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Phytoconstituents and Pharmacological Activities of Seeds of *Citrullus lanatus*: A Review

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Abstract: Herbal products are globally crucial because of their low side effect, affordability, and accessibility. Watermelon *Citrullus lanatus*) is a famous fruit in the indigenous system of folk medicine and is also known to contain bioactive compounds such as triterpenes, sterols, vitamins, cucurbitacin, and minerals. Fruits are used for cooling, strengthening, as aphrodisiac, and blood purifiers. *Citrullus lanatus* seeds are highly nutritious; they contain a good amount of protein, fat,vitamins, and mineral and the seeds are used to prepare shakes, mix into flour, and used for sauces. The seeds treat urinary tract infections, bed wetting, dropsy, and renal stones. This review aims to provide information on *Citrullus lanatus's* nutritional value and pharmacological actions.

Keywords: Herbal, Bioactive, Watermelon, Treatment, Fruit, Seed

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Introduction

Watermelon, a tropical plant, thrives in warm, sunny climates. It needs well-draining, fertile soil with a slightly acidic pH. Watermelon is grown from seeds and is commonly cultivated in Ghana's coastal regions, forest zones, and northern savannah areas (Eitzinger *et al*., 2022). Watermelons, scientifically known as *Citrullus lanatus*, are named for their high water content (around 93%). The "melon" part refers to their large, round shape and sweet, fleshy interior. The scientific name is derived from Greek and Latin roots. "Citrullus" comes from the Greek word "citrus," possibly referencing the fruit. "Lanatus" is Latin, meaning "wooly," referring to the seeds (Li *et al*., 2013).

Watermelons are versatile fruits with many uses. These can be eaten as a nutritious snack, a sweet dessert, as well as cool salad (Olumati, 2017). The watermelon juice can also be used to make delicious drinks. The sugar content and

Table 1: Proximate contents of watermelon seed (Rekha *et al*., 2016)

S. No.	Parameters	Values
1.	Moisture	6.4 %
2.	Fat	47.1 %
3.	Protein	68.4 %
4.	Fiber	1.2 %
5.	Ash	2.6 %
6.	Carbohydrate	25.1 %

sweetness are essential factors in determining the quality of different watermelon varieties. Despite their sweetness, watermelons are low in calories and are highly nutritious and thirst-quenching (Okonmah *et al*., 2011).Watermelon seeds are known to be exceedingly dietary; they are wealthy sources of protein, vitamins B, minerals (such as magnesium, potassium, phosphorous, sodium, press, zinc, manganese, and copper), and fat among others as well as phytochemicals (Braide *et al*., 2012).

Watermelon seeds, often overlooked, offer significant economic potential, especially in developing countries. These seeds can be processed into various products, such as snacks, flour, and sauces. The oil extracted from them is used in cooking and even in cosmetics. As demand for these products grows, watermelon seed cultivation can provide a valuable source of income for farmers and contribute to local economies (Jensen *et al*., 2011).

Watermelon seeds, often discarded after the fruit is eaten, have potential applications that remain largely unexplored. There is limited understanding of how different watermelon varieties impact their nutritional, phytochemical, and antioxidant properties. The purpose of this study is to examine the mineral profile, phytochemical content, antioxidant activity, and proximate composition of seeds from three different types of watermelon(Hassan *et al*., 2011).

Nutritional values

The natural product *Citrullus lanatus* carries 92% water, approximately 6% sugar and remaining is vitamins A, B, and C. Composition of dried seed without shell per 100 g incorporates protein 28.3 g, fat 47.4 g, water 5.1 g, vitality 2340 kJ (557 kcal), carbohydrate 15.3 g, Calcium 54 mg, Phosphorous 755 mg, thiamine 0.19 mg, riboflavin 0.15 mg, niacin 3.55 mg and folate 58 mg. The seed oil possesses oleic, palmitic, stearic corrosive, and glycosides of linoleic (Schippers *et al*., 2000). This medicinal plant serves as rich sources of vitamins, minerals, and compounds with cancer-preventive properties. These can be used to produce a variety of food products, which can help to meet dietary needs and fight various degenerative diseases (Sangita *et al*., 2016). The proximate, oil content and minerals of watermelon seeds are mentioned in Tables 1, 2and 3, respectively.

Historical Background

Citrullus lanatus was studied a long time ago in tropical Africa and subtropical Southern Africa specifically Namibia, Zimbabwe, Botswana, Mozambique, Zambia, and Malawi, and has been utilized by people since a long time (Paris *et al*., 2015). The development of different species of *Citrullus* in India began within the early eighth

Table 2: Oil Content of different varieties of watermelon Seed (Adejumo *et al*., 2015)

S. No.	Variety	Ether extract (%)
1.	Casheir	20.8
2.	Saddir	23.8
3.	Farrasha	23.5
4.	Kongo (kosti)	19.8
5.	Kongo (Gezira)	21.0
6.	Kongo (mixture)	25.0
7.	Seinnie (Dopa)	21.0
8.	Sheiria (Mixture)	27.5
9.	Sheiria (Dopa)	25.0

Table 3: Minerals of watermelon seed (Razavi *et al.,* 2006)

S. No.	Mineral	Quantity (mg/kg)
1.	Calcium	0.68
2.	Manganese	0.14
3.	Cobalt	0.03
4.	Copper	0.86
5.	Iron	1.87
6.	Sodium	10.5
7.	Potassium	53
8.	Magnesium	28
9.	Zinc	0.24

century after its presentation from an African landmass. Advance conveyance and presentation of *Citrullus* come to other nations and locales such as China, Southeast Asia, Japan, Europe, and America amid early post-Columbian times (Erhirhie *et al.*, 2013). Consequently, the development of *Citrullus* has been massively expanded all through the tropical locales of the globe due to its broadened utilization. It is commonly consumed when ripe as a fruit in summer due to its refreshing and soothing properties. There are various other critical employments due to which the quest of *Citrullus* has prospered (Mcgregor *et al*., 2012).

Bioactive Compounds/ Phytoconstituents in Watermelon Seed

Watermelon seed is well known for its dietary substance. Moreover, it has restorative well-being benefits against diverse incessant maladies such as diabetes. These health advantages originate from specific phytochemicals that make watermelon seeds superior to other grains in terms of promoting human health and wellness. Phenolic compounds display anticancer, anti-inflammatory, antiviral, and antioxidant impacts. Eight phenolic acids were identified from watermelon seeds, namely, 4-hydroxybenzoic acid, p-coumaric acid, gallic acid, ferulic acid, vanillic acid, syringic acid, caffeic acid, and sinapic acid. Phenolic compounds, often mentioned as bioactive substances, are auxiliary plant metabolites. They are predominant throughout the plant kingdom and can be found in different plant parts, both edible and non-edible, including mash, seeds, clears out, bark, and roots (Choudhury *et al*., 2022). They can exist in free frames or attached to proteins, sugars (glycosides), and other substances. They range

from simple particles to extremely complex ones. There are over 8,000 known chemical structures of phenolic compounds (Jaroszewska *et al*., 2023). Among the three assortments, dark red sweet type displayed the most noteworthy antioxidant action and had a significant phenolic component, which are well-known for their powerful anti-oxidant properties compared to other phyto-chemicals (Tabiri *et al*., 2016).

The watermelon seeds may be useful in treating a variety of ailments, including bronchitis, diabetes, nephritis, asthma, sinusitis, syphilis, and mental disorders, given their healthful and chemical makeup. Therefore, it is necessary to evaluate its pharmacological and wholesome potential, highlighting its natural qualities and advantages for wellbeing (Aravind *et al*., 2013). A vital component of human nutrition, watermelon, can be consumed fresh, packaged, in pulps, or in the form of juices. Its high calories and high-water content maintain homeostasis in body, producing energy. Its solid part holds important bioactive compounds, eminently citrulline, and lycopene (Mandizvo *et al*., 2022). Citrulline is an antioxidant that helps to promote blood vessel relaxation and fight atherosclerosis. It is changed over to arginine within the body, which produces nitric oxide (NO), a key atom in vasodilation (Omoniyi *et al*., 2020). Lycopene, the component of watermelon, is recognized for its antioxidant properties. Broadly, it has been associated to the anticipation of cancer and degenerative infections. Lycopene bears antioxidant properties because of its interesting non-cyclic structure with two unconjugated twofold bonds. This structure makes it compelling in neutralizing singlet oxygen, and acts as a powerful antioxidant. Watermelon has 40% more lycopene than tomatoes (Yimer *et al*., 2020). Watermelon mash contains vitamins and bioactive compounds. The eminent ones contain phenolic acids, lignans, coumarins, and stilbenes. These compounds are regularly found in diverse parts of the plant species, counting both the mash and seeds, with potential varieties in amounts (Falade *et al*., 2020). Organically dynamic compounds like tocopherols, watermelon seed oil contains large amounts of phospholipids and sterols, which have a beneficial effect on humans.

Significant concentrations of phenolic acids, flavonoids, terpenoids, alkaloids, steroids, carote-noids, and saponins have been found in watermelon seeds. Additionally, rutin and quercetin were also present (Abdulazeez *et al*., 2020). Investigation has shown that α-spinasterol has different physiological impacts, counting the balance of mitochondrial action, and quality expression of atomic receptors, and it moreover shows anti-tumor, antioxidant, and anti-inflammatory exercises (Jyoti and Jain, 2016). Watermelon seeds contain critical sums of saponins, alkaloids, and terpenoids (cucurbitacins) as their major compounds. Pectin, which is not an auxiliary metabolite, is additionally found in seeds, that control carbohydrate and cholesterol retention and supporting advantageous intestine microbes as a prebiotic specialist (Offuene *et al*., 2015). The analysis of fatty acids using gas-liquid chromatography-mass spectroscopy (GC-MS) of watermelon seeds showed a run of oily acids, calculating linoleic, stearic, palmitic, and oleic corrosive. These wet acids were found to be overwhelmingly present in seeds and were identified as the winning wet acids in WMSs oils with per cent composition as -- propanediol corrosive (3.74%), delta-tocopherol (5.16%), dioctyl esters (0.98%), carbonic acid (1.30%), oleic (17.84%), linoleic (13.77%), oleic (17.84%), linoleic (1.80%), oleic (17.84%), and palmitic acid (1.80%). Watermelon seeds are wealthy in protein (15-50%), counting egg whites, globulin, prolamin, and glutelin. Examining seed characteristics such as coat color, hardness, and biochemical composition (including lignin, cellulose, and hemicellulose) can aid in develop-ing nutritionally improved watermelon genotypes and value-added food products (Jacob *et al*., 2015; Nkoana *et al*., 2022). Table 4 illustrates

Table 4: Parts of watermelon along with their phytoconstituents

Part	Constituent
Seed	Beta carotene, Xanthophylls, Phenolics, Vitamin C, Lycopene (Sorokina *et al*., 2021) Protein- Albumin, Globulin, glutelin (Wani *et al*., 2011) Flavonoid, vitamin c, thiamine, polyphenolic compounds (Olamide *et al*., 2011) Terpene, steroid (Loiy *et al*., 2011) 2-dodecyclobutanon, 2-tetradcyclobutanone, cellulose radical (Sin *et al*., 2006) Glycoprotein-vicilin (Yadav *et al*., 2011) Amino acids- arginine, isoleucine, leucine. Mineral composition- Sodium, magnesium, calcium (Ojieh *et al*., 2008)
Seed Oil	High amount of higher fat acids- palmitic acid, stearic acid, linoleic acid. Higher amount is linoleic acid (Oluba *et al*., 2011). Total lipid content- oils- polyunsaturated fatty acids- oleic, linoleic fatty acid (Anhwange *et al*., 2010). Saturated fatty acid. Unsaturated fatty acid- tocotrienols (Oluba *et al*., 2011).

different parts of watermelon with their phyto-constituents.

Pharmacological activities of Citrullus lanatus

Bioactive substances can protect against metabolic waste and pathogens. Because of these beneficial effects, they can be used to create contemporary foods that may have addictive and defensive qualities. Because of its high concentration of bioactive chemicals and essential natural phytoconstituents, watermelon is regarded as food and a healing plant in African and Asian cultures (Reetapa *et al*., 2011). Watermelon bears anti-diabetic, hypogly-cemic, hypolipidemic, diuretic, anti-urolithiatic, and anthelmintic properties. Its seed extricates have illustrated antimicrobial properties, making them potential candidates for utilization in pharma-ceutical definitions against certain destructive microorganisms (Nadeem *et al*., 2022). Studies have shown antibacterial action in watermelon seed extricates against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*, and *Bacillus subtilis.* The ethanolic extricates from illustrated eminent pain-relieving and anti-inflammatory impacts over 3 to 24 h, conceivably credited to cucurbitacins, which are accepted to restrain COX 2 (Cyclooxygenase 2). The ethyl acetic acid derivatives from *Citrullus lanatus* seeds shows movement against certain microscopic organisms and parasites connected to respiratory, gastrointestinal, and urinary tract contaminations (Reetu *et al*., 2017). Table 5 represents the different pharmacological activities of watermelon seeds.

Anti-diabetic activity

Watermelon's anti-diabetic properties were considered in relation to ICR mice in a study. Mice have been nourished using diets with 10% watermelon substance powder (WM-P) or 1% watermelon skin ethanol extricates (WM-E). After 4 weeks, diabetes was actuated within the mice utilizing streptozotocin. The discoveries illustrated that WM-E supplementation strikingly diminished blood glucose levels and expanded serum levels. Additionally, the histological examination demonstrated that watermelon safeguards pancreatic cells, inferring a potential anti-diabetic attribute (Khalid *et al*., 2021).

Anti-inflammatory activity

Citrullus lanatus seed oil (CLSO) displayed anti-inflammatory activity in a rat model of carrageenan-induced paw edema. At 50 mg/kg and 100 mg/kg, the oil's efficacy was compared with that of the common anti-inflammatory

Table 5: Different pharmacological activities of *Citrullus lanatus* seeds (Vinhas *et al*., 2021)

S. No.	harmacological activities	Effects
1.	Cardiovascular Benefits	Diminished body weight pick up, diminished plasma cholesterol concentrations, progressed homeostasis of professional- and against-inflammatory cytokines, and constricted improvement of atherosclerosis in hypercholesterolemic mice
2.	Anti-hepatotoxic activity	Seed extricate hindered the rises of hepatic chemicals in serum, and enhanced the histopathological changes actuated by CCl4 in mice
3.	Weight loss and haematological benefit	Reduction of weight in Wistar rats; treatment of anaemia; depressing effects on platelet activity and leucocyte function
4.	Antiulcer and gastroprotective	Gastric Ulcer inhibition in rats
5.	Anti-diabetic	Blood glucose concentration is decreased by the methanolic extract of watermelon seed extract
6.	Anti-microbial	Activity against S. aureus (Staphylococcus aureus), E. coli (Escherichia coli), B. stubtilis (Bacillus subtilis) and P. aeruginosa (Pseudomonas aeruginosa).
7.	Anti-inflammatory	COX2 inhibitor
8.	Sexual enhancement	To increasing serum testosterone and luteinizing hormone.

medication diclofenac (10 mg/kg). The results revealed that both doses of CLSO and diclofenac significantly reduced the swelling and inflammation in the rat's paw induced by carrageenan, indicating the potential anti-inflammatory properties of CLSO (Patel *et al*., 2019).

Anti-Cancer Activity

Watermelons, like other natural products and vegetables, can lower cancer hazards due to their cancer-prevention agents. Lycopene, found in watermelons, may diminish prostate cancer cell development. Eating vitamin-A-rich natural products can protect against lung and verbal depth cancers, as per the National Cancer Foundation (Reetu *et al*., 2017).

Antioxidant activity

Antioxidant activity of *Citrullus lanatus* was evaluated using methanolic, chloroform, and ethyl as well as acetic acid extract. The degree of antioxidant activity was determined using the DPPH technique. *Citrullus lanatus* (MECL) seeds' methanolic extract showed the highest level of antioxidant potential (Nadeem *et al*., 2022).

Hepatoprotective activity

Citrullus lanatus seed oil illustrated hepatoprotective impacts against liver harm actuated by CCl_4 in rats. When compared to the negative control group, the 125 mg/kg and 250 mg/kg provoked a significant decrease in blood serum ALT, and AST. Moreover, histopathological examination of liver tissue affirmed the hepato-protective properties of *Citrullus lanatus* seed oil (Ahmed *et al*., 2020).

Antimicrobial activity

Different parts of *Citrullus lanatus* were studied for their antimicrobial properties. Extricates from stems, natural products, and seeds, utilizing

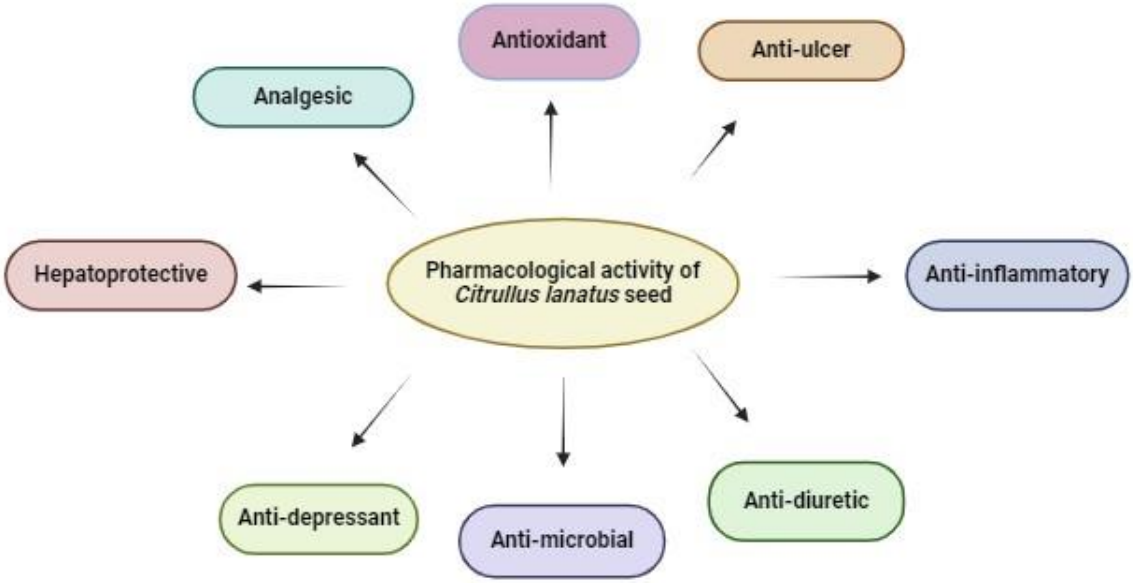

Fig. 1: Pharmacological activities of *Citrullus lanatus*

chloroform, hexane, and ethyl liquor, showed antibacterial impacts against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, and *Proteus vulgaris*. Moreover, these extricates illustrated antifungal movement against *Aspergillus niger* and *Candida albicans*. Also, *Citrullus lanatus* seed extricate, procured through cold maceration, showed good anti-bacterial activity against *Staphylococcus* species and *Pseudomonas aeruginosa* (Patel *et al*., 2019).

Anti-ulcerogenic activity

Citrullus lanatus has illustrated anti-ulcerogenic properties. When a methanolic extricate of its seeds was fed orally to rats in two diverse ulcer models (pyloric ligation and water drenching stretch), it altogether decreased the ulcer. Also, within the pyloric ligation show, it brought down gastric volume, free acid (Seshamamba *et al*., 2018).

Cardioprotective activity

It has been reported that when the male pale-skinned rats were given an adjusted calorie count that included *Citrullus lanatus* seeds, there were noteworthy reduction in serum triglyceride (TG) and VLDL-C (exceptionally Low-Density Lipoprotein Cholesterol) levels. Also, the treated group displayed diminished levels of serum levels of cholesterol, LDL (Low-Density Lipoprotein), and AI (Atherogenic List). HDL (High-Density Lipoprotein) values increased. These changes in lipid profiles propose potential positive impacts of *Citrullus* seed on cardiovascular well-being (Nkoana *et al*., 2022).

Other effects of Watermelon Seed

Antinutrients are substances that interfere with the digestibility, assimilation, and utilization of supplements and non-nutrients, blocking metabolic pathways and diminishing their bioavailability (Popova *et al*., 2019). Therefore, antinutrients must be decided to guarantee dietary security. The most common anti-nutritional factors found in watermelon seeds include phenols, alkaloids, hydrocyanic acid, tannins, phytates, and oxalates (Addo *et al*., 2018). Tannins are a bunch of polyphenols that tie and shape complexes with proteins, minerals, stomach-related proteins, and vitamins and repress their digestion within the body. Calcium, magnesium, copper, and zinc hinder its retention

by the digestive system. Oxalate shapes a complex with calcium and makes it inaccessible for absorption. This accelerates within the insoluble salts, which gather within the renal glomeruli in this way contributing to the improvement of renal disease (Dassanayake *et al*., 2012). Figure 1 represents the pharmacological activities of watermelon seeds.

Conclusion

The role of herbs in improving health keeps increasing as we discover new perspectives and possible advantages associated with lesser-known sources, such as watermelon seeds. These often-overlooked seeds have emerged as a guarantee in several perspectives of health and nutrition, greatly improving our knowledge of natural therapies. Originally thrown out as waste, watermelon seeds have become a nutritional powerhouse. Their huge line of essential supplements, which includes vitamins, minerals, and plant-based protein, make them a valuable addition to a modified diet. The proximity of amino acids and advancements in cancer prevention highlight their potential to foster heart well-being, related to stomach health, weight management. While the rising viewpoints and potential well-being benefits of watermelon seeds, it is imperative to preserve a basic approach. To establish precise dosages, activity tools, and long-term effects, more study is necessary. Furthermore, individual responses may vary, and caution should be exercised, particularly by people with underlying medical conditions or medication regimens. As we proceed to memorize more herbs and natural constituents, it is vital to grasp this newly discovered information regarding watermelon. This underscores how important it is to use evidence-based strategies to make informed decisions when pursuing overall well-being. In summary, the use of herbs in health and wellness may be a dynamic area that continues to unveil the abundant resources of nature. By mixing convention with logical thoroughness, we will open the total potential of these treasures while progressing all-encompassing and evidence-based approaches to well-being.

Ethical Statement

This is a review article hence no Ethical Approval needed.

Author Contributions

Mondal Banani-Editing and Supervision, *Ganguly Shayeri Chatterjee*-Reviewing, editing and supervision, *Dasgupta Ramesh Kumari*-Editing, *Mahanti Subarna*-Editing, *Karmakar Mriganka*-Writing original draft, *Sikder Chayanika*- Writing original draft, *Rai Shivam*- Writing original draft. All authors have read and agreed to the published version of the manuscript.

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Conflict of Interest

The authors declare no conflicts of interest.

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