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From Fruit to Pharma: A Review on the Phytochemicals, Extraction Methods, and Pharmacological Potential of *Citrullus lanatus* (Thunb.) Matsum. & Nakai

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A B S T R A C T

Objective: Watermelon, a tropical fruit with high water content, is rich in phytochemicals like cucurbitacins, flavonoids, glycosides, carotenoids, polyphenols, and amino acids. These compounds have anti-inflammatory and anticancer effects, and can help control blood pressure, glucose levels, and lipid metabolism.

Methodology: A complete database search was undertaken using terms such as' pharmacology','extraction methods,' ' nutrition profile,' '*Citrullus lanatus*', 'phytochemistry' to locate relevant material. Databases such as Google Scholar, SID, Magiran, PubMed, and Scopus were utilized to look for relevant publications, particularly ethnobotanical research on the issue.

Results: Watermelon exhibits a range of pharmacological activities, including antioxidant, anti-inflammatory, antimicrobial, anti-ulcer, antidiabetic, anti-obesity, laxative, and anticancer properties. The study emphasizes the need for effective and environmentally friendly extraction techniques, including supercritical fluid and ultrasound-assisted extraction, to separate bioactive components from watermelon

Conclusion: Environmentally friendly extraction methods and further research could advance its potential as a plant-based medication.

Keywords: Watermelon, Fruit, Phytochemicals, Pharmacological

➢ **How to cite this paper**

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Introduction

An herbaceous creeping plant of the Cucurbitaceae family is the source of the fruit crop known as watermelon (*Citrullus* lanatus (Thunb.) Matsum. & Nakai). Warm climates are ideal for this plant, which mostly generates offspring from its own seeds. This tropical plant needs at least 25 degrees Celsius and lots of sunlight to flourish. The ideal soil for watermelon is rich, well-drained, and somewhat acidic. The Northern Savannah parts of Ghana's shoreline, forest areas, and riverbanks are suitable for cultivation [1-2]. 3.1 million hectares of watermelons with an annual output capacity of 104 million tons are grown in Asia, Africa, and America. 67% of the world's output comes from China, making it the largest producer. According to the FAO, depending on the climate, ripening takes 80–110 days [3].

The *Citrullus lanatus* plant's fruit, dubbed the "water melon," is named after its maximum contains water content. The fruit was named "melon" because of its size and spherical shape, as well as its tasty and pulpy flesh. The scientific name for watermelon is derived from a blend of Greek and Latin. The scientific name "*Citrullus*" comes from the word "citrus," which alludes to the fruit. The word lanatus is Latin-derived and meaning "woolly." The plant has microscopic hairs on its stems and leaves. [4].

The watermelon, or Citrallus lanatus plant, is a fruit with maximum water content that is prized for its succulent flesh and huge, spherical form figure 1 illustrates the watermelon fruit. With the word "Citrullus" referring to the fruit, the scientific name is a blend of Greek and Latin roots. Watermelon's wild growth and variety of varieties suggest that it originated in southern Africa [5]. It has several herbaceous, sturdy, and powerful stems and may grow either ascending or prostrate. The middle lobe of the herbaceous, stiff leaves is the biggest. Because the plant is monoecious, it may produce both male and female blooms.

The stalk may grow up to 50 millimeters, while the fruit can have a diameter of up to 200 millimetres. The fruit weighs between 0.1 and 1 kg and varies in size from 5 to 70 cm. The fruit's flesh is yellow, and its seeds are flattened, oblong to elliptical, yellow to brown or black, and infrequently white [6].

Methodology

A complete database search was undertaken using terms such as' pharmacology','extraction methods,' ' nutrition value,' '*Citrullus lanatus*', 'photochemistry' to locate relevant material. Databases such as Google Scholar, SID, Magiran, PubMed, and Scopus were utilized to look for relevant publications, particularly ethnobotanical research on the issue.

Result

Here is the taxonomic classification of Citrullus lanatus (watermelon), along with a brief explanation for each level of classification:

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

Morphological characteristics:

The immature portions are heavily woolly with yellowish to brownish hairs, while the older sections lose their hair. It has several herbaceous stems that are quite robust and durable, reaching up to three meters in length. The leaves are simple, cordate, alternating on long petioles, and have seven shallow lobes with varying serrated edges. They are sharp, deep green, and have a diameter of 7 to 15 cm [7]. There are many hairs

on the abaxial side. They possess simple tendrils that spiral. It is the same plant that produces both male and female blooms. The male blooms appear in groups ahead of the females. Five golden petals and five greenish-colored sepals are included in each [8]. Hermaphrodite blooms are not always present. The spherical fruits are 14–20 cm long and have shallow grooves. It is greenish yellow on the skin. The flesh is called pepo, and it's juicy, flavorful, pale yellow, and nearly white. The smooth, light-brown, tiny seeds are 0.4 to 1.1 cm in length and 0.2 to 0.3 cm in width 3[9].

Chemical constitute:

Chemical composition: Citrullus lanatus seeds include flavanoids, alkaloids, tannins, amino acids, carbohydrates, cardiac glycosides, terpenoids, steroids, carotenoids, oils, and lipids, among other phytochemical components. Initially, citrulline, an amino acid, was isolated and evaluated using watermelon [10]. Watermelon is a good source of vitamin A (3%), numerous B complex vitamins, such as thiamine (Vit. B1), riboflavin (Vit. B2), niacin (Vit. B3), pantothenic acid (B5), vitamin B6, and folate (Vit. B9), which ranges from 1% to 3%, and vitamin C (14%). The mineral makeup is as follows: 1% zinc, 2% phosphorus, 2% potassium, 3% magnesium, 2% iron, and 1% calcium. It also includes oils and fatty acids that are very unsaturated. Aspartic acid, glutamine, and arginine are among the essential amino acids that are abundant in it [11].

Nutrients value

Watermelon is a hydrating and nutritious fruit rich in water, carbohydrates, and various vitamins and minerals. One cup of watermelon contains 46 calories, 12 grams of carbohydrates, and is a good source of vitamins A and C, as well as potassium as it is shown in table 1. It's also low in fat, cholesterol, and sodium.

Table 1: Nutrition value in the watermelon seed

Sl.no	Components	Concentration/Composition
	Proteins	25.2-35.6%
	Fats(lipids)	20-50%
	Carbohydrates	8-20%
	Minerals	Magnesium: 500-532mg/100g Iron:7-7.28mg/100g Zinc :10-10.24 mg/100g Calcium: 54 mg/100 g Phosphorus: 755 mg/100 g
	Vitamins	Vitamin A:70 mg kg−1 Vitamin C : 19.45 mg kg−1 Vitamin D : 8.76 mg kg−1 Vitamin B9: 1.84 mg kg−1

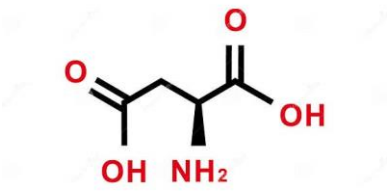
		Vitamin E : 3.53 mg kg−1 Vitamin K : 1.44 mg kg−
	Amino Acids	Phenylalanine: 5.15 g/100 g Arginine: 4.98 g/100 g Valine: 4.56 g/100 g
	Total phenols	1450–5400 mg GAE/100 g
	DPPH scavenging ability	56.93–94.46%
	Free radical scavenging activity	82-130µM Trolox/g

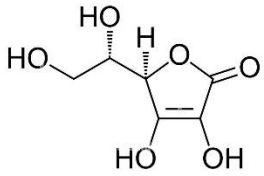
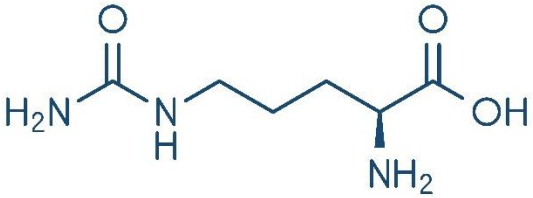
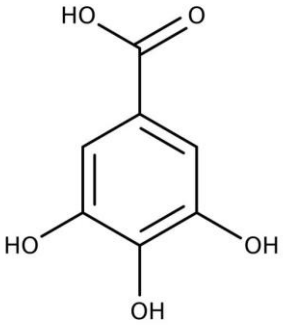
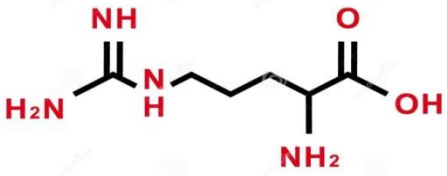
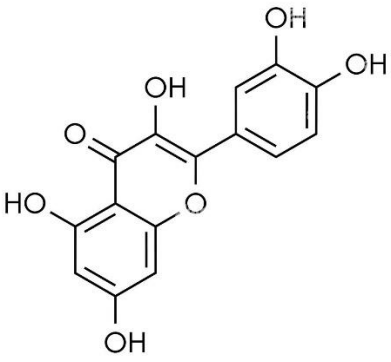
Discussion

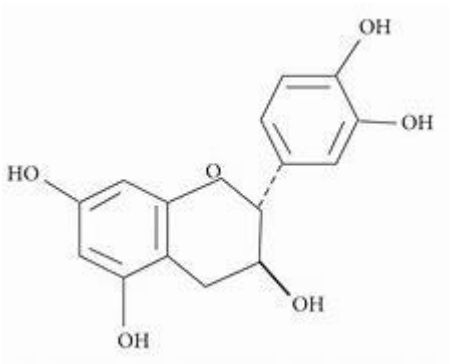
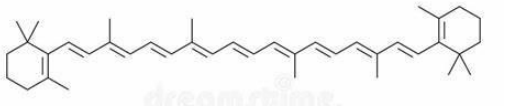
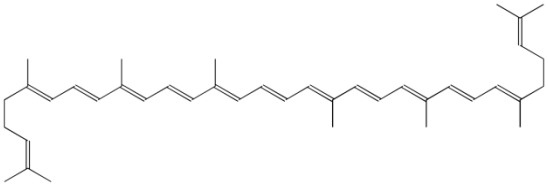
Phytochemical properties of the watermelon

Watermelon boasts a rich phytochemical profile, particularly with high concentrations of lycopene, citrulline, and various polyphenols, according to the National Institutes of Health (NIH). The structure and phytochemical of the watermelon is listed in the table the table 2.

Table 2: Bioactive compounds of watermelon

Sl.No	Phytochemical name	Structure
	Aspartic Acid	
	Glutamic acid	

	Ascorbic acid	
	Citrulline	
	Gallic acid	
	Arginine	
	Quercetin	

	Catechin	
	Beta carotene	
	Lycopen	

Traditional medicine uses cucurbitacins, which are tetracyclic triterpenoids found in plants, especially watermelon, to treat cancer and inflammatory illnesses. Terpenes, particularly the five-carbon isoprene unit isopentenyl pyrophosphate and dimethylallyl pyrophosphate, interact with regulatory proteins and have antioxidant properties [12]. They also function as NF-κB inhibitors in contemporary medicine, which responds to internal cues such as hypoxia and genotoxic stress as well as immune system disruptions. Cucurbitacin E is an anti-inflammatory that inhibits cyclo-oxygenase enzymes and neutralizes reactive nitrogen-containing compounds. Cellular ROS are not eliminated, although reactive nitrogen-containing compounds are reduced. Combining doxorubicin with cucurbitacin E increases the cytotoxicity against tumor cells while decreasing the size and bulk of the tumor [13].

Watermelon seeds contain compounds called glycosides that have anti-diarrheal effects. Linked to carbohydrate pairs, these molecules are chemical compounds that may coexist with other bioactive agents such as polysaccharides and thiol molecules. They are extremely reactive in physiological processes due to their diverse architectures and ease of hydrolysis by acids [14]. Glycosides are categorized according to their pharmacological or aglycone action. Saliva and gastric juice secretion are triggered by bitter principles such as andrographolide, diterpene lactone, amarogentin, and triterpenoid lactone. Anthracene glycosides regulate bowel movements and treat skin. Ingesting significant amounts of cyanogenic glycosides can be fatal and induce gastrointestinal distress because they break down to hydrogen cyanide. Appropriate processing and management are necessary to reduce the toxicity of cyanogenic glycosides in consumer food products [15].

Polyphenols are specifically polar phenolic molecules with functional hydroxyl groups that have properties that inhibit cancer, heart disease, and bacterial and viral infections. Reactive oxygen species are reduced, reactive nitrogen species are eliminated, and the enzymes that produce reactive oxygen species are inhibited. Anthraquinones, which are derived from anthracene, are widely recognized for their efficacious relief of stomachaches and constipation [16]. Flavonoids' structure affects

their antioxidant potential; aglycones have a higher level of activity than glycosides. Polyphenols can boost lipid oxidation and inhibit the enzymes that generate reactive oxygen species (ROS) with the aid of glutathione and mono oxygenase inhibitors [17]. Watermelon and winery by products include rutin and epicatechin, which have potent antiplatelet effects and reduce cholesterol. These interactions between molecules show that watermelon and its by products' cucurbitacins and polyphenols have prospective use as nutraceuticals, therapeutic agents, and functional foods for human health in general [18].

Pharmacological activities of the watermelon

Watermelon exhibits a range of pharmacological activities, including antioxidant, anti-inflammatory, antimicrobial, anti-ulcer properties, ant diabetics, obesity, laxative, and anticancer. The summary the pharmacological activity of the watermelon is given in the table 3.

Table 3: Pharmacological activities of the water melon

Sl.no	Pharmacological Activity	Effect	Reference
	Anti-inflammatory	inhibiting Cox2	[16]
	Sexual enhancement	Makes luteinizing hormone and testosterone levels in the blood higher.	[17]
	Antimicrobial	S. aureus, E. coli, B. tuberculis, and P. aeruginosa activity	[18]
	Weight loss and haematological benefits	Wistar rat weight loss, anemia treatment, and inhibition of leucocyte and platelet function.	[19]
	Anti-hepatotoxic activity	Seed extract reduced blood hepatic enzyme levels and ameliorated histopathological alterations caused by CCl4 in mice.	[20]
	Anti-diabetic	Methanolic seed extract induced a drop in blood glucose level in rats.	[21]

	Antiulcer and gastroprotective	Inhibiting gastric ulcers in rats	[22]
	Cardiovascular benefits	decreased body weight gain, decreased plasma cholesterol levels, improved pro- and anti-inflammatory cytokine balance, and reduced atherosclerosis development in mice with high cholesterol	[23]

Cardiovascular disease

A major cause of mortality worldwide, cardiovascular disorders also have substantial treatment expenses. The risk factors for these illnesses can be decreased with a diet rich in fruits and vegetables that is cardio-friendly [24]. Although direct consumption of l-Citrulline-rich fruits, such watermelon, might reduce oxidative stress and inflammation, it can also produce gastrointestinal discomforts [25]. When rats given a lot of fat were supplemented with watermelon, their lipid profiles, antioxidant status, and anti-inflammatory qualities increased. Fatty acid synthase (FAS), 3-hydroxy-3methyl glutaryl-coA reductase (HMGCR), sterol regulatory element binding protein (SERB), cyclooxygenase-2 (COX2), and nuclear factor-kB (NF-κB) are among the genes linked to lipid metabolism that it also controlled the expression of. The production of cholesterol and fatty acids depends heavily on these enzymes [26].

As a result, eating watermelon can help lower the risk factors for cardiovascular illnesses. Eating watermelon has been demonstrated to lower inflammation and oxidative stress, two major contributors to atherosclerosis. Rats on a high-fat diet had lower levels of C-reactive protein and the Cox-2 enzyme, which produces pro-inflammatory prostaglandins, was expressed less often [27]. Supplementing with watermelon decreases the inflammatory response and lowers Cox-2 activity [28]. According to research, eating watermelon every day decreased blood pressure, waist-to-hip ratio, body weight, and body mass index [29]. Additionally, in obese people, it enhanced antioxidant capacity and decreased triglycerides, low density lipoprotein cholesterol, and thiobarbituic acid reactive substance. Consuming watermelon on a regular basis might help lower risk factors for long-term conditions including heart disease [30].

Activity of watermelon in Obesity Management and Anti-Diabetic Snack

A major worldwide health issue, obesity is associated with lifestyle-related disorders and metabolic conditions including diabetes [31]. Obesity is a result of bad eating patterns and modern lifestyles, which include consuming fast food and processed meals rich in sugar. 10.5% of people in the United States have diabetes, while 45.8% of individuals are obese [32]. Type 1 diabetes is brought on by autoimmune reactions, whereas type 2 diabetes is brought on by insulin resistance. Diabetes-induced chronic hyperglycaemia can result in peripheral vascular disorders, cerebrovascular illnesses, retinopathy, neuropathy, nephropathy, and ischemic heart disease, among other consequences [33].

Symptoms of non-insulin-dependent diabetes include elevated glucose levels and decreased endothelial NO production. A precursor for NO generation, L-arginine has been demonstrated to improve vascular reactivity in animal models and hypercholesterolemia patients while lowering glucose levels in diabetic and obese rats [34].

However, l-arginine-rich diets have gained popularity since direct l-arginine consumption might result in gastrointestinal issues [21]. It has been discovered that watermelon juice dramatically raises plasma l-arginine levels, lowers glucose, free fatty acid, homocysteine, and methylarginines, and increases heart-related GTP cyclohydroxylase-1 and tetrahydrobiopterin levels as well as acetylcholine-mediated vascular relaxation [4].

Watermelon pomace juice has been suggested as a functional food to help fight obesity and diabetes because of its effects in animal models. In humans, watermelon juice can be a useful arginine supplement, improving cardiovascular and immunological response and helping to regulate whole body metabolism [15,18]. In obese people, watermelon consumption can lower blood pressure, enhance vascular function, and decrease body weight. Comparing watermelon to traditional refined carbohydrate snacks, it can also help with weight management by reducing hunger. Watermelon juice can also decrease hunger, according to studies [35].

Antioxidants

The human body produces reactive free radicals (ROS) through biochemical processes, which can harm cellular organelles and cause fatal illnesses [36]. Diets high in antioxidants, including plant-based diets, are crucial for preventing oxidative damage. Phenols, flavonoids, alkaloids, and terpenoids are examples of secondary metabolites that are essential to the relationship between plants and their surroundings because they protect plants and products from biotic and abiotic challenges and give them color and fragrance [37].
By scavenging or inhibiting the oxidation of low-density lipoproteins, a secondary metabolite's primary antioxidant potential is its capacity to detoxify harmful ROS. The antioxidant qualities of watermelon's lycopene and β-carotene include avoiding cataracts, suppressing retinal degeneration, lowering nitrogen oxide bioavailability, and shielding plasma lipoprotein architecture from oxidative stress [38].

Additionally, these pigments promote the growth of tumors and strengthen the immune system. Among carotenoids, lycopene is a potent antioxidant with a greater capacity to scavenge free radicals than both tocopherol and β-carotene [27]. Watermelon is a great option for a functional meal because of its high bioavailable lycopene content. A diet high in lycopene can preserve DNA and cellular membranes, control lipid production, and enhance the detoxification of free radicals [39].

The antioxidant qualities of fruits and vegetables are mostly attributed to polyphenolic chemicals, which are vital antioxidants [19]. For example, the hydrophilic antioxidant activity of watermelon is attributed to the presence of polyphenols. Watermelon is a good source of antioxidants since its fresh juice has 16.94–20.23 mg of gallic acid equivalent (GAE)/100 mL of polyphenols [40].

Moreover, watermelon may be used to boost beta-carotene levels and free radical scavenging activity in baked goods like cakes. 1, 1-diphenyl-2-picryIhydrazyl (DPPH) radical scavenging is more effective with this addition [41]. Watermelon rind powder's antioxidant properties can prolong its shelf life and enhance its useful ingredients, such as polyphenols. Numerous watermelon cultivars have been demonstrated to possess antioxidant potential and health-promoting compounds using in vitro experiments [36]. Red-fleshed watermelons are richer in lycopene and ascorbic acid, and they also have stronger antioxidant potential [42]. Because they include protein, fat, ash, fiber, salt, potassium, calcium, copper, magnesium, iron, phosphorus, and zinc, watermelon peels also have antioxidant potential [43].

Peel tissue has a high concentration of polyphenols, which help scavenge free radicals. Supplementing processed foods and food products with synthetic antioxidants such as butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) extends their shelf life and stability [50]. These artificial antioxidants must be replaced with natural ones because they may have drawbacks. To sum up, eating watermelon can greatly increase antioxidant potentials by both direct dietary

supplementation and indirect food supplementation [44].

Anticancer effect

Globally, cancer is a deadly illness with a high death rate. Watermelon's lycopene is one dietary component that can affect the molecular pathways of cancer. By influencing cell cycle machinery and lowering cyclin-dependent kinase (CDK) 1 and 3 activity in cancer cells, lycopene prevents DNA mutations and prevents tumor metastases. Because of its antioxidant qualities, it helps prevent malignant cells from proliferating and lessens oxidative stress [45]. The molecular basis for lycopene-mediated control of gene interaction is still being investigated, though. The equilibrium between cellular growth and planned cell death is upset by colon cancer, the second most deadly kind of cancer globally [46].

A healthy diet can help avoid the majority of colon cancers. It is possible that the tumoricidal properties of watermelon stem from the abundance of l-citrulline and its role in the production of endothelial nitric oxide (NO). Watermelon powder decreased the incidence of colon cancer in male Sprague-Dawley rats by lowering inflammation and oxidative damage to DNA, reducing abnormal crypt foci, and modifying the expression of enzymes that repair DNA [47]. With high mortality rates, breast and cervical cancers are the two most prevalent malignancies in women. The C33A cell line exhibits a high sensitivity to watermelon leaf extracts, which have been shown to have anti-proliferative effects on both cancer cell lines. Watermelon leaf extracts also have anti-cancer effects on leukemia, which is brought on by aberrant bone marrow blood cell growth [48]. Watermelon sprout phytochemicals prevent lung adenocarcinoma epithelial cell lines and human T-cell leukemia from proliferating excessively. By activating intercellular reactive oxygen species through NADPH oxidase, phytol-mediated cell death causes the cell cycle to stop in S-phase [56]. Important proteins including cyclin A, cyclin D, mitogen activated protein kinase (MAPK), and phosphatidylinositol-3-kinase (PI3K)/protein kinase b (Akt) are downregulated in this process [9]. Nevertheless, the phytol-induced cell death in cancer cell lines did not substantially correlate with the apoptosis mechanism [6]. In order to find prospective medication candidates for a variety of terrible malignancies, more research on the identification and extraction of phytochemicals with effective anti-cancer activity is necessary. Because of its phytochemicals, which fight damaging oxidative stress and affect important metabolic pathways, watermelon consumption also shows potential health advantages against a number of life-threatening disorders [49].

Antiulcer properties

The inflammatory bowel disease ulcerative colitis results in inflammation of the mucosa throughout the intestinal system. The elimination of ulcers, crypts, and goblet cells are its defining features. The second most deadly malignancy, colorectal cancer, can develop from chronic stages. Psoriasis, ankylosing spondylitis, and rheumatoid arthritis are among the numerous connected conditions that are linked to it [50-52]. Reduced l-arginine absorption by colonocytes is one of the symptoms. A precursor of l-arginine, watermelon can help cure ulcerative colitis by boosting antioxidant activity, reducing levels of pro-inflammatory cytokines, and enhancing other clinical indicators. Supplementing with watermelon enhanced nitric oxide levels, cellular kinetics, and colon crypt micro-architecture, according to recent research.

Synergistically, this increase in NO levels boosts the production of peroxisome proliferator-activated receptor-γ (PPAR-γ), which reduces oxidative stress and inflammation [53]. The expression of cyclin D1, a key protein in the Wnt signalling pathway, can be reduced in ulcerative colitis-affected mice by watermelon supplementation. This is associated with colon cancer because the Wnt signalling system encourages cell division instead of proliferation. The antioxidants in watermelon may help lower 8-OHdG levels, which may contribute to colorectal cancer development [40]. Oxidative stress, which is caused by too many reactive oxygen species, can damage DNA and encourage

the development of cancer. Because watermelon prevents oxidative stress and shields DNA from harm, it can help lower the amount of 8-OHdG. This may aid in preventing mice from developing colorectal cancer [54-55].

Laxative

Citrullus lanatus fruit pulp aqueous extract was tested for its laxative properties in albino Wistar rats. The rats were split up into five groups, each with six rats. At 250, 500, and 1000 mg, aqueous fruit pulp extract from Citrullus lanatus fruit pulp was administered to Groups 3, 4, and 5. The first group served as a control, while sodium picosulfate, a standard, was administered to the second group.

Safety and toxicity profile

Rats were used to test the acute toxicity of Citrullus lanatus extracts. Citrullus lanatus seed oil (CLSO) n-hexane extract was assessed using the acute toxic class technique in accordance with OECD standard no. 423. Citrullus lanatus seed oil has been demonstrated to be safe at doses up to 2,000 mg/kg body weight. Mice were also used to assess the toxicity of an aqueous extract of roots and leaves. Since no mice perished throughout the monitoring period, the state food and drug agency conducted a maximal tolerance study, per GLP 2003. Despite receiving a single, maximum oral dosage of 43.5 g/kg at two different times (7 am and 5 pm), no mice perished over the seven-day period. Following oral administration, the Citrullus lanatus ethanolic extract demonstrated no mortality, even at the maximum dosage level of 2000 mg/kg body weight of the extract.

Extraction methods

Bioactive molecule extraction from plant matrices is crucial for many businesses, such as food, pharmaceutical, and chemical industry [52]. Alkaloids, terpenoids, flavonoids, and phenols are among the compounds that offer health benefits. However, the extraction procedure has a significant influence on their effectiveness and quality. Achieving the maximum volume and bioavailability requires improving extraction techniques. The extraction techniques used have an impact on time, cost, purity, and recovery. Pre-extraction units must perform operations including cleaning, cutting, size reduction, and drying in order to increase extraction rates [53].

Solvent-based extraction techniques, including maceration, percolation, decoction, reflux extraction, and Soxhlet extraction, are widely used in the food and pharmaceutical industries due to their versatility and ease of use. These techniques use factors such as polarity, ionic strength, heat, and mechanical force [54].

This technique involves applying pressure on pulverized watermelon seeds, then centrifuging and filtering the mixture to extract the oil from the plant matter [55].

There are drawbacks to this simple and reasonably priced method of extracting bioactive compounds, including a long extraction time and a low extraction rate. It works best for extracting thermolabile compounds since they decompose at higher temperatures [56]. Among the factors influencing extraction efficiency are the kind of solvent, extraction duration, sample size, extraction temperature, and solid/solvent ratio. While Soxhlet extraction and maceration with methanol suppress DPPH radicals, maceration at room temperature can be used to remove phenolic compounds from oil mixtures. With an IC50 ranging from 1.41 to 2.60 mg mL−1, these substances exhibit potent antioxidant properties [57].

Bioactive compounds can be effectively extracted by filtering through plant material in a percolator [58]. A fresh solvent is introduced after a plant sample that has been pulverized is soaked in boiling water and macerated for many hours. Processing time and product volume are reduced by this method. However, not all bioactive compounds may be suitable for percolation, which requires a percolator [59].

Using the heat-stable extraction method of decoction, compounds that are soluble in water can be extracted. Following treatment with water

or an aqueous solution, plant material is cooled, filtered, and strained. It is not suitable for volatile and thermolabile compounds, though, and due to limitations in mass and kinetic transfer, it could be less successful, resulting in a poorer yield and quality of extracted molecules [60,61].

Also referred to as solid-liquid extraction, this technique works better than percolation and maceration since it uses less solvent and takes less time. In order to extract oil, plant material is combined with a solvent; the vapours cool and return to the flask. While this approach works well for heat-stable substances, it is not the best for thermo labile ones [62,63]. Soxhlet extraction It is a traditional process for removing bioactive compounds from plant sources that incorporates elements of reflux and percolation processes. This technique constantly pushes solvent through the sample, resulting in higher extraction capacities and shorter extraction times than standard approaches [55]. However, it may cause some bioactive substances to break down when heated, therefore its usage is restricted to heat-stable molecules. Older extraction techniques including maceration, percolation, decoction, reflux extraction, and Soxhlet extraction are still important because of their versatility and ease of usage [58]. Grape skin has been used to extract phenolic compounds using both standard and non-traditional methods. Variables such as temperature, extraction time, and solvent choice affect the amount and caliber of recovered bioactive compounds [64,65].

The drawbacks of traditional extraction techniques like Soxhlet and maceration include lengthy extraction durations, significant solvent consumption, and the possibility for sensitive chemicals to degrade:

Watermelon seed lipids may be extracted via supercritical fluid extraction (SFE), which offers improved bioactive ingredient preservation, reduced solvent usage, and increased efficiency [59]. Nonpolar and moderately polar chemicals may be effectively extracted with SFE since it employs CO2 as the solvent. Since watermelon seeds have a significant content of unsaturated lipids, they react negatively to the high temperatures used in traditional extraction methods [66]. By allowing oil to be extracted from almonds at reasonable temperatures, SFE prevents lipid nutritional changes. Due to its low solvent residue and high yield of bioactive lipids per unit of raw material, watermelon seeds can be used to extract commercial food-grade oil [67].

A method known as microwave-assisted extraction (MAE) may be used to extract antioxidants from watermelon seeds, which include tocopherol, flavonoids, and phenolic compounds. With this method, less solvent is used and greater extraction rates are achieved by simultaneously heating the solvent and seed matrix with microwave radiation [68,69]. In terms of recovering phenolic compounds with powerful antioxidant properties, MAE is highly effective. For the efficient extraction of bioactive compounds from both plant and animal sources, it is widely used due to its many benefits, which include faster extraction rates, shorter processing times, and improved solvent penetration. Biologically active chemicals may be separated from natural matrices using MAE, which is also environmentally acceptable because it employs water or other Earth-friendly solvents [70,71].

A hydro-thermo-mechanical technique called instant controlled pressure drop (DIC) technology employs pressure variation and auto-vaporization to improve the quality of organic goods including food, cosmetics, and medicinal biopolymers [72]. A vacuum chamber, an extraction vessel with a heating jacket autoclave, an extract collection chamber, and a pressure drop valve make up the DIC system. When processing food powders that are sensitive to temperature, such as apples and onions, DIC may be a suitable alternative [65]. For fragile fruits like strawberries, it works especially well, maintaining their quality while increasing extraction efficiency. DIC is a useful technique in the food and nutraceutical sectors because of its mild processing and improved functioning [73].

Proteins and polyphenols may be extracted from watermelon seeds using an enzyme-assisted extraction (EAE) technique. In order to extract bound proteins and polyphenols, celluloses and pectinase are used to break down the cell walls of

seeds. Additionally, EAE reduces the surface barrier, making solvent extraction simpler [74]. Polyphenol yield is influenced by variables such as enzyme-to-sample ratio and particle size. The process uses the enzymes in a sample and maintains the pH of the enzymes while keeping the solvent at a low temperature [75]. Energy is saved by stopping the hydrolysis process by inactivating the enzyme at 80–90°C. It is good for the environment because EAE utilizes water and pH levels are controlled. However, it takes three to four hours to eliminate.

It is an economical and energy-efficient technique for watermelon seed protein and polyphenol extraction. It shortens the extraction time and raises the concentration of polyphenols by weakening cell membranes, which permits matrix diffusion and solvent access. PEFE is used in sugar extraction and wine production to regulate polyphenol extraction and maximize colorant yields, and it is appropriate for sensitive components such as fatty acid profiles. It has no adverse effect on the flavour or taste of the extracted oil [76].

Pulsed electric field extraction (PEFE) is a cost-effective and energy-efficient method for extracting proteins and polyphenols from watermelon seeds. By weakening cell membranes, which allows matrix dispersion and solvent access, it raises the concentration of polyphenols and reduces the extraction time [77]. PEFE is suitable for sensitive materials like fatty acid profiles and is used in winemaking and sugar extraction to control polyphenol extraction and optimize colorant yields. There is no negative impact on the extracted oil's flavor or taste [78].

Ultrasound-assisted extraction (UAE) for watermelon seeds is a highly effective method for extracting oils and antioxidants. Due to its ability to reduce extraction time and solvent requirements, this approach is both cost-effective and ecologically benign [79]. Oils high in unsaturated fatty acids, tocopherols, phenolic compounds, and antioxidants are particularly well-recovered by UAE. Heat and oxidation-sensitive bioactive can be effectively removed from food with its help [80]. Ultrasound is appropriate for extraction and complementing other technologies since it increases heat and mass transfer rates when used in conjunction with other extraction techniques. According to a research, pomegranate peels may effectively extract phenolic compounds using ultrasonic and pressurized liquid extraction (PLE), which facilitates the extraction of bioactive components [81]. Ultrasonic extraction and supercritical fluid extraction (SFE) are the most researched methods. Using a variety of extraction techniques in the processing of high-quality products can improve the extraction of phenolic compounds and provide new ways to access bioactive compounds from natural sources [82].

Conclusion

Watermelon, or Citrullus lanatus, is a rejuvenating tropical fruit that also contains a wealth of essential minerals and pharmacologically active plant components. Cucurbitacins, polyphenols, flavonoids, carotenoids, and amino acids like L-citrulline and L-arginine provide a wealth of varied medicinal benefits. According to scientific research, it helps against cardiovascular disease, diabetes, obesity, oxidative stress, inflammation, and some types of cancer. Watermelon is a good crop for making functional foods and for use in medicines because of its anticancer, anti-inflammatory, antioxidant, laxative, and anti-ulcer properties. Furthermore, the development of environmentally friendly extraction methods including enzyme-assisted extraction (EAE), ultrasound-assisted extraction (UAE), and supercritical fluid extraction (SFE) has made it easier to isolate these bioactive substances in a productive and sustainable manner. These new techniques maintain the phytochemicals' functional integrity, making industrial and medicinal solutions safer and more effective. Last but not least, C. lanatus has enormous promise as a medicinal and nutraceutical medication. Watermelon can advance as a plant-based medication for a variety of illnesses and as a useful resource for the creation of plant-based medications as long as investigations into its bioactive components, mechanism of action, and pharmacological use continue.

Limitations and Future Research

The review acknowledges that while the therapeutic potential of watermelon is promising, more research is needed to fully understand its efficacy and safety. Future research directions include:

Optimizing extraction methods: Exploring different solvents, temperatures, and extraction times to maximize the yield and purity of bioactive compounds.

Identifying specific bioactive compounds: Further investigating the individual phytochemicals responsible for the observed pharmacological effects.

Exploring novel applications: Investigating the use of watermelon by-products in functional foods, nutraceuticals, and pharmaceuticals, including the development of innovative formulations.

Conducting clinical trials: Evaluating the efficacy and safety of watermelon extracts and by-product extracts in humans.

Statement And Declaration

No organization provided the author any assistance for the work that was turned in.

Ethics approval

The Declaration of Helsinki's tenets were followed in the conduct of this investigation.

Competing interests

Regarding this article's content, the author has declared no conflicting interests.

Consent to participate and funding

Nill.

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