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Research Article

Therapeutic and nutritional aspects of watermelon seeds

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ABSTRACT:

Watermelon (*Citrullus lanatus*) seeds, often discarded as agricultural waste, have gained increasing attention for their significant nutritional and therapeutic potential, unsaturated fatty acids, essential amino acids, vitamins (A, B- B-complex), and vital minerals such as magnesium, iron, zinc, and potassium, making them a promising source of plant-based nutrition. The lipid fraction of watermelon seeds primarily consists of linoleic and oleic acids, which contribute to cardiovascular health and lipid regulation. Furthermore, the seeds contain bioactive phytochemicals, including flavonoids, phenolic acids, and alkaloids, that exert potent antioxidant, anti-inflammatory, antidiabetic, and antimicrobial effects. Experimental and clinical studies have highlighted their hepatoprotective and nephroprotective potential through modulation of oxidative stress pathways and inflammatory mediators. Additionally, watermelon seed oil has shown promise in skin health, metabolic regulation, and functional food formulation. Despite this, research gaps persist regarding standardised extraction, compound isolation, and large-scale human trials to validate their pharmacological efficacy and safety. The growing global demand for sustainable, plant-derived nutraceuticals positions watermelon seeds as a valuable functional ingredient for health promotion and waste reduction.

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INTRODUCTION

Watermelon (*Citrullus lanatus*), a member of the family Cucurbitaceae, is one of the most widely cultivated and consumed fruit crops in the world. It is valued for its refreshing taste, hydrating flesh, and nutritional richness. According to the Food and Agriculture Organisation (FAO, 2022), global watermelon production exceeded 100 million metric tons, with China, Turkey, Iran, India, and

Brazil ranking as leading producers. The fruit is predominantly consumed fresh, though processed products such as juices, jams, and seed oils have gained increasing attention. Despite the extensive use of its edible pulp, watermelon seeds, representing nearly 4-5 % of the fruit's weight, are often discarded as waste during processing and consumption (Anwar *et al.*, 2022).

This also overlooks a potential reservoir of nutrients and bioactive compounds beneficial to human health.

Traditionally, watermelon seeds have been valued in various cultures for their nutritional and medicinal benefits. In several African and Asian regions, the seeds are roasted, ground, or boiled and incorporated into local cuisines as protein-rich ingredients (Badifu & Ogunsua, 1991; Egbuonu, 2015). In Nigeria and parts of India, the ground seeds are used to prepare soups, sauces, and snacks, whereas in traditional Chinese and Ayurvedic medicine, watermelon seeds have been utilised for treating urinary tract infections, hypertension, and liver disorders (Choudhary *et al.*, 2020; Deme *et al.*, 2021). Their cultural relevance reflects a long-standing empirical understanding of their therapeutic potential.

From a nutritional standpoint, watermelon seeds are an excellent source of macronutrients and micronutrients. They contain approximately 30- 35 % protein, 40-50%fat, and 10-15% carbohydrates (Adeyemi *et al.*, 2020). The seed oil is rich in unsaturated fatty acids, especially linoleic acids, which play a crucial role in cardiovascular health (Oluba *et al.*, 2008; Nyam *et al.*, 2009). Furthermore, they provide essential amino acids such as arginine and tryptophan, minerals including magnesium, phosphorus, iron, and zinc, and vitamins such as arginine and tryptophan, minerals including magnesium, phosphorus, iron, and zinc, and vitamins such as niacin, folate, and vitamin E (Yadav *et al.*, 2017).

These components collectively contribute to muscle repair, immune regulation, metabolic balance, and antioxidant defence.

Beyond their nutritional composition, watermelon seeds harbour various phytochemicals and bioactive compounds—flavonoids, phenolic acids, alkaloids, saponins, and tannins—that exhibit strong antioxidant, antimicrobial, anti-inflammatory, and antidiabetic activities (Zannou *et al.*, 2020; Olayemi *et al.*, 2020). Modern pharmacological studies have provided evidence for their hepatoprotective, nephroprotective, and cardioprotective properties through modulation of oxidative stress pathways and inflammatory markers (Rahman *et al.*, 2013; Anwar *et al.*, 2022). The presence of citrulline and arginine enhances nitric oxide synthesis, improving vascular function and reducing hypertension (Collins *et al.*, 2007). This growing body of evidence suggests that watermelon seeds can serve as functional food ingredients with significant nutraceutical potential.

Despite these promising findings, the utilisation of watermelon seeds remains limited, particularly in commercial food and pharmaceutical industries. Most global watermelon production still focuses on the flesh, while the seeds are discarded or underexploited. Research on seed valorisation, extraction optimisation, and bioactive compound standardisation is comparatively

scarce. There is also a lack of comprehensive reviews consolidating nutritional, phytochemical, and pharmacological data to establish watermelon seeds as a sustainable and health-promoting resource (Giwa & Akanbi, 2021). Moreover, variations in cultivation conditions, seed maturity, and processing techniques can significantly influence the chemical composition and therapeutic efficacy, indicating a need for standardised comparative analyses (Adepoju *et al.*, 2019).

With increasing global interest in plant-based diets, functional foods, and sustainable agriculture, revisiting the potential of watermelon seeds is both timely and necessary. They align with the current emphasis on zero-waste utilisation and circular food systems, offering opportunities for value addition and environmental conservation (FAO, 2022). Moreover, their high nutrient density and low cost make them suitable candidates for addressing nutritional deficiencies in developing nations.

The objective of this review is to provide a comprehensive overview of the botanical, nutritional, and phytochemical composition of watermelon seeds, and to summarise their therapeutic and pharmacological aspects, including antioxidant, anti-inflammatory, hepatoprotective, and antioxidant, anti-inflammatory, hepatoprotective, and antidiabetic properties. This paper also aims to identify current research gaps, highlight emerging applications in functional foods and nutraceuticals, and suggest future directions for sustainable utilisation.

By consolidating available literature, this review contributes to a deeper understanding of *Citrullus lanatus* seeds as a potential nutraceutical resource, supporting ongoing efforts toward waste valorisation, food security, and integrative health research.

Botanical and Cultivation Profile of *Citrullus lanatus*: Botanical Classification and Taxonomy

Watermelon (*Citrullus lanatus* (Thunb.) Matsum. & Nakai) belongs to the family Cucurbitaceae, which also includes cucumber, pumpkin, and squash (Robinson & Decker-Walters, 1997). It is classified under the genus *Citrullus*, comprising several wild and cultivated species distributed across Africa and Asia (Paris, 2015). The taxonomy of *Citrullus* has undergone revisions, with four main species recognised: *C. colocynthis*, *C. monospermous*, *C. amarus*, and *C. lanatus*, the latter being the domesticated edible watermelon (Renner *et al.*, 2017). Chromosome number is $2n = 22$, and the plant is monoecious with separate male and female flowers borne on the same vine (Wehner, 2008).

Morphology and Growth Habit

Watermelon is an annual, herbaceous, trailing vine with deeply lobed leaves and tendrils that enable spreading up

to 3–5 meters (Wehner, 2008). The stems are angular and hairy, and the plant produces yellow, unisexual flowers. Male flowers are more numerous, whereas female flowers arise at nodes on lateral branches (Robinson & Decker-Walters, 1997). The fruit is a pepo (a modified berry) that varies in size, shape, and colour across cultivars. It has a thick rind, juicy flesh rich in carotenoids and lycopene, and numerous flat seeds embedded within the mesocarp (Paris, 2015). Seeds are small, obovate, and range in colour from black to brown, white, or mottled depending on the variety (Nerson, 2005). The 1000-seed weight varies between 30 and 120 g, depending on cultivar and environmental conditions (Wehner, 2008).

Cultivation and Global Distribution

Watermelon is believed to have originated in the arid regions of northeastern Africa, particularly in the Kalahari Desert (Paris, 2015). It spread through trade routes to Asia, the Middle East, and the Mediterranean region. Today, *C. lanatus* is cultivated extensively in tropical and subtropical zones across Africa, India, China, the Middle East, and South America (FAO, 2022). China remains the world's largest producer, followed by Turkey, Iran, India, and Brazil, contributing over 70% of total global output. In India, watermelon cultivation thrives in Rajasthan, Maharashtra, Tamil Nadu, and Uttar Pradesh, especially in sandy loam soils under irrigated conditions (Kumar *et al.*, 2020).

Environmental and Agronomic Requirements

Optimal watermelon growth occurs in well-drained sandy loam soils with a pH range of 6.0–7.5 (Wehner, 2008). The crop requires high sunlight exposure and moderate rainfall. The ideal temperature for germination is 25–30 °C, while fruit development is optimal between 22–28 °C (FAO, 2022). Water stress, nutrient deficiency, and low pollination rates can drastically reduce fruit yield and seed viability. The crop is generally grown in open fields with a spacing of 2–3 m between rows, and pollination is mainly insect-mediated, primarily by honeybees. Harvesting typically occurs 80–100 days after sowing (Nerson, 2005).

Seed Yield and Post-Harvest Characteristics

Each mature watermelon can produce 300–800 seeds, depending on variety and growing conditions. Seed yield averages 400–600 kg per hectare (Wehner, 2008). The seeds are manually extracted, washed, and sun-dried to reduce moisture below 8% for safe storage (Kumar *et al.*, 2020). Seed oil yield ranges between 35–50% based on extraction method, cultivar, and maturity stage (Anwar *et al.*, 2022). Roasted or fermented seeds are commonly consumed in Africa and Asia, whereas cold-pressed seed

oil is gaining industrial interest due to its stability and nutritional profile (Nyam *et al.*, 2009).

Phytochemical Constituents

Watermelon seeds contain a variety of phytochemicals, including phenolic acids (gallic, ferulic, and caffeic acids), flavonoids (quercetin, kaempferol), alkaloids, tannins, saponins, and glycosides (Olayemi *et al.*, 2020; Egbunu, 2015). These compounds contribute to antioxidant, hepatoprotective, and anti-inflammatory properties, making the seeds valuable for nutraceutical applications (Choudhary *et al.*, 2019). The phytochemical composition is influenced by genotype, soil fertility, and post-harvest processing, with roasted and germinated seeds showing enhanced antioxidant activity due to the release of bound phenolics (Yadav *et al.*, 2017).

Nutritional Composition of Watermelon Seeds

Watermelon (*Citrullus lanatus*) seeds represent a rich reservoir of nutrients and bioactive compounds that offer both nutritional and therapeutic potential. Though often discarded during fruit consumption, these seeds are a concentrated source of macronutrients, micronutrients, and phytochemicals comparable to other oil-bearing seeds such as pumpkin, flax, and sunflower.

Macronutrient Composition

Proteins

Watermelon seeds contain approximately 27–35% protein, depending on cultivar and growing region (El-Adawy & Taha, 2001). The seed proteins are predominantly globulins and albumins, with essential amino acids such as arginine, lysine, tryptophan, and methionine (Hassan *et al.*, 2020). Arginine, a nitric oxide precursor, plays a vital role in cardiovascular regulation and immune defence (Ehiowemwenguan *et al.*, 2014). Protein isolates from watermelon seeds have demonstrated high digestibility and balanced amino acid profiles comparable to soy protein (Oyelade *et al.*, 2008). Such protein content makes the seeds suitable for incorporation into plant-based food formulations and protein supplements.

Lipid Profile

Lipids account for 35–40% of watermelon seed weight, with unsaturated fatty acids forming the major fraction. Linoleic acid (C18:2), oleic acid (C18:1), and palmitic acid (C16:0) are predominant (Yadav *et al.*, 2021). These fatty acids are beneficial for cardiovascular and metabolic health due to their hypocholesterolaemia and anti-inflammatory effects (Anhwange *et al.*, 2010). Watermelon seed oil exhibits a favourable omega-6 to omega-9 ratio, comparable to safflower and sesame oils (Umerie & Enebeli, 2016). The oil is also rich in

tocopherols (vitamin E) and phytosterols, enhancing its oxidative stability and shelf life (Kumar *et al.*, 2018).

Carbohydrates and Fibre

Carbohydrate content varies between 15–25%, comprising both soluble and insoluble fractions. The seeds provide dietary fibre ($\approx 4\text{--}6\%$), which supports gastrointestinal health and glycemic control (Azhari *et al.*, 2014). The low glycemic carbohydrate composition renders them suitable for diabetic diets (Ejечи & Okoko, 2019). Additionally, fibre-rich seed flour has shown potential as a functional ingredient in bakery and snack products (Shukla & Srivastava, 2018).

Micronutrient Composition

Minerals

Watermelon seeds are a significant source of essential minerals, including magnesium, iron, zinc, potassium, calcium, copper, and phosphorus (Akpambang *et al.*, 2008). Magnesium levels ($\sim 530\text{ mg}/100\text{ g}$) contribute to neuromuscular regulation and glucose metabolism (Fayemi *et al.*, 2019). Iron ($7\text{--}9\text{ mg}/100\text{ g}$) supports haemoglobin synthesis and prevents anaemia, while zinc enhances immune and reproductive function (Elinge *et al.*, 2012). Potassium and phosphorus content promote electrolyte balance and bone integrity, respectively. These nutrient densities make watermelon seeds comparable or even superior to cashew or almond kernels in micronutrient value (Adedeji *et al.*, 2015).

Vitamins

The seed oil and kernel fractions contain notable amounts of vitamins A, E, and B-complex (B1, B2, niacin, and folate) (Hassan *et al.*, 2020). Vitamin E (tocopherol) contributes antioxidant capacity, preventing lipid peroxidation (Kamel *et al.*, 2016). Vitamins B1 and B3 are essential for energy metabolism and nervous system function. Trace levels of vitamin A precursors (carotenoids) support visual and immune health (Mohdaly *et al.*, 2012).

Phytochemical Profile

Watermelon seeds possess a broad spectrum of phytochemicals, including flavonoids, saponins, alkaloids, tannins, phenolic acids, and phytosterols (Ojeh *et al.*, 2008). Phenolic compounds like caffeic, ferulic, and gallic acid contribute to antioxidant and anti-inflammatory effects (Kumar *et al.*, 2018). The seeds' total phenolic content ranges from $5\text{--}8\text{ mg GAE/g}$, with significant free radical scavenging activity (Abdel-Rahman *et al.*, 2020). Phytosterols such as β -sitosterol and stigmasterol reduce intestinal cholesterol absorption, enhancing cardiovascular protection (Gido *et al.*, 2019). Moreover,

saponins and alkaloids contribute antimicrobial and hepatoprotective properties (Abiodun & Adeleke, 2010).

Comparison with Other Edible Seeds

Compared to other edible seeds such as pumpkin (*Cucurbita pepo*), flax (*Linum usitatissimum*), and sunflower (*Helianthus annuus*), watermelon seeds exhibit competitive nutritional potential. While pumpkin seeds have higher zinc and iron content, watermelon seeds offer superior magnesium and arginine levels (Azhari *et al.*, 2014). Their lipid profile closely resembles that of sunflower seeds, but with a better oxidative stability index due to tocopherol enrichment (Yadav *et al.*, 2021). Unlike flax seeds, which are high in omega-3 fatty acids but prone to rancidity, watermelon seed oil remains stable under heat, making it suitable for edible applications (Elinge *et al.*, 2012). Thus, they can serve as a cost-effective alternative source of plant protein and oil in developing countries.

Effect of Processing, Roasting, and Germination

Processing significantly alters the nutritional and phytochemical characteristics of watermelon seeds. Roasting enhances flavour and digestibility but can decrease thermolabile vitamins such as vitamin C and folate (El-Adawy & Taha, 2001). Germination and fermentation improve amino acid availability, mineral bioaccessibility, and antioxidant activity due to enzymatic hydrolysis of antinutritional factors like phytic acid (Shukla & Srivastava, 2018). Studies have shown that germinated seeds exhibit higher total phenolic content and enhanced antioxidant enzyme activity, making them suitable for functional food use (Farida *et al.*, 2018). Conversely, excessive heating can induce oxidative degradation of lipids and partial loss of essential fatty acids (Mohdaly *et al.*, 2012).

In summary, watermelon seeds are nutrient-dense functional ingredients, offering a balance of macronutrients, micronutrients, and phytochemicals. Their nutritional equivalence to other common seeds, combined with their low cost and availability, supports their potential for sustainable food product development and nutraceutical innovation.

Therapeutic and Pharmacological Aspects of Watermelon (*Citrullus lanatus*) Seeds

Watermelon (*Citrullus lanatus*) seeds, traditionally considered agricultural waste, have emerged as a reservoir of bioactive compounds demonstrating significant pharmacological potential. Extensive phytochemical investigations have identified alkaloids, phenolic acids, flavonoids, tannins, saponins, and unsaturated fatty acids as the major constituents contributing to their therapeutic value (Egbonu, 2018).

These bioactive molecules confer antioxidant, anti-inflammatory, antidiabetic, antihyperlipidemic, hepatoprotective, nephroprotective, cardioprotective, antimicrobial, and antiparasitic properties, validated through both *in vitro* and *in vivo* experimental models.

Antioxidant Activity

Watermelon seed extracts possess potent antioxidant capacities due to their rich polyphenolic and flavonoid profiles. Studies using assays like DPPH (2,2-diphenyl-1-picrylhydrazyl) and FRAP (Ferric Reducing Antioxidant Power) revealed that ethanolic and methanolic extracts of *C. lanatus* seeds scavenge free radicals in a concentration-dependent manner (Eneche *et al.*, 2020). These effects are attributed to compounds such as gallic acid, catechin, and rutin (Okunlola *et al.*, 2021). Additionally, the lipid peroxidation inhibition suggests potential protection against oxidative stress-induced cellular damage (Abdel-Rahman *et al.*, 2019). Antioxidant activity also supports cardiovascular and hepatic protection through suppression of reactive oxygen species (ROS) generation.

Anti-inflammatory and Analgesic Activity

Inflammation is a major component of chronic diseases, and bioactive compounds in watermelon seeds—particularly flavonoids and alkaloids—demonstrate significant anti-inflammatory properties (Abiodun & Adeleke, 2019). Experimental rat models using carrageenan-induced paw oedema have shown marked inhibition of inflammation following administration of methanolic seed extract (Bello *et al.*, 2020). The mechanism involves downregulation of COX-2 and TNF- α pathways, indicating a nonsteroidal-like mode of action (Onoja *et al.*, 2017). Furthermore, analgesic activity was evidenced in hot-plate and tail-flick tests, supporting traditional claims of pain relief (Okoh *et al.*, 2022).

Antidiabetic and Antihyperlipidemic Effects

The hypoglycaemic potential of *C. lanatus* seeds is associated with the presence of alkaloids, saponins, and unsaturated fatty acids that modulate glucose metabolism (Uchegbu *et al.*, 2018). Diabetic rat models demonstrated significant reductions in fasting blood glucose, serum triglycerides, and total cholesterol after oral administration of aqueous and ethanolic seed extracts (El-Adawy *et al.*, 2019). These effects are mediated by enhanced insulin secretion and glucose uptake through the activation of AMP-activated protein kinase (AMPK) pathways (Eze *et al.*, 2020). The seeds also exhibited hypolipidemic activity by increasing HDL and reducing LDL levels, comparable to standard drugs like metformin (Olayemi *et al.*, 2019).

Hepatoprotective, Nephroprotective, and Cardioprotective Actions

Watermelon seed oil and extracts have demonstrated remarkable protective effects on vital organs. Hepatoprotective effects were observed against paracetamol- and CCl₄-induced liver toxicity in rats, with improved serum markers (ALT, AST) and restored histopathology (Hassan *et al.*, 2018). The nephroprotective action is attributed to high arginine and polyphenol content, which enhances renal blood flow and reduces oxidative stress (Egbuonu, 2018). Cardioprotective benefits arise from the presence of citrulline, a nitric oxide precursor that improves endothelial function and reduces arterial stiffness (Wu *et al.*, 2020). Together, these findings support *C. lanatus* seeds as a potential nutraceutical for organ protection.

Antimicrobial and Antiparasitic Effects

The antimicrobial potency of *C. lanatus* seed extracts has been validated against several Gram-positive and Gram-negative bacteria, including *Staphylococcus aureus*, *Escherichia coli*, and *Salmonella typhi* (Dutta *et al.*, 2018). Ethanolic extracts demonstrated higher efficacy compared to aqueous ones, possibly due to better solubility of phenolics in alcohol. The antifungal potential against *Candida albicans* and *Aspergillus niger* was also notable (Oladipo *et al.*, 2019). Antiparasitic properties, particularly against *Plasmodium* and *Trypanosoma* species, have been attributed to alkaloid and saponin fractions that interfere with parasite metabolism (Nwosu *et al.*, 2020).

Mechanisms of Action and Bioactive Compounds

The therapeutic potential of watermelon seeds can be mechanistically linked to their diverse phytoconstituents. Phenolic acids act as free radical scavengers; flavonoids inhibit lipid peroxidation and inflammatory mediators, while saponins exert cholesterol-lowering effects by binding bile acids. Arginine and citrulline enhance nitric oxide synthesis, promoting vasodilation and cardiovascular health (Wang *et al.*, 2019). Additionally, the seed oil's high linoleic acid content contributes to lipid profile modulation and anti-inflammatory effects (Akinsanmi *et al.*, 2021).

Pharmacological Activities of Watermelon (*Citrullus lanatus*) Seeds

Overall Implications

The pharmacological potential of *C. lanatus* seeds is multifaceted, encompassing antioxidant, metabolic, and organ-protective roles that support their integration into functional foods and phytotherapeutic formulations. However, there remains a paucity of standardised clinical studies validating these results in humans. Future

research should focus on bioavailability, dosage optimisation, and safety profiling to translate these benefits from bench to bedside.

Health Benefits & Functional Food Applications of Watermelon (*Citrullus lanatus*) Seeds

Watermelon (*Citrullus lanatus*) seeds, often considered agricultural waste, are now emerging as an excellent source of bioactive nutrients with substantial implications for human health and functional food development. Their composition—rich in proteins, essential fatty acids, minerals, vitamins, and phytochemicals—contributes to multiple physiological and preventive health benefits. The increasing interest in natural plant-based products and sustainable nutrition has positioned watermelon seeds as a versatile ingredient in nutraceuticals, cosmetics, and traditional medicine (Amin & Rahman, 2020; Kumar & Sharma, 2022).

Role in Human Diet and Functional Foods

Watermelon seeds are increasingly being incorporated into dietary formulations due to their high protein (28–35%), lipid (40–50%), and mineral content (Oyeleke *et al.*, 2018). The seeds provide a balanced amino acid profile comparable to soybean, rich in arginine, tryptophan, and lysine—key for muscle growth and metabolic regulation (Adeniyi *et al.*, 2022). Their lipid fraction, dominated by linoleic and oleic acids, supports cardiovascular health and anti-inflammatory functions (Okoro *et al.*, 2021).

Functional food industries utilise roasted or defatted seed flour to enrich bakery and confectionery products, energy bars, and protein supplements (Onwuka *et al.*, 2022). The oil extracted from watermelon seeds serves as a healthy edible oil, offering a nutty flavour with a stable oxidative profile (Egbuna *et al.*, 2018). Moreover, sprouted watermelon seeds exhibit enhanced antioxidant activity and bioavailability of phenolic compounds, making them suitable for germinated functional blends (Singh & Patel, 2021). Watermelon seed powder has also been integrated into gluten-free formulations to improve protein density and sensory characteristics (Rahman *et al.*, 2021). Given their high magnesium and zinc content, regular consumption can aid in maintaining normal glucose metabolism, nerve function, and immunity (Oladunmoye *et al.*, 2020).

Nutraceutical and Pharmaceutical Applications

The biochemical richness of watermelon seeds has significant nutraceutical potential. Bioactive compounds such as citrulline, arginine, flavonoids, and phenolic acids exert antihypertensive, antioxidant, and hepatoprotective effects (Kumar & Sharma, 2022; Oladunmoye *et al.*, 2020). These compounds help modulate nitric oxide production, regulate lipid metabolism, and mitigate

oxidative damage, which collectively contribute to cardiovascular protection (Mansour *et al.*, 2020).

Pharmaceutical studies demonstrate that watermelon seed extracts can serve as adjunct therapies in managing metabolic disorders such as diabetes, dyslipidaemia, and hypertension (Okafor *et al.*, 2021). The oil fraction, owing to its unsaturated fatty acids, is also explored for encapsulation in soft gels and nutraceutical supplements. Recent investigations have highlighted its potential in designing nanoemulsions and lipid-based drug delivery systems due to its high oxidative stability and bioavailability (Adeniyi *et al.*, 2022).

Furthermore, the seed's protein hydrolysates possess antioxidant peptides that can be used in anti-ageing and stress-resistance formulations (Bamidele & Fasogbon, 2019). Such functional applications bridge the gap between dietary consumption and preventive pharmacology, aligning with the growing global nutraceutical trend.

Cosmetic, Skin, and Hair Health Benefits

Watermelon seed oil has gained substantial attention in the cosmetic and personal care industry due to its emollient, moisturising, and antioxidant properties (Abdelwahab *et al.*, 2021). The oil is light, non-greasy, and easily absorbed into the skin, making it suitable for formulations in facial serums, lotions, and hair oils (Nwankwo *et al.*, 2020).

Its linoleic and oleic acids restore skin barrier function and maintain hydration, while vitamin E and polyphenols combat oxidative damage and premature ageing (Rahman *et al.*, 2021). Watermelon seed oil is also used in anti-acne and scalp rejuvenation products because of its antimicrobial action against *Propionibacterium acnes* and *Malassezia* species (Uchegbu *et al.*, 2019). The zinc and magnesium content further promotes keratinocyte regeneration and collagen synthesis (Singh & Patel, 2021). Hair formulations utilising defatted seed extract enhance hair strength and reduce follicular inflammation, owing to their essential amino acids and antioxidants (Okoro *et al.*, 2021). Such evidence underscores the seeds' transition from food waste to a premium cosmetic resource.

Traditional and Folk Medicinal Uses

In traditional medicine, watermelon seeds have been employed as natural remedies for urinary tract infections, intestinal worms, and hypertension (Eze & Nwodo, 2018). African and Indian systems of medicine use powdered seeds as diuretics, tonics, and anti-inflammatory agents (Amin & Rahman, 2020). Decoctions of the seeds are consumed for kidney cleansing and as cooling agents in heat-related illnesses (Ogunleye *et al.*, 2018).

Ethnomedical literature describes watermelon seeds as beneficial for reproductive health, aiding in hormone balance and sperm quality due to arginine and zinc content (Okafor *et al.*, 2021). The Ayurvedic concept recognises them as “Sheetal” (cooling) and “Balya” (strengthening), promoting vitality and tissue regeneration (Bamidele & Fasogbon, 2019).

Recent integration of traditional insights with laboratory evidence has validated many of these uses, reinforcing the seeds’ multifunctional therapeutic potential and paving the way for standardised herbal formulations.

Functional and Cosmetic Applications of Watermelon (*Citrullus lanatus*) Seeds

Toxicological and Harmful Effects of Watermelon (*Citrullus lanatus*) Seeds

Although *Citrullus lanatus* (watermelon) seeds are generally recognised as safe and nutritionally beneficial, understanding their potential toxicological implications is crucial for their incorporation into functional foods and nutraceuticals. Despite their rich nutrient and bioactive compound profile, watermelon seeds—like many plant seeds—contain certain anti-nutritional factors that can interfere with nutrient absorption, enzyme activity, and overall metabolic balance if consumed excessively or improperly processed.

Anti-Nutritional Factors

Raw watermelon seeds contain a variety of anti-nutritional compounds, including phytates, oxalates, tannins, saponins, trypsin inhibitors, and lectins, which can negatively influence nutrient bioavailability (Ezeh *et al.*, 2018).

- Phytates (phytic acid) form insoluble complexes with essential minerals such as calcium, zinc, and iron, thereby reducing their intestinal absorption.
- Oxalates can bind with calcium to form calcium oxalate crystals, which may contribute to kidney stone formation in predisposed individuals (Singh *et al.*, 2021).
- Trypsin inhibitors interfere with proteolytic enzyme activity, reducing protein digestibility, while tannins may impair iron absorption and cause gastrointestinal irritation at high levels (Mohammed & Musa, 2019). However, most of these compounds are thermolabile and significantly reduced by roasting, boiling, fermentation, or germination (Olaofe *et al.*, 2013).

Common Anti-Nutritional Factors in Watermelon Seeds and Their Effects

Anti-Nutritional Factor	Physiological Effect	Reduction Method
Phytate	Binds minerals (Fe, Zn, Ca), reduces bioavailability	Soaking, germination, fermentation
Oxalate	Can form calcium oxalate crystals (kidney risk)	Boiling, roasting
Trypsin inhibitor	Reduces protein digestibility	Heating, fermentation
Tannin	Reduces iron absorption, causes GI discomfort	Roasting, enzymatic treatment
Saponin	May cause hemolysis in large amounts	Boiling, dilution

Toxicity and Overconsumption Effects

Studies on the acute and sub-chronic toxicity of watermelon seed extracts in animals reveal a high margin of safety. In rats, oral administration of ethanolic seed extract at doses up to 2000 mg/kg body weight produced no observable adverse effect level (NOAEL), with normal haematological and biochemical parameters (Oladunmoye *et al.*, 2020).

However, excessive consumption—particularly of unprocessed or raw seeds—may lead to digestive discomfort, flatulence, or intestinal blockage, due to their high fibre and oil content. Rare allergic responses, such as itching or mild gastrointestinal distress, have been reported in sensitive individuals (Ahmed *et al.*, 2022).

Furthermore, excessive intake of seed oil may result in high caloric load and lipid imbalance if not moderated. Since watermelon seed oil is rich in unsaturated fatty acids, oxidation during improper storage can lead to the formation of peroxides and free radicals that contribute to oxidative stress (Umaru *et al.*, 2019).

Toxicological Findings from Animal and Human Studies

Toxicological evaluations in animal models consistently indicate that watermelon seed and oil are non-mutagenic, non-cytotoxic, and non-carcinogenic under normal dietary concentrations.

- A 90-day sub-chronic study in Wistar rats revealed no histopathological alterations in the liver, kidney, or spleen after daily consumption of seed oil (Eze & Okafor, 2021).
- In contrast, minor hepatic enzyme elevation was observed in animals fed very high doses (>3000 mg/kg), suggesting potential hepatic stress at unrealistic consumption levels.
- Human data are scarce; however, traditional consumption patterns across African and Asian populations indicate long-term safety when seeds are roasted or boiled before intake (Agbo *et al.*, 2020).

Processing and Reduction of Toxic Compounds

Processing is a key factor in mitigating toxicity. Techniques such as roasting, boiling, fermentation, and germination effectively reduce anti-nutritional compounds by denaturing proteins, degrading phytates, and breaking down complex polyphenols.

- Roasting (120–150°C for 10–15 minutes) significantly decreases tannin and oxalate levels without major nutrient loss (Fagbemi *et al.*, 2017).
- Fermentation improves mineral bioavailability and enhances the sensory and functional quality of the seeds.
- Germination increases antioxidant activity and reduces phytic acid through endogenous phytase activation (Ijarotimi & Keshinro, 2019).

Thus, processed watermelon seeds are not only safe for human consumption but also serve as valuable ingredients for the development of functional foods and nutraceutical formulations.

Regulatory and Safety Considerations

The Food and Agriculture Organisation (FAO) and World Health Organisation (WHO) have not reported any toxicity concerns regarding watermelon seeds or their oil when consumed as part of a normal diet. However, quality control during processing, avoidance of rancid oil, and proper storage under low humidity and temperature are necessary to prevent oxidation and microbial contamination.

Additionally, research is needed to establish safe upper intake levels and to assess long-term metabolic effects through clinical trials.

Conclusion

While watermelon seeds are predominantly safe and beneficial, unprocessed seeds may contain anti-nutritional compounds that can reduce nutrient absorption or cause mild gastrointestinal distress if consumed in large amounts. Appropriate processing methods, such as roasting, fermentation, and germination, effectively minimise these risks. Overall, current evidence supports the toxicological safety of *Citrullus lanatus* seeds, making them a sustainable, health-promoting ingredient in food and nutraceutical industries.

Processing and Value-Added Products of Watermelon (*Citrullus lanatus*) Seeds

Watermelon (*Citrullus lanatus*) seeds, once regarded as agricultural waste, have gained increasing industrial and nutritional significance due to their high protein, lipid, and bioactive compound content. Proper processing enhances the safety, stability, and functional value of the seeds, while also enabling their conversion into a wide range of value-added products. This section discusses

the key processing methods—roasting, sprouting, defatting, and oil extraction—and explores industrial applications such as food fortification, biodiesel production, and cosmetic formulations.

Processing Techniques

1. Roasting

Roasting is one of the oldest and most common processing methods used to enhance the flavour, texture, and digestibility of seeds. It significantly reduces anti-nutritional compounds such as tannins, phytates, and trypsin inhibitors, while increasing the availability of amino acids and antioxidants (Fagbemi *et al.*, 2017). Roasting temperatures between 120–150°C for 10–15 minutes improve sensory attributes and shelf stability without major nutrient losses.

However, excessive heating may cause Maillard reactions, leading to the degradation of thermolabile vitamins such as vitamin E and partial denaturation of essential fatty acids (Umaru *et al.*, 2019). Controlled roasting, therefore, ensures both palatability and nutrient retention.

2. Sprouting and Germination

Germination activates endogenous enzymes, which hydrolyse complex macromolecules into simpler, more digestible forms. Studies have shown that sprouted watermelon seeds exhibit elevated levels of free amino acids, vitamin C, and total phenolic content, enhancing their antioxidant potential (Ijarotimi & Keshinro, 2019). Furthermore, germination for 48–72 hours under controlled humidity (25–28°C) effectively reduces phytate and oxalate concentrations by up to 60%.

Sprouted seeds can be utilised in energy bars, smoothies, and health snacks, providing a nutrient-dense, functional ingredient.

3. Defatting

Defatting refers to the removal of oil content through mechanical or solvent extraction, resulting in a high-protein, low-fat seed meal. The defatted flour retains essential amino acids and can be used in bakery and confectionery formulations as a protein supplement (Eze *et al.*, 2021). The protein concentrate derived from defatted watermelon seed has shown superior emulsifying and foaming properties, making it suitable for food fortifiers, meat analogies, and dairy substitutes (Olaofe *et al.*, 2013).

Oil Extraction

Oil extraction is a major value-enhancing process. Watermelon seed oil is extracted using cold pressing, solvent extraction (n-hexane), or supercritical CO₂ methods.

- Cold pressing preserves bioactive compounds like tocopherols and sterols.
- Solvent extraction yields a higher oil percentage (~45–55%) but may require purification to remove residual solvents.
- Supercritical CO₂ extraction is a clean, eco-friendly method producing high-quality oil with excellent oxidative stability (Ogunlesi *et al.*, 2020).

The extracted oil is light-yellow, rich in linoleic (C18:2, 55–65%), oleic (C18:1, 15–25%), and palmitic acids (C16:0, 10–15%), with natural antioxidants like α -tocopherol, making it ideal for food, cosmetic, and biodiesel applications (Ezeh *et al.*, 2018).

Major Processing Methods and Their Effects on Watermelon Seeds

Processing Method	Primary Objective	Effect on Nutrients	Industrial Application
Roasting	Flavour enhancement, anti-nutrient reduction	Reduces phytates, increases digestibility	Snack and bakery inclusion
Germination	Improve bioavailability	Increases vitamins and phenolics	Health foods, cereals
Defatting	Reduce oil content	Concentrates protein	Bakery, food fortifiers
Cold Pressing	Preserve antioxidants	High tocopherol retention	Edible oil, cosmetics
Solvent Extraction	Maximise oil yield	High oil recovery (~50%)	Industrial oil, biodiesel
Supercritical CO ₂ Extraction	Chemical-free extraction	High oxidative stability	Premium oil products

Seed Oil Applications

1. Food Industry

Watermelon seed oil possesses a favourable fatty acid composition comparable to sunflower and safflower oils, making it suitable as a culinary oil or salad dressing. Due to its mild flavour and high smoke point (~230°C), it is used for frying and baking applications (Adegoke *et al.*, 2019).

Moreover, it is rich in polyunsaturated fatty acids (PUFAs) and natural antioxidants, beneficial for cardiovascular health. Defatted flour left after oil extraction serves as a high-protein byproduct for functional food development.

2. Biodiesel Production

Watermelon seed oil has emerged as a potential non-edible feedstock for biodiesel production due to its fatty acid profile and oil yield. Transesterification of seed oil using methanol and sodium hydroxide as catalysts produces biodiesel with comparable cetane number, viscosity, and calorific value to standard diesel fuel

(Mohammed *et al.*, 2020). This provides a sustainable and eco-friendly bioenergy alternative, particularly in agricultural regions with abundant watermelon cultivation.

3. Cosmetic and Pharmaceutical Applications

The high concentration of linoleic acid and vitamin E makes watermelon seed oil valuable in cosmetic formulations. It acts as a natural emollient, improving skin hydration, elasticity, and barrier repair. The oil's non-greasy texture and quick absorption properties make it ideal for facial serums, lotions, and hair-care products (Agbo *et al.*, 2020). Additionally, the bioactive compounds exhibit anti-inflammatory and antioxidant effects, supporting their inclusion in nutraceutical capsules and herbal ointments.

Packaging, Storage, and Shelf Life

Watermelon seed products are sensitive to oxidation and moisture absorption, which can compromise quality. Proper packaging materials, such as vacuum-sealed laminated pouches or nitrogen-flushed bottles, are essential to prevent rancidity and maintain oil stability (Umaru *et al.*, 2019). Storage at temperatures below 25°C and relative humidity <60% is recommended to prolong shelf life up to 6–9 months. For defatted flours and germinated products, incorporation of natural antioxidants like rosemary extract or vitamin E can further delay lipid oxidation. Furthermore, studies indicate that microencapsulation of seed oil using maltodextrin or gum arabic improves oxidative stability and enables its use in functional beverages and powdered supplements (Eze & Okafor, 2021).

Conclusion

Processing of watermelon seeds not only enhances their nutritional quality and safety but also expands their industrial utility across the food, cosmetic, and biofuel sectors. Techniques such as roasting, germination, and oil extraction transform these underutilised seeds into high-value ingredients with significant economic and health potential. Optimisation of extraction technologies and innovative packaging methods will further strengthen their role in sustainable food systems and the nutraceutical market.

Research Gaps and Future Prospects

Despite the growing body of literature supporting the nutritional and pharmacological potential of *Citrullus lanatus* (watermelon) seeds, substantial gaps persist in current scientific understanding. Most studies to date have been *in vitro* or **animal-based**, with limited translation into clinical or large-scale human studies. The need for standardised, evidence-based evaluations remains critical for integrating watermelon seed products

into mainstream nutraceutical and pharmaceutical industries.

1 Lack of Large-Scale Human Trials

Most studies examining watermelon seeds' therapeutic effects—such as antioxidant, antihyperlipidemic, and hepatoprotective activities—have been confined to laboratory or small animal models (Ezeh *et al.*, 2018; Fagbemi *et al.*, 2017). There is a notable absence of randomised controlled trials (RCTs) assessing dose-dependent effects, long-term safety, and efficacy in human populations. Without such data, the translation of preclinical results into validated nutraceutical recommendations remains limited. Future research should prioritise multicentre clinical trials to confirm bio-efficacy and establish standardised dosage ranges.

Standardisation of Extracts and Bioactive Compounds

Current studies employ varied extraction solvents (ethanol, hexane, methanol, water) and protocols, leading to inconsistencies in the reported composition and biological activity of watermelon seed extracts (Ogunlesi *et al.*, 2020). Lack of phytochemical standardisation hinders the reproducibility of results across laboratories. A unified analytical framework—using advanced chromatographic and spectrometric techniques (HPLC, LC-MS, NMR)—is necessary to identify and quantify key bioactive compounds, including tocopherols, phenolic acids, and unsaturated fatty acids. Such standardisation will facilitate regulatory approval and commercial product development.

Bioavailability and Mechanistic Exploration

Although watermelon seeds are rich in antioxidants, polyphenols, and essential fatty acids, the bioavailability and metabolic pathways of these compounds remain poorly understood. Very few studies have explored absorption kinetics, biotransformation, or tissue distribution of active components (Adegoke *et al.*, 2019). Moreover, the mechanisms underlying their antidiabetic or anti-inflammatory effects—whether through modulation of insulin signalling, lipid metabolism, or oxidative stress pathways—require molecular-level clarification using omics-based approaches such as metabolomics and proteomics (Agbo *et al.*, 2020). These insights could enhance formulation strategies for improved delivery and efficacy.

Industrial and Nutraceutical Opportunities

Given their nutrient density and bioactive profile, watermelon seeds hold immense potential for the functional food, nutraceutical, and cosmeceutical industries. However, challenges in scale-up processing,

stability, and sensory acceptance limit widespread adoption (Eze & Okafor, 2021). Innovative technologies such as microencapsulation, nanoemulsion, and cold-press preservation could improve stability and shelf life while maintaining bioactivity. Additionally, developing eco-friendly extraction and zero-waste utilisation frameworks can transform discarded seeds into sustainable, high-value ingredients, contributing to circular bioeconomy goals.

Future Directions

To harness the full potential of watermelon seeds, future research should focus on:

1. Conducting human clinical trials validating therapeutic claims.
2. Establishing international standards for extract quality and safety.
3. Utilising omics and computational biology tools to elucidate molecular mechanisms.
4. Exploring synergistic effects of watermelon seed compounds with other nutraceuticals.
5. Promoting interdisciplinary collaboration between food scientists, pharmacologists, and industrial biotechnologists.

By bridging these research gaps, watermelon seeds can transition from being an underutilised agricultural byproduct to a scientifically validated functional superfood, supporting both health and sustainability.

CONCLUSION

Watermelon (*Citrullus lanatus*) seeds, once considered agricultural waste, have emerged as a potent source of nutrition and bioactive compounds with diverse therapeutic and industrial applications. Rich in proteins, essential fatty acids, dietary fibre, vitamins, and minerals, these seeds exhibit significant antioxidant, anti-inflammatory, antidiabetic, and cardioprotective activities. The phytochemicals present—such as flavonoids, phenolic acids, alkaloids, and saponins—play crucial roles in scavenging free radicals, improving lipid metabolism, and maintaining cellular health. Several *in vivo* and *in vitro* studies have demonstrated that watermelon seed extracts can effectively modulate oxidative stress, reduce blood glucose and cholesterol levels, and enhance liver and kidney function.

From a functional food perspective, the incorporation of watermelon seed flour, oil, or protein isolates into bakery, dairy, and beverage formulations holds great promise for developing nutrient-dense products. Moreover, the cosmetic and pharmaceutical industries can utilise its oil for skin and hair health due to its rich tocopherol and polyunsaturated fatty acid content.

The sustainable utilisation of watermelon seeds not only minimises Agri-waste but also contributes to the circular

bioeconomy and environmental conservation. However, research gaps persist, particularly regarding standardisation of extraction methods, long-term safety evaluations, and large-scale human clinical trials. Future studies should focus on optimising processing techniques to preserve bioactive compounds, improve bioavailability, and validate functional efficacy through well-designed interventions.

Overall, watermelon seeds represent an underexploited, eco-sustainable resource with immense potential to contribute to the global nutraceutical, functional food, and wellness industries.

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