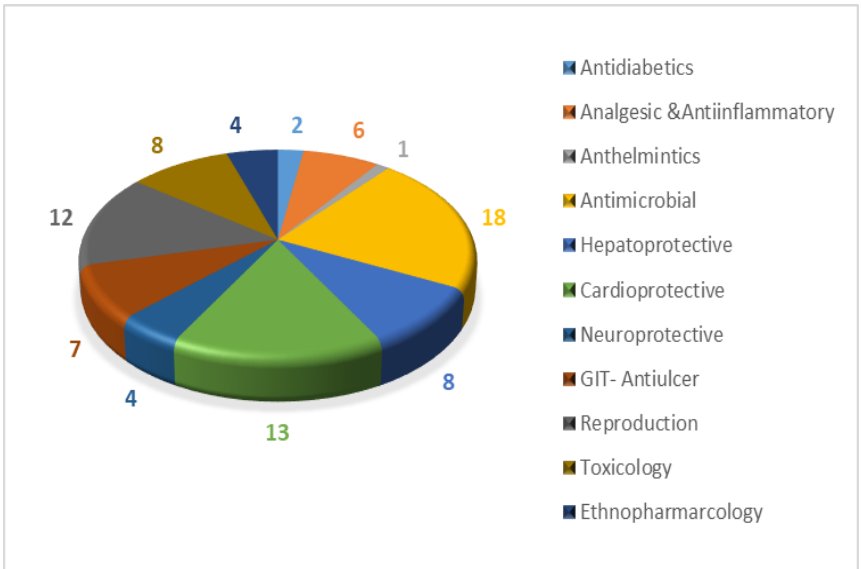



Figure 4: Pie chart showing reviewed pharmacological published articles on different parts of *Citrullus lanatus* in last ten years.

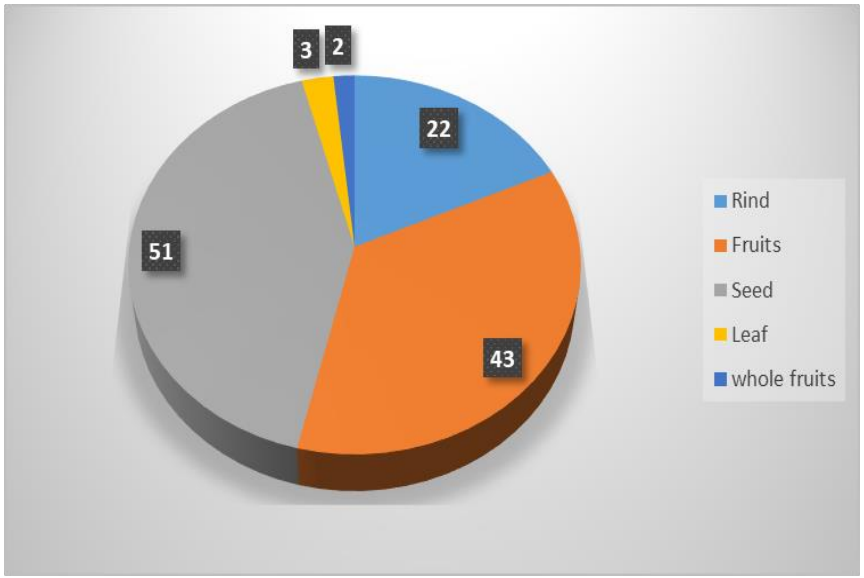
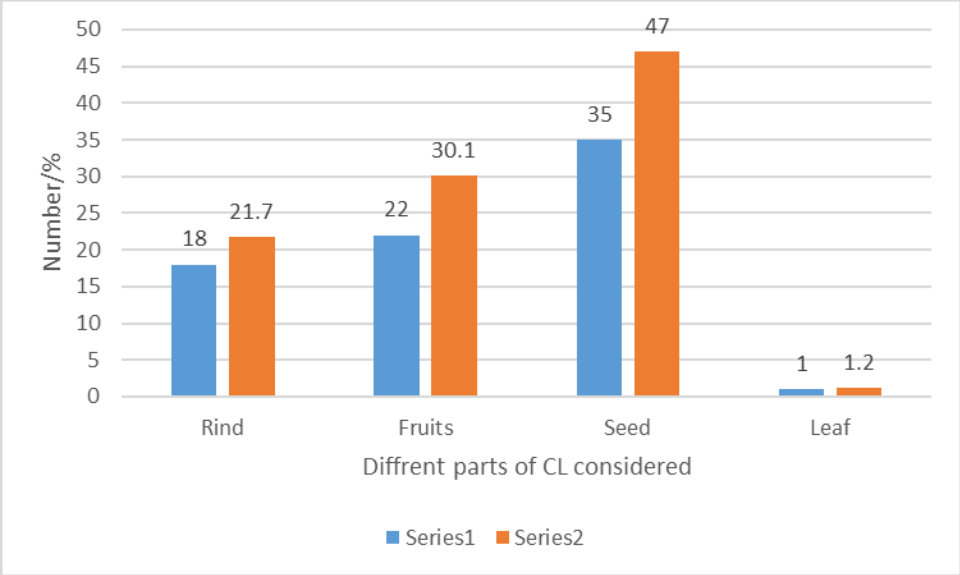



Figure 5: Pie chart of published articles reviewed on different parts of *Citrullus lanatus* in the last ten years.




Bar/Series1 = Number of published articles considered in the part of CL.Bar/Series 2 = Percentage of published articles considered in the part of CL

Figure 6: Bar chart of number / percentage of published articles on pharmacological review of different parts of *Citrullus lanatus* in last ten years.

**Discussion**

The one hundred and twenty-one (121) published articles considered in this review for different parts of CL in the last ten years are extensive but not exhaustive. It is believed that it can give an idea of the available knowledge on phytochemical, proximate, antioxidants, pharmacology, and medicinal importance of different parts of CL in the period considered (Jan. 2010 to April 2021). Also, it will help to confirm the traditional claims of the use of CL in treating some ailments in our environment.

In considering publications for different parts of CL it was observed that CL fruits received the highest level of attention considering the phytochemicals, proximate, and antioxidant potentials found in them such as saponin, alkaloids, total phenol, lycopene, anthraquinones, flavonoids, phobatanin (Oseni and Okoye, 2013); vitamin A, cucurbitacin E, flavonoids, vitamin C, thiamine, riboflavin, polyphenolic compounds, terpene, steroid, flavonoid, glycoprotein-vicilin (Rajasree *et al.* 2016, Gupta *et al.*2018, Nagal *et al.* 2012, Tlili *et al.* 2011b); citrulline content (Munglue *et al.*, 2013, Tarazona-Díaz *et al.*, 2013, Poduri *et al.* 2013, Bailey *et al.* 2016, Oseni *et al.* 2015) the ethyl acetate fractions of CL fruits obtained from different geographical sites with higher content of total phenols and flavonoids (Singh *et.al.* 2020); CL fruit contains high percentages of moisture, carbohydrates, and low percentage of fat (Hind Abd-alluh and Abu-Hiamed, 2017). The seed also received attention due to the alkaloids, flavonoids, tannins, amino acids, carbohydrates, cardio glycosides, terpenoids, steroids, carotenoids (Varghese et.al. 2013). It was observed that the ethanolic and petroleum ether of CL seeds contain steroids, alkaloids, flavonoids, terpenoids, and saponins (Sani 2015, Hong *et al.* 2018). It was also recorded that the carbohydrates found in CL seed are also beneficial Elkhedir and

Mustafa (2015), Romdhane *et al.,* (2017), as well as the protein (Morais *et al.,* 2017).
While CL rind is found to contain glycosides, saponins, flavonoids, steroids, and protein (Azad *et al.,* 2015, Feizy *et al.,* 2020, Kumar *et al.,* 2012). But saponins, steroids, terpenes, carbohydrates, anthraquinones, and terpenes were found in the methanolic extract of CL leaf by only one team of the researchers (Alebiosu and Yusuf, 2015). In reviewing the pharmacological published articles on different parts of CL considering different fields.

**Antimicrobial**

The seed was observed in this review to enjoy the highest attention on antimicrobial activity with different claims such as Babaiwa *et al.,* (2017) emphasizing the use of the ethyl acetate extract of CL seeds to treat a wild range of bacterial due to the presence of some chemical compounds such as fatty acids, hexamethyl-2-ethyl acridine, gamma- tocopherol and methyl phthalate. The aqueous and methanolic extract of CL seed powder had been shown to have good antimicrobial properties (Sola *et al.,* 2019). The antimicrobial efficacy of methanolic extract of CL seed was reported by Sathya and Shoba (2014). Other groups of authors that attested to the good antibacterial effects of CL seed were Adunola *et al.,* (2015); Braide *et al.,* (2012); Sathya and Shoba (2014); Babaiwa *et al.,* (2020) and Gill *et al.,* (2010). Hameed *et al.,* (2020) emphasized the importance of melanin found in crude chloroform, hexane and ethanol leaves, stem, fruits, and seeds extracts of CL as a good antibacterial agent due to the presence of tannins, saponins, flavonoids, cyanogenic glycosides found in the extract. Braide *et. al.,* (2012) reported the phytochemical and antibacterial properties of CL seeds. The ethanolic extract of CL rind had been shown to contain antioxidant such as phenolic substance this make it exhibit an excellent antimicrobial efficacy by the ethanolic extract of CL rind when incorporated at 0.10% level in pork patties (Kumar *et al.,* 2018). Watermelon rind powder had been shown to improve growth parameters and serves as probiotics and prebiotics (Doan *et al.,* 2021). While CL fruits have been proven to be effective against some bacteria and fungal strains (Thirunavukkarasu and Ramanathan 2010). Meanwhile, Siddiqui *et al.,* (2018) reported the anti-urolithiasis and diuretic effects of CL fruits.

**Cardioprotective**

Watermelon seed had been shown to decrease atherogenic index, LDL, serum cholesterol, and liver glycogen whereas increasing the HDL in the experimental animal model (Oyenihi *et al.,* 2016). While Fan *et al.,* (2020) and Karikpo *et al.,* (2018) confirmed watermelon seed extract to possess significant cardioprotective potential by ameliorating structural integrity of the cardiac muscles and significantly ($p<0.05$) reducing the levels of creatine kinase and dehydrogenase which a marker of cardiac injury. The aqueous extract of *Citrullus lanatus* fruit had been shown to possess hematinic effects (Akintunde *et al.,* 2020. Kolawole *et al.,* 2017) demonstrated the presence of phenol, alkaloids, saponins, tannins, and steroids in watermelon juice to have anti-oxidative effects.
The citrulline and arginine found in watermelon flesh, seeds, and rind fed to humans have been shown to later metabolize nitric oxide which is an important vasodilator in the body (Biswas and Chattopadhyay 2017; Rajasree *et. al.,* 2016). The watermelon rind had also been investigated and confirmed to cause cardiovascular system protection (Akintunde *et al.,* 2017; Abu-Hiamed, 2018); Fan *et al.,* 2020) due to the presence of phytochemicals constituents.

**Reproduction**

The dietary consumption of CL fruit had been shown to ameliorate infertility with the enhancement of *Carica papaya* seeds extract in the animal model (Amedu and Idoko 2016a). Jimoh *et al.,* 2021 revealed that CL fruits in dextrose saline enhance rooster semen kinetics, seminal oxidative stability, and egg fertility. The reproductive activities in the body can be improved by the antioxidants found in the aqueous extract of CL fruit (Daramola *et al.,* 2018). Khaki *et al.,* 2014). Also, the level of testosterone in the body can be upregulated by CL fruit extracts (Salvador and Marin 2019). Mohammed and Al-Bayati 2014 confirmed that the citrulline and lycopene found in watermelon rinds can enhance some reproductive indices in

male mice. This was also reported for CL seed (Khaki *et al.,* 2014). The hypophyseal axis and sexual behavior of male Wistar rats are upregulated by the ethanolic extract of CL rind (Atuadu *et al.,* 2018). Kolawole *et al.,* (2014) also reported that CL rind improves semen parameters, reproductive hormones, and testicular oxidative status. The methanolic extract of CL seeds had been shown to upregulate sperm parameters, testosterone level, and testicular cytoarchitecture in the animal model study (Godspower *et al.,* 2015). Ebeye *et al.,* (2015) reported the histomorphological effect of aqueous extract of CL fruits in the animal model. While Onyeso *et al.,* (2016) revealed the hypoglycaemic influence of hydro-methanolic seed extract with co-administered caffeine, which can ameliorate impaired testicular and avoid sperm killing or testicular damage caused in alloxan-induced diabetes male Wistar rats. This was established with the knowledge of watermelon fruits and citrulline having potent tocolytics with deregulating force produced by calcium entry that arise by different pathways, including oxytocin stimulation. The major mechanism was suggested to stimulate the Nitric Oxide-cyclic guanosine monophosphate (cGMP) relaxant pathway (Onyeso *et al.,* 2016).

**Analgesic and Anti-inflammatory**

The oral methanolic extract of CL seed has been reported to have anti-inflammatory activity and free radical scavenging activity. This was traced to the presence of phytochemical substances such as carbohydrates, alkaloids, steroids, saponins, flavonoids, tannins, and phenolic compounds (Sarika *et al.,* 2013; Madhavi *et al.,* 2012; Gill *et al.,* 2010). Wahid *et al.,* (2020) investigated that the ethanol extracts of CL seeds have good analgesic and anti-inflammatory effects due to the presence of cucurbitacin A, B, or E in the seeds which are thought to inhibit the COX 2 pathway. The presence of glycosides, saponins, flavonoids, steroids, and protein in the methanolic extract of CL rind had been shown to have good analgesic and anti-inflammatory effects (Azad *et al.,* 2015). The possible antipyretic and anti-inflammatory activities of methanolic extract of *C. lanatus* rind were associated with the flavonoids and/or the alkaloidal components of the extract (Kolawole and Dapper. 2016).

**GIT: Antiulcer**

The *Citrullus lanatus* seed has been investigated to possess good antioxidant and anti-ulcerative potential due to the presence of bioactive compounds like flavonoids, saponin, and tannins (Lucky and John 2012; Gill and Sood 2011; Bhardwaj *et al.,* 2015). The methanolic extract of CL seeds has been shown to have an ulcerative protective effect due to its anti-secretory potential along with its cytoprotective (Alok, *et.al.,* 2012). Swapnil, *et al.*, (2011) reported that aqueous fruit pulp extract of CL has significant laxative activity. Francis *et al.,* 2013 reported the significant gastro-protective effect of *Citrullus lanatus* juice or fruit.

**Neuroprotective**

The ethanolic watermelon seed extract has been shown to have significant immunoreactivity to neurofilament protein antibody to improve cognitive functions (Finbarrs *et al.,* 2018; Owoeye *et al.,* 2018). Incorporating watermelon rind in flour for cake production has enhanced nutritional quality, chemical and functional properties (Imoisi *et al.,* 2020). It is worth noting here that the neuroprotective potentials of *Citrullus lanatus* fruit or juice are yet to be investigated.

**Toxicology**

The ethanolic watermelon seed in diet had been revealed to cause a significant decrease in body weight and not significantly alter the weight of the liver and brain (Oyenihi *et al.,* 2021; Garuba *et al.,* 2017). Belemkar and Shendge (2021) improved on the study using an animal model to investigate the effects of ethanolic extracts of CL seed and observed that it does not alter behavioral changes, biochemical, hematological, and histopathological lesions in the experimental animal. While Aigbiremolen *et al.,* (2019) confirmed that *Citrullus lanatus* seeds had no renal morpho-functional changes in the experimental animal. It is also on record that *Citrullus lanatus* can be incorporated into the cake to improve the nutritional values (FDA, 2018).

**Antidiabetic**

The alkaloids, flavonoids, terpenoids, saponins, and anthraquinones found in ethanol and petroleum extract of CL seed had been shown to have antidiabetic effects in the animal model (Sani 2015). In the study of Hong *et al.,* (2018) CL fruit or juice consumption had been shown to upregulate hepatic gene expression of endothelial nitric oxide synthase and downregulate the expression of fatty acid synthase, 3-hydroxy-3-methylglutaryl-CoA reductase, sterol regulatory element binding protein 1, sterol regulatory element-binding protein 2, cyclooxygenase-2, and nuclear factor–κB p65. It is worth noting here, that antidiabetic effects of different parts of CL have not received much attention on treatment and experimental work to complement the claims in their use in ethno-veterinary medicine.

**Hepatoprotective**

*Citrullus lanatus* seed oil possesses in vivo antioxidant capacity which can protect liver cells from damage caused by toxic agents due to its richness in linoleic acid and other saturated fatty acids (Madhavi *et al.,* 2012; Eke *et. al.,* 2021; Bazabang *et. al.,* 2018). The aqueous and methanolic extracts of watermelon seeds had been shown to have hepatoprotective activity on salt and paracetamol-induced liver damage in female white rats (Omotoso 2018). Adebayo (2014) also reported that the leaf extract of *Citrullus lanatus* had hepato-protective potentials on carbon tetrachloride -induced liver damage in rats. Enemali *et al.,* (2020) investigated and confirmed that CL fruits juice had a protective effect on the liver of acetaminophen-intoxicated albino rats. Makaepea *et. al.,* 2019 and Sorokina *et. al.,* 2021 reviewed natural products found in CL fruit and emphasized that the products have good hepatoprotective effects. It is worth noting that throughout this search there is a dearth of information on hepatoprotective effects of CL rind.

**Anthelmintics**

The fatty oils found in aqueous and alcoholic extracts of CL seed have been shown to paralyze tapeworms and roundworms (Varghese *et. al.,* 2013). This review also discovered that there is little information on the anthelmintics potentials of CL.

**Ethnopharmacology**

The medicinal importance of using CL to treat fatigue, typhoid, malnutrition, scanty urination, asthma attack, indigestion, hypercholesteremia, arthritis had been established in different parts of *Citrullus lanatus* (Khulakpam *et al.,* 2015).

**CONCLUSION**

With the abundance availability of CL fruits throughout the world, there are a lot of inherent values that can be enjoyed through the exploitation of all different parts of CL but there are yet to be explored. Meanwhile, more studies still needed to be done to open up the hidden treasures in this valuable medicinal fruit (watermelon) as listed in the recommendations below:

**Recommendations**

i. This review confirms that *Citrullus lanatus* rind has not received much attention as *Citrullus lanatus* fruit or juice and *Citrullus lanatus* seeds did in all the areas considered (phytochemical, antioxidant, proximate, and pharmacological).
ii. Also the whole fruit of *Citrullus lanatus* which is a possibility of feeding to livestock has not received much attention. The scientific knowledge of the whole fruit of CL is required to understand the Phytochemical, proximate, and antioxidants potentials to foresee the possible medicinal importance of the whole fruits in the life of livestock to be fed with the whole fruits.
iii. They still need to study more on the hepatoprotective and anthelmintic abilities of different parts of *Citrullus lanatus* generally especially on the rinds.
iv. There are need for more studies to investigate effects of different parts of *Citrullus lanatus* on tumour growth and treatment.

**Conflict of Interest**

The authors have no conflict of interest to declare.

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