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Phytochemical And Pharmacological Overview Of *Citrullus Lanatus*: Insights From Fruit Flesh, Seeds, Rind, Leaves, And Roots

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Abstract: Citrullus lanatus *(watermelon) is a globally cultivated cucurbitaceous crop valued not only for its edible fruit flesh but also for the nutritional and medicinal properties of its seeds, rind, leaves, and roots. Increasing evidence shows that these underutilized parts contain diverse phytochemicals, including carotenoids, amino acids, flavonoids, tannins, saponins, and essential fatty acids. Lycopene and citrulline dominate the fruit flesh, contributing to antioxidant and cardiovascular benefits, while seeds provide proteins, oils, and polyunsaturated fatty acids with hypoglycemic and antimicrobial effects. The rind, rich in citrulline and polyphenols, demonstrates wound healing and antioxidant activities, whereas leaves are reported to possess anti-inflammatory and antimicrobial compounds. Roots, though less studied, are traditionally employed for diuretic and laxative purposes, with emerging evidence of hepatoprotective potential. Collectively, these findings highlight watermelon as a valuable source of nutraceuticals and potential therapeutic agents. This review underscores the phytochemical richness and pharmacological relevance of* Citrullus lanatus *beyond its fruit flesh, drawing attention to seeds, rind, leaves, and roots as promising reservoirs of bioactive compounds. Further research through bioassay guided isolation, mechanistic studies, and clinical validation is essential to optimize utilization of watermelon derived products in functional food and drug development.*

Keywords: *Citrullus lanatus*, Watermelon, Phytochemicals, Pharmacological activities, Nutraceuticals, Traditional medicine, Bioactive compounds

1. Introduction

Watermelon (*Citrullus lanatus*, family Cucurbitaceae) is one of the most widely consumed fruits worldwide and represents a major horticultural commodity with both economic and nutritional importance. Global consumption has traditionally focused on the sweet, watery flesh, which is valued for its refreshing quality and high content of lycopene, citrulline, and other antioxidants. However, in recent years, scientific attention has expanded beyond the edible flesh to explore the potential of nonflesh parts such as seeds, rind, leaves, and roots. These components, once regarded as waste, are now increasingly recognized as valuable reservoirs of bioactive compounds with diverse applications in health and industry (Perkins Veazie et al., 2001; Acun et al., 2025).

Watermelon seeds are rich in proteins, lipids, and micronutrients such as magnesium, zinc, and iron. They also provide essential fatty acids, particularly linoleic and oleic acids, which contribute to their nutritional and pharmacological relevance. The rind, which constitutes a significant proportion of fruit biomass, contains dietary fiber, pectin, citrulline, and polyphenols. These compounds are associated with antioxidant, antimicrobial, and wound healing effects, offering promising opportunities for waste valorization and functional food development.

Beyond these more studied parts, ethnobotanical records demonstrate that watermelon leaves and roots hold cultural and medicinal significance in different regions. Leaves are employed in traditional medicine for treating gastrointestinal complaints, malaria, and inflammatory disorders, while root preparations are valued for their diuretic and laxative properties (Rotimi et al., 2023). Preliminary phytochemical studies confirm the presence of flavonoids, alkaloids, tannins, and saponins in these tissues, which supports their continued pharmacological exploration.

This chapter provides a holistic overview of *Citrullus lanatus*, integrating findings from analytical chemistry, preclinical pharmacology, and clinical nutrition. By synthesizing evidence across different plant parts, the chapter highlights the whole plant perspective, moving beyond the conventional focus on fruit flesh. Particular emphasis is placed on the valorization of agricultural byproducts, positioning watermelon as a sustainable source of bioactive compounds for functional foods, nutraceuticals, and therapeutic applications. In doing so, this work aims to stimulate further multidisciplinary research into the nutritional and medicinal value of *Citrullus lanatus* as well as its potential role in advancing global food and health security.

2. Scope and Methodology

The literature search that informs this chapter included PubMed, Web of Science, Scopus, ScienceDirect, Google Scholar and select open access journals through August 2025. Keywords included Citrullus lanatus, watermelon, rind, peel, seeds, seed oil, citrulline, lycopene, phytochemistry, antioxidant, antimicrobial and valorization. Inclusion criteria were peer reviewed original research, reviews, clinical trials, and food science studies that reported phytochemical composition, extraction and analytical methods, in vitro and in vivo bioactivity, safety or product development. Preprints and ethnobotanical surveys were considered when they added experimental phytochemical or pharmacological data. Non English articles were excluded. Data were organized by plant part and by topic: phytochemistry, analytical methods, pharmacology, toxicology and applications. For key factual statements and quantitative data, recent up to 2025 sources are cited.

3. Phytochemical Composition by Plant Parts

3.1 Fruit Flesh

The edible flesh is dominated by water and simple carbohydrates but also contains carotenoids and free amino acids of biomedical interest. Lycopene is the principal carotenoid in red and pink cultivars and accounts for much of the antioxidant capacity reported in in vitro assays and observational associations with reduced cancer risk in some epidemiologic studies (Giovannucci, 2002; Perkins-Veazie et al., 2001). Citrulline, a non-protein amino acid, is present at high concentrations in many cultivars and serves as a precursor to arginine and nitric oxide, supporting vascular function and exercise recovery reported in human trials (Collins et al., 2007; Luo et al., 2024). Minor quantities of phenolic acids and flavonoids have been quantified in comparative analyses of flesh and peel, and levels vary with genotype, maturity and agronomic factors (Perkins-Veazie et al., 2001; Liu et al., 2018).

3.2 Seeds

Watermelon seeds are nutrient dense. Modern compositional studies report crude protein commonly between 25 and 40 percent and oil yields typically in the 30 to 40 percent range depending on cultivar and extraction method (El-Adawy & Taha, 2001; Nissar, 2025). Fatty acid profiling consistently shows predominance of polyunsaturated fatty acids with linoleic acid (C18:2 n-6) as the major component and oleic acid as the principal monounsaturated fatty acid (Siol et al., 2025). Seeds also contain tocopherols, phytosterols, saponins, phenolics and proteins that may confer antioxidant, hypoglycemic and antihypertensive effects in preclinical models. Seed oil has been evaluated for edible oil, cosmetic and topical applications while defatted seed meal holds promise as a protein ingredient (El-Adawy & Taha, 2001; Nissar, 2025).

3.3 Rind and Peel

Rind represents a substantial proportion of fruit mass, often 30 to 50 percent, and contains fiber, pectin, citrulline, phenolic compounds and flavonoids (Tarazona-Díaz et al., 2013; Ben Romdhane et al., 2024). Recent extraction and fractionation studies find that rind is a tractable source of polyphenols and citrulline with appreciable antioxidant capacity when processed via gentle drying and green extraction approaches that preserve heat labile constituents (ACS Food Science study, 2024; Mohseni, 2025). Rind derived pectins and polysaccharide fractions have been characterized for food texturizing and functional fiber applications with reported yields that depend on cultivar and extraction solvent conditions (Ben Romdhane et al., 2024).

3.4 Leaves and Aerial Parts

Leaves contain flavonoids, tannins, saponins and some alkaloids. Ethnopharmacological uses of leaves include decoctions for fever and gastrointestinal complaints. Phytochemical screening and antimicrobial assays frequently report inhibitory activity against bacteria and fungi in vitro, though most studies are preliminary and lack compound level identification or in vivo confirmation (Athanasiadis et al., 2023). Quantitative profiling of flavonoid subclasses in leaves is limited and variable by harvest stage.

3.5 Roots

Roots are the least studied plant part with sparse phytochemical data. Screening often detects alkaloids, tannins and terpenoids consistent with ethnobotanical claims of diuretic and laxative use. Contemporary mechanistic or isolation studies from roots are uncommon and represent a clear research gap.

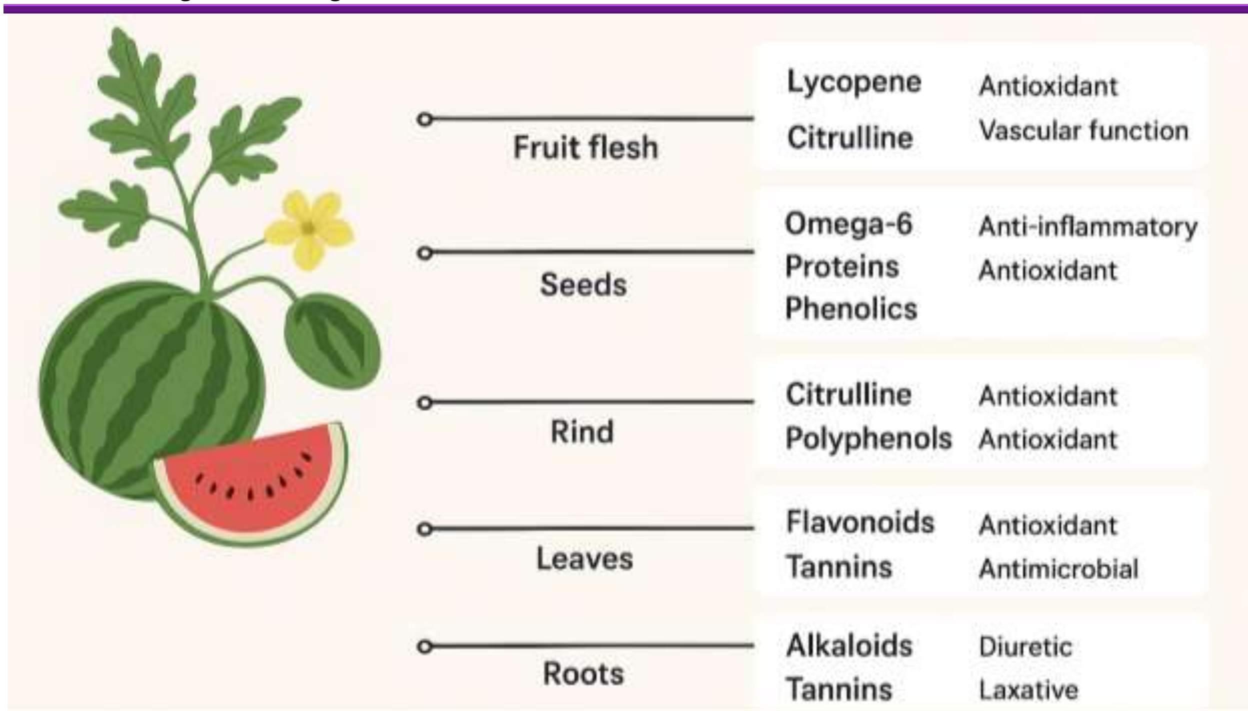

Figure 1. *Schematic overview of* Citrullus lanatus *parts, major phytochemicals and reported bioactivities.*

4. Analytical and Experimental Methodologies

4.1 Sample Collection and Preprocessing

Best practice for preserving labile carotenoids and citrulline in flesh and rind is rapid processing, freezing and lyophilization or cold drying. For seeds, moderate drying prior to mechanical decortication improves oil quality and reduces microbial spoilage. Many recent studies detail the influence of harvest maturity and storage on phytochemical stability and emphasize reporting of cultivar and post harvest handling to enable comparisons across studies (Quandoh et al., 2025; Tarazona-Díaz et al., 2013).

4.2 Extraction technologies

Traditional solvent extraction using aqueous methanol, ethanol or acetone mixtures remains common for polyphenols. Seed oil extraction uses Soxhlet with hexane at research scale and cold pressing for edible oil preparation. In the last decade, green extraction techniques including ultrasound assisted extraction, pressurized liquid extraction and supercritical CO2 have been increasingly applied to rind and seeds to improve selectivity and reduce solvent residues. Comparative studies show ultrasound enhancing phenolic yields from rind while supercritical CO2 is effective for nonpolar carotenoids and seed oil recovery (Mohseni, 2025; ACS Food Sci Tech, 2024). Spray drying and microencapsulation of citrulline from rind have been developed to stabilize extracts for functional ingredient use (Barón et al., 2021).

4.3 Chromatographic and Spectrometric Analysis

HPLC coupled to diode array detection and LC-MS/MS is the standard for carotenoid and phenolic profiling. Carotenoid analysis often requires pretreatment to saponify lipid matrices and use of isocratic or gradient HPLC with authentic standards for quantification. Fatty acid composition of seed oils is routinely determined after esterification to fatty acid methyl esters and analysis by GC-FID or GC-MS. NMR remains valuable for structural elucidation of isolated novel constituents. Method validation with external standards, limits of detection and recovery experiments are increasingly reported in high quality studies to permit cross study comparison (Siol et al., 2025).

4.4 Bioassays and Pharmacology

In vitro antioxidant assays such as DPPH, ABTS, FRAP and ORAC continue to be used for screening. Antimicrobial evaluation follows CLSI broth microdilution for minimal inhibitory concentration determination. Enzymatic assays for antidiabetic screening include alpha amylase and alpha glucosidase inhibition. In vivo rodent models assess antihypertensive, hypoglycemic and hepatoprotective endpoints. Clinical intervention studies with citrulline or watermelon preparations use randomized controlled designs measuring blood pressure, arterial stiffness and exercise recovery; pooled analyses show modest systolic and diastolic reductions in middle aged and elderly populations (Luo et al., 2024; Rodríguez-Carrillo et al., 2025).

Table 1: **Comparative summary of extraction approaches, typical yields and main compounds for each watermelon plant part**

Plant part	Typical extraction methods used in literature	Typical reported yields or content ranges reported	Main compounds / classes recovered	Representative sources

Fruit Flesh	Cold aqueous extraction for juices; solvent extraction with methanol/ethanol for phenolics; hexane/acetone for carotenoids after saponification; lyophilization for samples	Lycopene variable by genotype e.g., 10 to 120 mg/kg fresh weight reported across cultivars; citrulline ranges vary widely depending on cultivar and maturity; water content ~90%	Lycopene, β-carotene, citrulline, some phenolic acids and flavonoids	Perkins-Veazie et al., 2001; Tarazona-Díaz et al., 2013; Liu et al., 2018.
Seeds	Cold pressing and solvent extraction (n-hexane) for oil; Soxhlet/hexane for research yields; aqueous methanol for phenolics; defatting followed by protein extraction	Oil yields typically 30 to 40% seed mass depending on cultivar and moisture; crude protein 25 to 40%	Seed oil rich in linoleic acid (major PUFA), oleic acid (MUFA), tocopherols, phytosterols; proteins and saponins in meal	El-Adawy & Taha, 2001; Siol et al., 2025; Nissar, 2025.
Rind and Peel	Aqueous or hydroalcoholic extraction for polyphenols and citrulline; ultrasound assisted extraction and supercritical CO2 for nonpolar compounds; pectin extraction with acidified water followed by alcohol precipitation	Pectin yields reported from rind vary widely for method and cultivar; water soluble polysaccharide yields e.g., 8–34% reported in some studies; antioxidant extract yields vary with solvent	Citrulline, phenolic acids, flavonoids, pectins, soluble fibers, polysaccharides	ACS Food Sci Tech 2024; Ben Romdhane et al., 2024; Mohseni, 2025.
Leaves	Aqueous decoction and hydroalcoholic extraction for ethnobotanical studies; methanolic extracts for screening	Yields variable and generally lower than other parts; flavonoid content depends on harvest stage	Flavonoids, tannins, saponins, alkaloids; moderate antioxidant and antimicrobial activity reported	Athanasiadis et al., 2023; Fokou et al., 2009.
Roots	Aqueous and methanolic extracts in preliminary screens; limited modern extraction studies	Sparse quantitative data; screening detects alkaloids, terpenoids, tannins	Alkaloids, tannins, terpenoids; ethnopharmacological diuretic and laxative uses reported	Limited modern studies; select ethnobotanical reports and screening papers.

5 Pharmacological Evidence by Therapeutic Area

5.1 Vascular Function and Cardiovascular Risk Factors

Citrulline is the lead translational molecule from watermelon research. Oral citrulline increases arginine and nitric oxide bioavailability, improving endothelial function and lowering blood pressure in randomized trials and meta analyses. A recent meta-analysis found reductions in systolic and diastolic pressure among older adults and suggested that combined citrulline and arginine supplementation yields larger effects than either alone (Luo et al., 2024). Clinical doses used in trials vary but commonly range between 3 and 6 g daily for citrulline equivalents, while whole fruit interventions deliver lower amounts and are dependent on serving size and cultivar (Collins et al., 2007; Luo et al., 2024). Mechanistic studies support increased nitric oxide mediated vasodilation as the principal pathway. Despite promising results, heterogeneity in formulations and small sample sizes remain limitations.

5.2 Antioxidant and Ant-inflammatory Effects

Lycopene, flavonoids and phenolic acids present in flesh and rind contribute to antioxidant capacity in vitro and to reductions in oxidative biomarkers in preclinical models. Human data are limited but observational and interventional work with red watermelon suggests cardioprotective antioxidant effects and benefits on exercise induced oxidative stress (Perkins-Veazie et al., 2001; Tarazona-Díaz et al., 2013). Seed derived tocopherols and phenolics also contribute to antioxidant profiles documented in compositional studies.

5.3 Metabolic Effects and Antidiabetic Potential

Seed extracts and compounds such as saponins have produced hypoglycemic effects in rodent models through mechanisms that include inhibition of carbohydrate digestive enzymes and antioxidant mediated pancreatic protection. Human clinical evidence for metabolic endpoints remains scarce and limited to small pilot studies; thus more rigorous randomized trials of seed derived preparations are needed to substantiate preclinical findings (Nissar, 2025).

5.4 Antimicrobial and Antiparasitic Activities

Crude extracts from rind, leaves and seeds show in vitro activity against Gram positive and Gram negative bacteria and some fungi. Ethnopharmacological claims of antiparasitic effects have some experimental support in small animal models, but bioassay guided isolation of active molecules is still limited. Advances in antimicrobial screening and isolation would aid in identifying lead compounds for further development (Athanasiadis et al., 2023).

5.5 Other Reported Effects

Preclinical studies report hepatoprotective effects for certain aqueous and methanolic extracts, and mixed results for reproductive health markers in animal models. Human clinical data outside vascular endpoints remain sparse and are typically small and preliminary.

6. Valorization, Food Technology and Product Development

Large volumes of rind and seeds create an imperative for circular economy solutions. Recent product development research through 2024 and 2025 demonstrates successful incorporation of watermelon byproduct powders into pasta, bread and snack matrices, improving fiber and antioxidant content while reducing waste (Acun et al., 2025; Ben Romdhane et al., 2024). Fermentation and enzymatic treatments can upgrade nutritional quality of rind for animal feed and human ingredients; microencapsulation and spray drying enable stabilization of citrulline or phenolic extracts for functional ingredient use (Barón et al., 2021; Acun et al., 2025). Commercial translation requires scale up studies, sensory optimization and regulatory safety dossiers.

7. Safety and Toxicology

Watermelon flesh is safe for general consumption; relevant safety considerations involve sugar content for diabetics and rare food allergy. Concentrated extracts, seed oil, rind powder and encapsulated citrulline require compositional characterization and toxicology testing. Clinical trials of citrulline up to 6 g daily report good tolerability with occasional mild gastrointestinal symptoms. Chronic toxicity and genotoxicity data for concentrated extracts, especially intended for nutraceutical markets, remain inadequate and should be prioritized (Luo et al., 2024; Nissar, 2025).

8. Research Gaps and Priority Recommendations

1. Standardization of materials and methods. Researchers should report cultivar, harvest maturity, post harvest handling and extraction conditions to improve reproducibility.
2. Bioavailability and pharmacokinetics. Comparative studies of citrulline from whole flesh, rind concentrates and purified supplements are required to inform dose selection.
3. Clinical endpoints beyond vascular surrogates. Large randomized trials are needed for metabolic, hepatic and exercise recovery endpoints.
4. Bioassay guided isolation for antimicrobial leads. Compound level identification from active extracts is an unmet need.
5. Safety data for concentrated preparations. Subchronic and chronic toxicology studies must precede broad nutraceutical claims. These priorities align with recent reviews and experimental studies calling for a translational pipeline from byproduct chemistry to validated health products (Meghwar, 2024; Nissar, 2025).

9. Conclusion

A whole plant perspective on *Citrullus lanatus* reveals diverse bioactive compounds across flesh, seeds, rind, leaves and roots that support nutritional, pharmacological and industrial applications. Citrulline and lycopene are the most translationally advanced compounds with clinical evidence for vascular benefits, while seed oils and rind polyphenols offer promising functional ingredient opportunities. Priorities include method standardization, bioavailability research, larger clinical trials and safety dossiers to enable commercialization and sustainable valorization of watermelon byproducts.

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