Review

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Review

Health Promoting Properties and Applications of Nutrients and Bioactives of Watermelon and Its By-Products

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Abstract: The increasing demand by consumers for popular healthy fruits, such as the watermelon (*Citrullus lanatus*), generate substantial bio-wastes, making it imperative to harness the value of these by-products. Watermelon has low-calorie content and several other nutritional benefits that make it suitable for weight management and heart-healthy diets. Within this article, the nutritional composition and bioactives of watermelon which are strongly linked to the prevention of cardiovascular disorders (CVD), cancer, and age-related conditions, will be thoroughly reviewed. In addition, the therapeutic potential effects of watermelon consumption, such as anti-inflammatory, cardio-protective and anti-cancer properties, are also examined, with emphasis to the importance of incorporating watermelon into regular diets for overall health improvement. Additionally, the study explores various applications of watermelon by-products in functional foods, contributing to meeting recommended daily nutrient allowances, as well as in other functional products like cosmetics, with health promoting properties. In conclusion, this comprehensive review underscores the role of watermelon and its by-products for the development of products that can contribute to the prevention of chronic diseases and promote overall well-being.

Keywords: watermelon; valorization; by-products; bioactives; antioxidant; anti-inflammatory; anti-cancer; cardio-protective; functional foods; cosmetics

1. Introduction

According to World Health Statistics 2023 for monitoring health for the sustainable development goals of the World Health Organization (WHO) the major problems that predominates in the contemporary world today are chronic disorders. Such diseases could provoke more than 40 million deaths per year, which accounts for 74% of all deaths worldwide, due to cardiovascular disorders (CVD), cancer, chronic respiratory diseases and diabetes-related kidney disease [1]. It is well-established that chronic inflammation and its associated oxidative stress and thrombo-inflammatory manifestations are implicated in the propagation and development of these disorders, while it has also been observed that switching into healthy dietary habits plays an anti-inflammatory vital role in the prevention of these chronic disorders, improving thus life quality [2–4]. Fruits and vegetables are key components of healthy dietary patterns possess a great variety of micronutrients, such as carotenoids and phenolic compounds and other bioactive molecules with antioxidant, anti-inflammatory and antithrombotic properties [5,6]. Consumption of diverse fruit species relates to a lower chance of acquiring certain diseases, such as coronary heart disease or cancer, due to their bioactive substances [7].

Citrullus lanatus (CL), commonly known as watermelon, seems to be such a rich in bioactives healthy fruit. Watermelons (*Citrullus lanatus*) belongs to the *Cucurbitaceae* family tropical fruits and is one of the world's most cultivated fruits, with significant economic importance [8,9]. 7% of the worldwide fruits and vegetables production area is the one that watermelon cultivated in. Watermelons are primarily grown in Asia (79.5%), Africa (7.5%), and America (6.9%). Although production and consumption of this fruit are expanding gradually in the Mediterranean basin, China produces 67% of the total quantity, while having the highest consumption rates [10].

Watermelon consumption is increasing due to its sweetness and refreshing taste, high moisture content and appealing colors ranging from red to yellow or to pink. As a fruit, it is a low in calories, salt, cholesterol and fat fruit [11–13], and thus a popular and widely consumed fruit [14], due also to being thirst-quenching and nutritive, with an abundant content in nutrients, minerals and phytochemicals with numerous biological benefits [13], that are linked to healthy-eating and improved human health [15,16]. Subsequently, watermelon consumption has been associated with several health benefits, including improving cardiovascular health, high blood pressure in hypertensive patients, decreasing LDL oxidation, and fighting against age-related degenerative diseases, and certain types of cancer [14,15,17].

The increasing amounts of bio-wastes from agri-food by-products globally per annum, as well as their economic, social, and environmental impact have prompted research towards the appropriate and effective utilization of such wastes. In general, fruit, vegetable, and cereals by-products are popular due to their significant nutritional content and have the potential for supporting healthy diets, while wasted pulp can be incorporated into food products providing “ready to eat” bioactive components. Natural antioxidants in fruit and vegetable waste have sparked public and scientific curiosity. For example, flavonoids, and phenolic bioactive compounds from such by-products have received considerable attention due to their physiological effects such as antioxidant, anti-inflammatory, and anti-tumor activities, as well as their low toxicity when compared to synthetic phenolic antioxidants such as butylated hydroxyanisole, butylated hydroxytoluene, and propyl gallate [18,19]. Subsequently, several studies aim to replace synthetic antioxidant additives in foods by investigating the functionality of natural sourced antioxidants, such as those contained in agri-food wastes [20–22].

Watermelon’s by-products, such as its rind, remnants of its flesh/pulp (40%) and its seeds (60%) contain substantial amounts of such bioactives and phytochemicals [23,24]. The nutrients in the watermelon rind can help humans and animals reach RDA (recommended daily allowance) consumption to maintain good nutritional status and, thus, good health [25], while watermelon seeds also contain several nutrients (proteins, minerals, vitamins, lipids) and bioactives. The nutrients and bioactives of watermelon by-products like those found in rind and seeds, if recovered appropriately, they can be valorized and utilized as functional ingredients for novel functional products.

Here, the nutritional composition, bioactive compounds, mechanism of action, and therapeutic properties of watermelon and its by-products is thoroughly reviewed. In addition, the rising issues of agro-waste utilization of watermelon’s by-products is also examined, while emphasis is given to the valorization of its bioactives as ingredients for novel functional foods, supplements, nutraceuticals, or even drugs and cosmetics. Limitations and future perspectives for the benefits of this popular fruit and its by-products is also further discussed.

2. Nutritional composition, bioactives’ content and associated health benefits of watermelon and its y-products

2.1. Nutritional composition, bioactives’ content and associated health benefits of watermelon

Watermelon is characterized by a chunky rind and a fleshy middle with various colors. According to Oberio and Sogi [26], watermelon fruits yield 55.3% juice, 31.5% rind, and 10.4% pomace. The nutrition composition of flesh, juice, rind/peel, rind powder, and seeds of watermelon,

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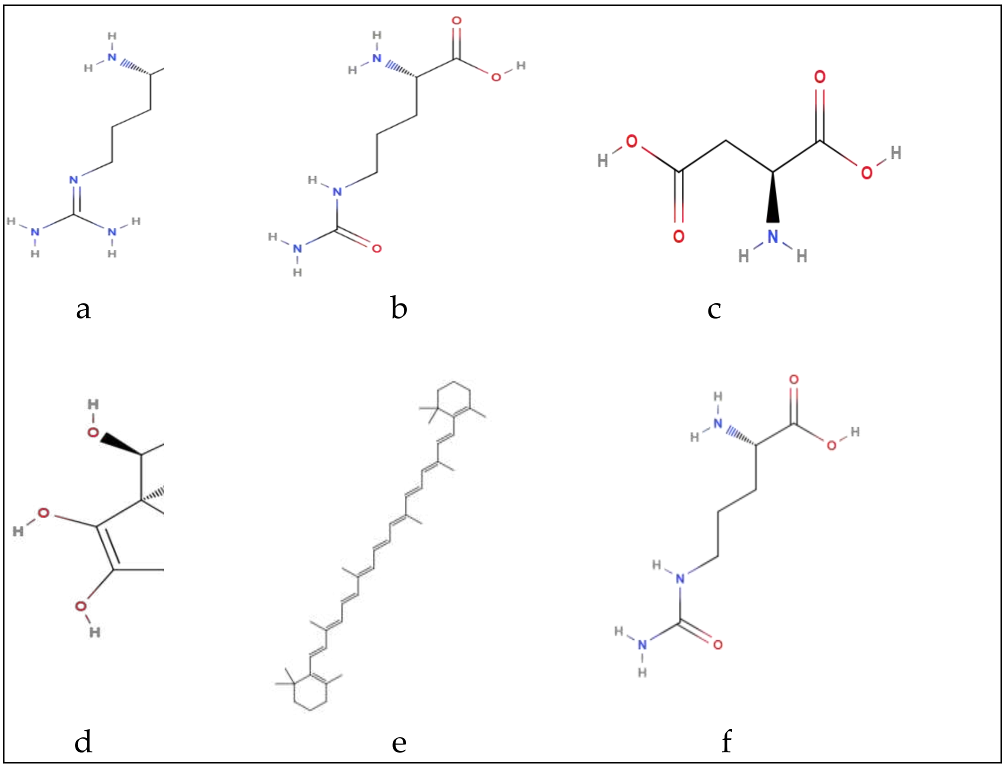
has been evaluated through a number of studies. The flesh and rind portion are low in fat while seeds are high in crude fat content whereas, crude fiber content was found high in the rind portion as compared to other parts (**Table 1**).

Table 1. Proximate composition of watermelon and its by-products (g/100g) [27–44].

	Fruit			By-products		
	Flesh	Juice	Pulp	Seed	Peel	Rind
Compounds	**Quantity g/100g**			**Quantity g/100g**		
Moisture	91.45	90.1-92.42	11.5	3.39-8.5	8.78	5.12-94.62
Ash	0.25	0.1-0.37	3.66	2.48-4.9	5.31	0.46-20
Protein	0.61	0.4-0.84	3.33	17.75-49.7	2.88	0.63-21
Crude fat	0.15	0.05-0.027	0.5	13.7-50.5	2.33	0.08-15
Carbohydrates	7.55	7.55	73.35	6.06-46.3	70.04	4.2-80.75
Crude fiber	0.4	0.4-0.7	7.66	2.1-40.75	10.66	2.6-23

The sweetness of the watermelon is mainly attributed to a combination of sucrose, glucose, and fructose [17]. Sucrose and glucose make up 20-40% of the total sugars in a ripe watermelon, while fructose makes up 30-50% [17]. Nevertheless, watermelon has a low energy density and is hence advised for weight management [13]. Watermelon is a good source of nutrients, minerals and vitamins [45], such as phosphorus, magnesium, calcium, and iron, as well as thiamine, riboflavin, niacin, folate and A, C and E vitamins [14,16,46]. It is also a source of several amino acids (**Figure 1**) and especially of citrulline, a non-essential amino acid that helps muscle relaxation [47].



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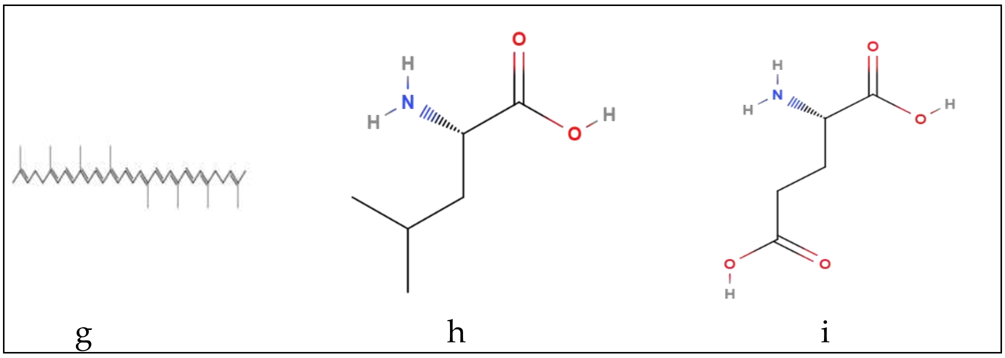

Figure 1. Structures of the most important micronutrients in watermelon (adopted from Jebir and Mustafa [48] (a) Arginine, (b) Citrulline, (c) Aspartic acid, (d) Ascorbic acid, (e) Beta-carotene, (f) Citrulline, (g) Lycopene, (h) Leucine and (i) Glutamic acid. Structures were obtained from https://molview.org/ (accessed on the 21st of September 2023).

Thus, watermelon is a nutrient-dense, thirst-quenching fruit with few calories [49] and its consumption may also be advantageous in maintaining acid-base balance in the body, which is crucial in normal physiology, hunger, and digestion [15]. Its vitamin content makes it beneficial for normal vision and skin health, cholesterol control, normal appetite, and nervous system function, and it may be involved in normal muscle contraction [50,51].

On the other hand, the leading organic acids that contribute to the peculiar watermelon flavor are malic, citric, and oxalic acids [52]. Watermelon flesh is red, yellow, and pink due to the presence of carotenoids such as β-carotene and its acyclic isomer, lycopene, lycopene [53]. The content of watermelons' microconstituents varied since it depends on cultivar, level of maturity, and provenance [54–57]. These carotenoids possess antioxidant, anti-inflammatory, and hypotensive beneficial effects for human health [58,59], while they can scavenge free radicals with therapeutic impact in several manifestations, including cancer and CVD, too [60–62]. Lycopene is also shown to have analgesic and anti-inflammatory properties [63,64], anti-ulcerative properties [65,66], and antibacterial properties [63,67]. Overall, lycopene is a primary bioactive compound present in watermelon, contributes several health benefits such as, antioxidant, anti-inflammatory antiproliferative, antihyperglycemic antidiabetic and cardio-preventing and protecting properties [8,57,68,69].Watermelon juice's lycopene-rich nature and health benefits, according to Kim et al. and Jumde et al. [13,69], make it a good choice for preparing additional functional foods to increase utilization.

On the other hand, vitamins, minerals and specific amino acids, watermelon also contains a variety of other bioactive compounds, including phenolic compounds and alkaloids are distributed and concentrated differently in the flesh, rind, leaves, and seeds, as depicted in **Figure 2** [10,70–72]. Some of these phytochemicals could prevent diseases like hypertension and arthritis [11], while according to Bailey et al. watermelon juice supplementation improves vascular health in hypertensive people [73]. Watermelon contains comparably more antioxidants than popular fruits like tomatoes, strawberries, and guavas [15]. Nevertheless, apart from the antioxidant protection, watermelon bioactive compounds demonstrate numerous health benefits, including reduced risk of CVD, aging-related ailments, obesity, diabetes, and various cancer-fighting effects [10,74–77], suggesting that incorporating watermelon in the diet can effectively reduce such chronic disease [8,14].

Watermelon has been considered an excellent dietary source of bioactive phenolics. Phenolic compounds can be found in great numbers in the seeds [78] and higher in all portions except flesh [77]. Abu-Reidah et al. reported that 23 compounds of watermelon flesh belong to the flavonoid families [79]. Mushtaq et al. found myricetin and quercetin in rind [80] while apigenin, naringenin-7-*O*-glycoside, rutin, amentoflavone, quercetin, quercitrin, kaempferol and luteolin in seeds were determined by Jimoh et al. and Sultana & Ashraf [78,81]. Major bioactive compounds present in watermelon and by-products such as peel, rind, and seed are depicted in **Figure 2**. Watermelon fruits contain other phytochemical compounds too, like cucurbitacins and their glycoside derivatives,

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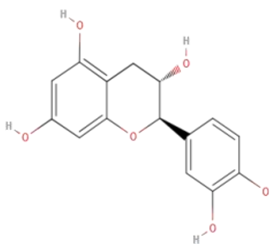
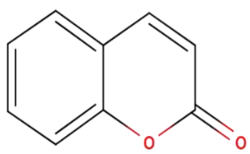
which have a unique medicinal significance due to their potential biological activities like hepatoprotection, anti-inflammatory, anti-tumor, antimicrobial, and anti-helminthic effects (**Figure 3**) [82,83].

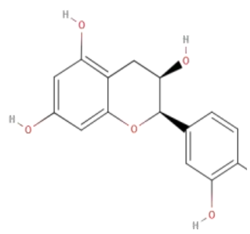
Thus, watermelon's health benefits are greatly linked to its nutrient composition and its high content in a number of bioactive compounds, mostly phytochemicals, with anti-inflammatory, antioxidant and anti-cancer properties that contribute to health and the prevention of chronic diseases [82,84–88]. Because of these qualities, and due to its watermelon is a desirable functional food high lycopene, vitamin A, vitamin C, antioxidant and anti-inflammatory bioactives' content, watermelon is a great functional food [39,63,89].

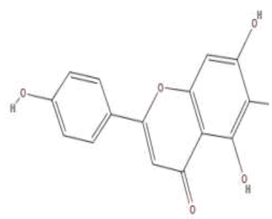
2.2. Nutritional composition, bioactives' content and associated health benefits of watermelon by-products

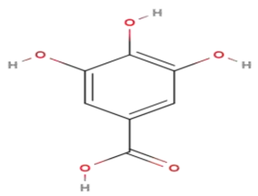
Watermelon by-products are usually its rind, peel, seeds and pulp. Watermelon rind (WR) is an integral part of watermelon. It is a thick white flesh between the outer green skin and the interior-colored flesh that contributes to about one-third of the total fruit mass mostly discarded despite being comestible. Watermelon rind contains starch, non-starch polysaccharides, sugars, resistant starch, oligosaccharides, and pectin [90]. Nutrition composition of watermelon and by-products is given in **Table 1**. Fresh WR has 95% moisture, but dry WR powder contains water (9-17%), crude protein (6-21%), fat (0.66-15%), dietary fiber (12-23%), ash (12-20%), and total carbohydrates (42-65%) including sugars, pectin, cellulose, lignin and hemicellulose [14,35,42,91]. The minerals content of rind are reported as; Fe (0.28mg/kg), Na (1.16mg/kg), K (4.83mg/kg), P (5.17mg/kg), Mg (8.22mg/kg), Zn (19.80mg/kg), and Ca (28.70mg/kg) [43,92]. Watermelon rind is also a rich source of citrulline, flavones, saponin, sterols, terpenoids and phenolic compounds, which are bioactives compound providing antioxidant properties and other health promoting effects [93].

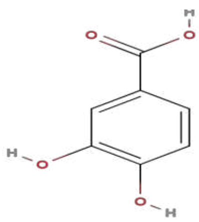

Catechin (1)

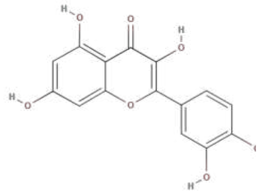

Coumarin (2)

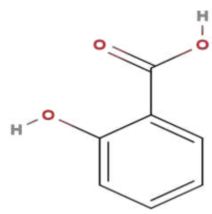

Epicatechin (3)

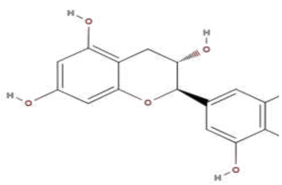

Flavonoid (4)

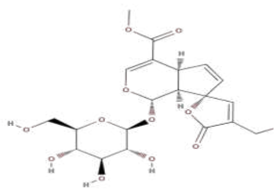

Gallic acid (5)

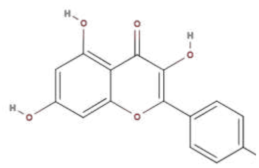

Protocatechuic acid (6)

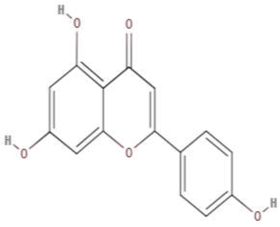

Quercetin (7)

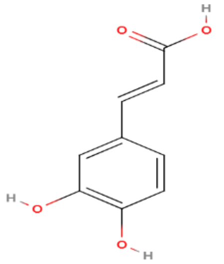

Phenolic acid (8)

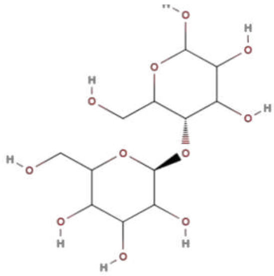

Gallocatechin (9)

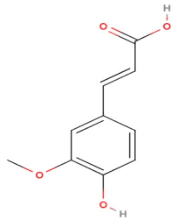

Iridoid (10)

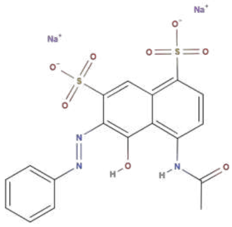

Kaempferol (11)

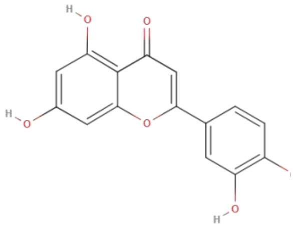

Apigenin (12)

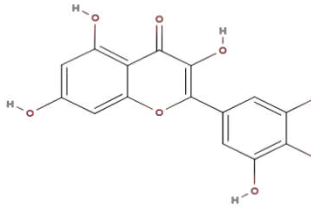

Caffeic acid (13)

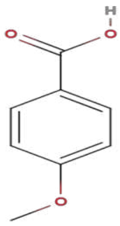

Cellulose (14)

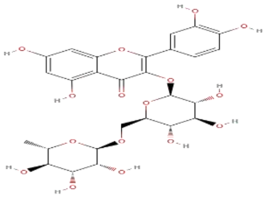

Ferulic acid (15)

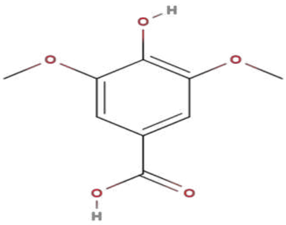

Lignin (16)

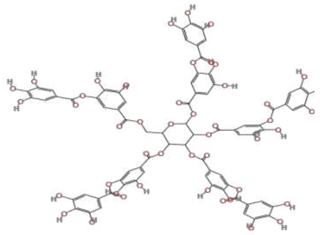

Luteolin (17)

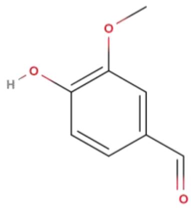

Myricetin (18)


p-Anisic acid (19)


Rutin (20)


Synergic acid (21)


Tannin (22)


Vanillin (23)

By-products (peel, rind, seed)

Figure 2. Major bioactive compounds in watermelon and its by-products. Structures were obtained from https://molview.org/ (accessed on the 21st of September 2023). Bioactives numbered as 1-11 are mostly found in watermelon fruit, while bioactives 12-23 are mostly found in its by-products (rind, peel and seed).

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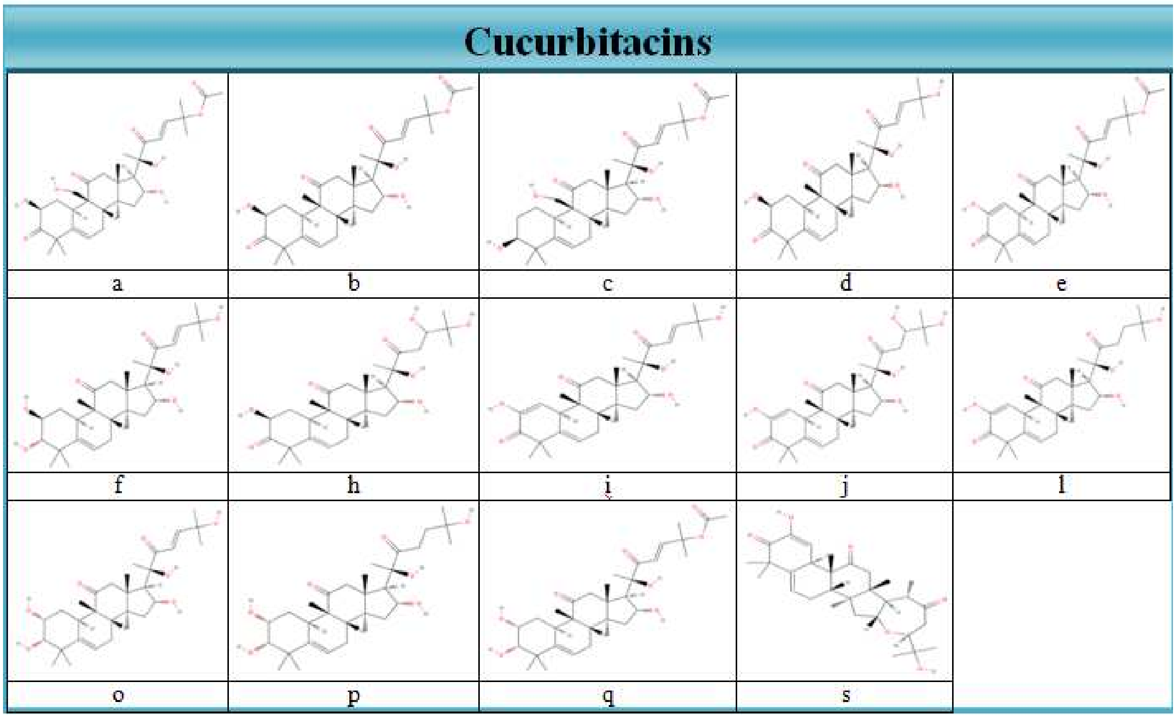

Figure 3. Chemical structure of the main cucurbitacins (adopted from Zamuz et al. [24]). Structures were obtained from https://molview.org/ (accessed on the 21st of September 2023).

Watermelon seeds are abundant in protein, minerals (including magnesium, potassium, iron, zinc, sodium, phosphorus, copper, and manganese), B vitamins, lipids and unsaturated fatty acids like stearic, palmitic, linoleic, and oleic acid, as well as several bioactive phytochemicals [94]. It also contains a lot of carbohydrates, including glucose, sucrose, and fructose, as well as carotenoids like carotene [95]. Watermelon seeds contain also a significant amount of arginine, contributing to their therapeutic properties [96], as this amino acid can decrease ulcerative colitis symptoms, but also it increases antioxidant capacity [97,98]. Due to the existence of many nutritious benefits, watermelon seeds have applications in a variety of culinary products. Sola et al. found that watermelon seed extracts contain antimicrobial capabilities [99]. Furthermore, roasted watermelon seeds are used by customers as an appetite stimulant and to alleviate constipation [83]. Nutrients and valuable bioactive compounds are given in **Table 2**.

Table 2. Nutrients and other valuable and bioactive compounds of watermelon and its by-products [27–44].

Parts	Carbohydrates	Anti-nutrients	Vitamins	Minerals	Amino acids	Phenols	Fatty acids
WMR	Galactose Xylose Arabinose Glucose Glucoranic acid Mannose Rhamnose Glucuronic acid	Oxalates Alkaloids Phytates Saponin Tanin Flavonoids Phenols	A B1 B2 B3 B6 C	Fe Mn P Ca Na Zn Cu K Mg	Citrulline phenylalanine Valine Leucine Tyrosine Lysine	Gallic acid, Synapic acid, Hydroxycinnamic acid, Quercetin, m-Coumaric acid, Chlorogenic acid, Syringic acid, p-coumaric acid, myricetin, caffeic acid, vanillic acid, 4-hydroxybenzoic acid, p-anisic acid.	**Saturated** Myristic acid, Palmitic acid, Margeric acid, Stearic acid, Arachidic acid, Behenic acid, Lignoceric acid. **Unsaturated** Elaidic acid, Linolenic acid, Linoleic acid, Vaccenic acid Oleic acid, Docosahexaenoic acid, Eicosadienoic acid, eicosenoic acid, hypogeic acid, vaccenic acid, gondoic acid.
Seed	Galactose Arabinose Glucose Sucrose Mannose Fructose Xylose	Oxalates Alkaloids Phytates Saponin Tannin Phenols Flavonoids	A B1 B2 B3 B6 B12 D E K	Fe Mn P Ca Na Cu Zn Cr K Mg Pb	Arginine Phenylalanine Lysine Leucine Iso-leucine Aspartic acid Glutamicacid, Serine Valine Cysteine Glycine	Gallic acid, Caggeic acid, Syringic acid, Sinapic acid, Rosmarinic acid, Vanillic acid, Prochatechuic acid, Leuteolin, Flavonoids, Flavone, Chlorogenic acid, Apigenin, Phenolic acid,	**Saturated** Myristic acid, Arachidic acid, Pentadecyclic acid, Margeric acid, Behenic acid, Stearic acid, Lignoceric acid. **Unsaturated** Palmitoleic acid, Gadoleic acid, Linolenic acid, Linoleic

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					Histidine Threonine Alanine Proline Methionine	4-hydroxybenzoic acid, Ferulic acid, Coumaric acid.	acid, Oleic acid, Erucic acid.
Peel	Galactose Xylose Arabinose Glucose Glucoranic acid Mannose Rhamnose Glucuronic acid	Alkaloids Saponin Tanin Flavonoids Phenols	A B1 B2 B3 B6 C	Fe Mn P Ca Na Zn Cu K Mg	Citrulline Phenylalanine Valine Leucine Tyrosine Lysine	Gallic acid, Synapic acid, Hydroxycinnamic acid, Quercetin, m-Coumaric acid, chlorogenic acid, syringic acid, p-coumaric acid myricetin caffeic acid vanillic acid 4hydroxybenzoic acid, p-anisic acid.	**Saturated** Myristic acid Palmitic acid Margaric acid Stearic acid Arachidic acid **Unsaturated** Linolenic acid Linoleic acid Oleic acid
Pulp	Fructose Sucrose Glucose	Flavonoids Glycosides Tannins Phenols Saponins Tannins	A B_1 B_6 C E	Ca Fe Mg Zn Na K	Citrulline Leucine Glutamic acid, Aspartic acid Arginine	Carotenoids Quercetin, Luteolin Gallic acid Coumarin Aviprin	Linoleic acid Oleic acid Palmitic acid Stearic acid Linolenic acid

*WMR= watermelon rind.

2.3. Molecular-Biochemical-Cellular Mechanisms of Action of of the most Bioactive Compounds present in Watermelon and Its By-Products: A Molecular Perspective

The most abundant bioactive constituents of watermelon and its by-products are several subclasses of cucurbitacins and polyphenols. Cucurbitacins are tetracyclic triterpenoids, derived from Cucurbitaceae family plants, while more than 100 species of such micro-constituents have been found in about 30 different species of Cucurbitaceae family [100]. Some of the different species of Cucurbitaceae family are the Bryonia [101], Cucumis [102] and Momordica [103], while cucurbitacins have also been identified, in lower amounts, in Polemoniaceae [104], Scrophulariaceae [105], and Thymelaeaceae species [106], too. From a chemical standpoint, cucurbitacins have a signature highly oxidized tetracyclic nucleus, since containing several of oxygen-containing groups at different positions [107]. Structurally, cucurbitacins are categorized into 12 primary forms, namely, cucurbitacin A to T [108]. It is reported that cucurbitacins demonstrate potential biological activities, based on the target cells, such as, anti-oxidant, anti-inflammation, anti-microbial, anti-diabetic, anti-rheumatic, anti-tumor, and so on [109–111].

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Considering the bioactivity of cucurbitacins, their low water solubility and lipophilicity contribute to enhanced antitumor effectiveness. This effect is facilitated by increased solubility and targeting following local and systemic administration, especially in their glycosylated forms, which have demonstrated the ability to prevent free radical and oxidative damage [110]. In terms of their anti-inflammatory activity, cucurbitacins have been found to block the activity of tumor necrosis factor alpha (TNFα) in lymphocytes and macrophages; simultaneously, they inhibit the function of nuclear factor-kappa-B (NF-κB) [112–115]. For instance, cucurbitacin R, has been proven effective against pain and inflammation in several different studies [116].

In addition to the aforementioned activities, several derivatives of cucurbitacins derivatives, namely, cucurbitacin B, D, E, and I, have been found to manifest anti-multiplication effects on various human cancer cell lines and tumor xenografts, including those associated with breast, brain, liver, lung, skin, prostate and uterine cervix cancers [109,110,117–119]. Noteworthy, cucurbitacin glycosylated derivatives (B and E) extracted from *Citrullus colocynthis* have demonstrated antigrowth effects on human breast cancer cells, through the conglomeration of cells in the phase II of growth/mitotic phase (G2/M phase) of the cell cycle and the induction of apoptosis, simultaneously [109]. Moreover, cucurbitacin R and 23, 24-dihydrocucurbitacin B extracted from the roots of *Cayaponia tayuya* were found to suppress cellular proliferation and/or initiate apoptosis in colon cancer cell lines [115,120]. Other studies suggest that, the simultaneous intake of cucurbitacins and anti-cancer medication led to improved results; the co-intake of doxorubicin and cucurbitacin E led to marked cytotoxicity towards tumor cells in vivo and in vitro resulting in diminished tumor dimensions and mass [121]. A similar trend was observed when comparing single medication with the simultaneous intake of cucurbitacin B with medication (docetaxel), on human laryngeal cancer cell line (Hep-2) [122].

On the other hand, polyphenols are products of plant secondary metabolism, found within the nucleus, the mesophyll cells and other regions where the generation of the reactive oxygen species (ROS), take place [123]. Polyphenols, including flavonoids, are produced through the phenylpropanoid pathway have been shown to exhibit several health promoting activities [124,125]. The functional hydroxyl group of polar phenolics give them the ability to scavenge free radicals and bind metal ions [126–128]; metal chelation is a key factor in preventing radical generation that could lead to the biomolecular damage [129]. In addition, many studies have demonstrated that polar phenolics have the capability to activate several protective enzyme systems in the human body, while simultaneously are able to manifest protective impacts against numerous human diseases, including, cancer, cardiovascular diseases and bacterial and viral infections [130,131].

Polar phenolic compounds have several different activities, with their distinctive trait being their ability to function as antioxidants. This behavior is attributed to the arrangement of functional groups surrounding the nucleus; the substitution and the configuration of the hydroxyl groups in the B ring, also significantly affect the antioxidant activity mechanisms, including chelating metal ions like iron and copper, and scavenging reactive oxygen species (ROS) and reactive nitrogen species (RNS) [132,133]. Additionally, the position, structure, and number of sugars in flavonoids (glycosylated forms) significantly affect their antioxidant properties with aglycone forms generally exhibiting better antioxidant efficacy than their respective glycosylated counterparts [134].

The mechanisms through which antioxidants, i.e., polyphenols, act, include the reduction of the ROS formation, either by binding to compounds involved in the production of the free radicals or by inhibiting enzymes, the scavenging of ROS and the enhancement of the human organism's antioxidant defense [135]. As for the enzyme inhibition, polyphenols exhibit inhibitory effects against the ones responsible for ROS generation, such as glutathione and monooxygenase, while enzymes such as NADH oxidase and mitochondrial succinoxidase are also implicated in such processes [136]. In addition, flavonoids serve as potential protective compounds against lipids oxidation through several different pathways [137].

For instance, epicatechin and rutin have been proven as stable, robust molecules that may effectively inhibit lipid peroxidation in vitro [138]. Additionally, quercetin has been demonstrated to

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chelate and stabilize iron [139]; the ethanol extract of winery by-products containing epicatechin and quercetin exerts a potent anti-platelet effect [140].

During oxidation on the B ring of flavonoids possessing a catechol group, they form a stable radical known as orthosemiquinone, rendering them potent scavengers. In contrast, flavones lacking the catechol group tend to be weaker scavengers due to their tendency to form unstable radicals [141].

It should also be mentioned that apart from their general antioxidant capacity, specific phenolic compounds have also been found to possess potent anti-inflammatory activities with several health promoting properties [142]. For instance some phenolic compounds have shown anti-cancer potency through inhibiting the synthesis of potent thrombo-inflammatory mediators implicated in cancer growth and metastasis [2], while they have also shown strong antiplatelet activities [140,143] and a general anti-inflammatory potency in renal cells and blood cells that contribute in the reduction of risk for developing several disorders related to the inflammatory manifestations of these cells [144,145].

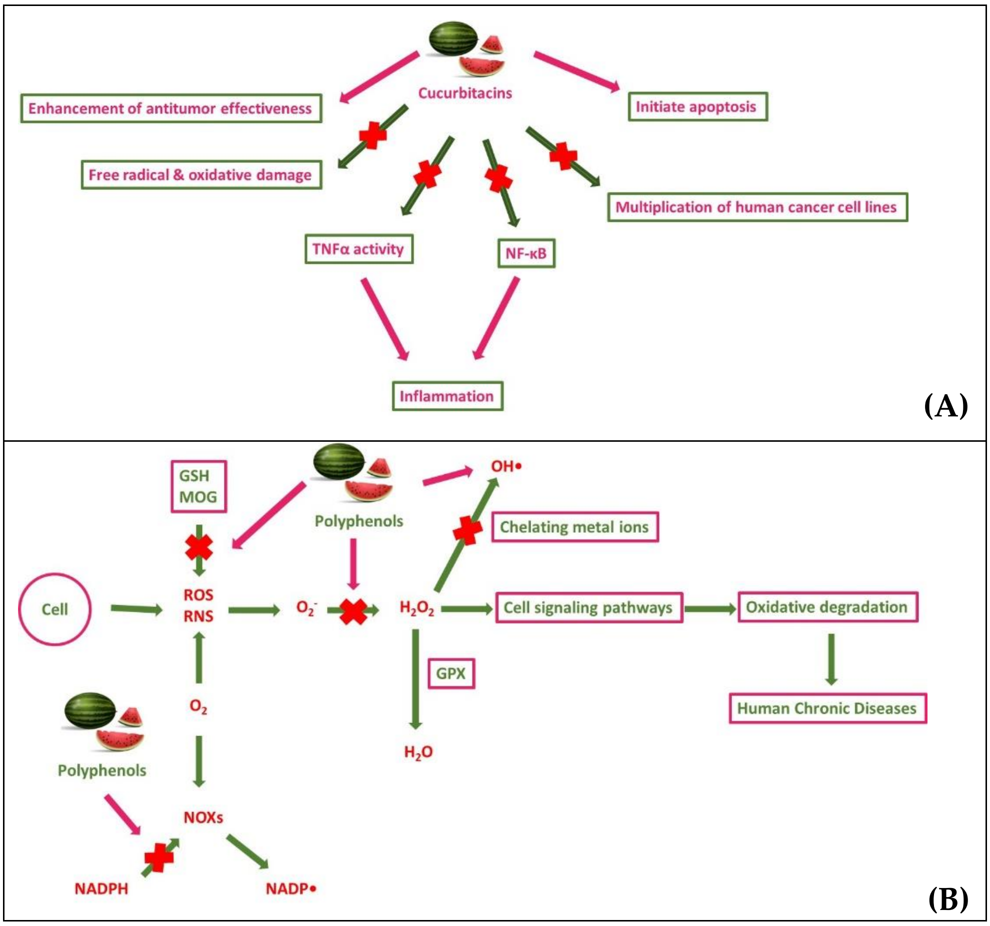

Figure 4. The biochemical mechanisms of (A) Cucurbitacins and (B) Polyphenols, of watermelon and its by-products. TNFα: tumor necrosis factor alpha; NF-κB: nuclear factor-kappa-B; ROS: reactive oxygen species; PNS: reactive nitrogen species; GSH: glutathione; MOG: monooxygenase; GPX: glutathione peroxidase; NOXs: NADPH oxidases. .

3. Health promoting effects associated with watermelon and its by-products bioactives

3.1. Antioxidant and anti-inflammatory properties and associated health promoting effects

Citrullus lanatus is a great sources of a variety of antioxidant bioactives, such as vitamins, phenolic compounds and carotenoids [10,70–72,146–150]. According to Choudhary et al. [15], citrulline is a non-essential amino acid with significant antioxidant effects [151], which can be metabolized in arginine with anti-inflammatory properties [152]. Watermelon, contains a high concentration of vitamin C, a more hydrophilic antioxidant that inhibits iron oxidation and scavenges free radicals [153]. Due to the plethora of antioxidants, watermelon has a higher antioxidant potential than strawberries, tomatoes, and guava, which along with their anti-inflammatory and anti-cancer protection [15,16], can improve the human health [154]. Epidemiological studies show that phytochemicals present in watermelon have substantial therapeutic benefits [8,14,69] helpful for the functions of the liver, kidney, and brain [45]. Researchers have associated the hepatoprotective effect in our body to antioxidant activity of phytochemicals found in watermelon [155].

Epidemiological studies showed that watermelon has several therapeutic properties, including anti-inflammatory properties [15,16,150,156]. Aqueous extracts of edible watermelon portions helps prevent anti-inflammatory diseases [157]. In addition, the lipid soluble lycopene, an essential antioxidant of watermelon and watermelon juice (WJ) [158–160], also possess strong anti-inflammatory properties [8,63,64,161,162]. In addition, carotenoids in watermelons provides practical therapeutic activities to prevent anti-inflammatory diseases [163]. Several processes have been developed for its extraction and purification from watermelon and WJ due to its antioxidant and anti-inflammatory potential [164]. Watermelon sourced lycopene also aids in cholesterol reduction [84,165–169]. Lycopene takes part in anticancer mechanisms too, by inhibition of invasion and metastasis, regulation of cell proliferation, induction of phase 2 enzymes, modulation of cytokine expression, redox and hypocholesterol emic effects [162]. The absorption pathway of lycopene starts from the ingestion of watermelon in the form of cis-lycopene, through the gastro-intestinal tract, enter the bloodstream through chylomicron mediated mechanism, and finally stored in adipose tissue dense organs, liver, prostate and adrenal gland [8].

WJ has also become of interest to consumers, due to its rich content in phytochemicals, including lycopene, with antioxidant anti-inflammatory and antihypertensive properties [8,170,171]. More specifically WJ contains significant amounts of the highly bioavailable form of lycopene, the cis-isomeric lycopene [172], as well as L-citrulline, an amino acid and antioxidant that can be metabolized to L-arginine, an essential amino acid, which is used in the synthesis of nitric oxide and plays an essential role in cardiovascular and immune function [172]. Thus, WJ consumption has been proven to raise the lycopene level, as well as L-citrulline and L-arginine levels in human blood [173].

Watermelon by-products also contain antioxidant and anti-inflammatory bioactives with health promoting properties. The research conducted for evaluating the effect of extracts of watermelon by-products on rats fed for 12 weeks resulted in a decrease in LDL and total cholesterol, and body fat and showed anti-inflammatory properties [174–177]. Singh Gill investigated different extracts (ethyl acetate, chloroform, and methanol) of watermelon seeds for their antioxidant activity through DPPH method and they found that the maximum antioxidant activity was obtained in methanolic extracts of the seeds [178]. Gill et al. studied the antioxidant potential of watermelon seed extract in rodent models [179]. DPPH and H_2O_2 perform to evaluate the free radical scavenging activities. It was determined that the methanolic extract has good antioxidant potential to use in the future for nutraceutical purposes.

Adebayo et al. also found methanolic extracts of watermelon seed contain phytochemical compounds with strong antioxidant activities to protect the damaging effects on cells [180]. It is widely used to treat various diseases and has several therapeutic activities [181]. Rahman et al. studied the in-vitro activities of watermelon seed extracts through n-hexane, chloroform, and ethanol as solvents [182]. All extracts showed high antioxidant potential as measured by DPPH, FRAP, H_2O_2, and NO scavenging activities. Still, it depends on the extraction method, as hexane extract showed more antioxidant potential than the chloroform and ethanol extracts [182]. It is also reported that seed extract is a good reservoir of antioxidants that mitigate the oxidative stress in stressed rats [183]. Watermelon seed ethanol extracts showed potent anti-inflammatory properties too [184]. Antioxidant activities were recorded in seed oil too, with several applications in making cosmetic products from watermelon by-products [185].

In addition, watermelon seed flour supplementation and its ethanol extracts are effective against inflammation and chronic pain due to their anti-inflammatory power [184,186]. It has been stated that the watermelon rind flour incorporation into the diets of rats improved antioxidant activity, lipid profile, and had significant anti-inflammatory capabilities [186]. Besides, it has been associated with

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lowering the level of low-density lipoprotein, cholesterol and triglyceride levels and increases antioxidant capacity in obese persons [187].

Sajjad et al. evaluated the administration of 50g of watermelon seed to male and female rats for 40 days resulting in a decrease in blood pressure due to cations and phytochemicals showing antioxidant activities [40]. Moreover, the process of seed protein hydrolysis can aid in producing antioxidant peptides, too [188]. Seed protein hydrolysates include the globulin fractions with antioxidant activities observed for ethanol-induced stressed rat [189] and purified peptides helped to protect HepG2 cells from hydrogen peroxide-induced damage by increasing antioxidative enzymes activities [188]. Wen et al. studied that the seed protein hydrolysate had great antioxidant potential in acidic pH or a temperature >100°C or neutral environment with gastrointestinal digestion treatment [190]. Seed protein hydrolysate or isolates can be used as a functional ingredient or an alternative to synthetic antioxidants to prevent the adverse effects of drugs [191].

Watermelon and its peel extracts also have antioxidant and anti-inflammatory properties due to the presence of unsaturated fatty acids, carotenoids, and phenolic components, similar to those found in extracts of watermelon seeds [192]. For example, watermelon rind methanol extracts showed potential anti-inflammatory properties [193]. In addition, watermelon rind extracts are also rich in quercetin, a strong antioxidant compound that helps to reduce nitrogen and reactive oxygen species [194]. Moreover, watermelon rind extract with the combination of banana peel extract showed the highest antioxidant activities as compared to banana peel extract [195]. Furthermore, polysaccharides in rind extract possess excellent antioxidant activity against reactive oxygen species and DNA damage induced by hydroxyl radical at 5mg/ml concentration [14].

3.2. Cardio-protective health promoting effects

Watermelon is a rich source of phytochemicals and minerals, low in sodium, cholesterol, and fat therefore, it is suitable for heart health and blood pressure [17,196]. It is a rich source of lycopene, beta-carotene, and unsaturated fatty acids that as aforementioned possess strong antioxidant and anti-inflammatory properties, offering cardio-protective benefits by reducing oxidative stress and inflammation, and thus lowering the risk of CVD and other associated manifestations [8,52,62,68,154,161,197]. Watermelon supplementation in obese individuals suffering from hypertension and high blood pressure, has been proven to lower both hypertension and blood pressure [198]. WJ is a great source of compounds with cardioprotective properties, including arginine, citrulline, and lycopene [199]. The non-essential amino acid, citrulline, present in all parts of the watermelon, has cardio-protective activities as it relaxes as well as dilates the blood vessels [174,193,200]. Moreover, Tarazona-Diaz et al. reported that WJ contributed to reducing both muscle soreness and the recovery heart rate in athletes after 24 hours, proving the potential of WJ as a functional drink for athletes [201].

In addition, the rich content of watermelon seed oil in antioxidants seem to prevent chronic disorders, including CVD [202]. Moreover, an in-vivo study on watermelon seed extracts showed great potential for cardio-protective effect, by reducing creatine kinase and lactate dehydrogenase, which are considered as indicators of heart disease [161,203]. Watermelon derived saponins also have been found to possess pharmaceutical potential to prevent CVD and other chronic diseases [162].

3.3. Anti-cancer health promoting effects

A number of studies suggest that the rich content of watermelon in lycopene slows down tumor growth, while lycopene supplementation can help in the prevention of cancer of many organs [204]. Lycopene has a repressive role in gene mutation [205]. It interferes with mechanisms involved in cancer cell growth cycle and carcinogen metabolism [206]. It is noteworthy to mention that lycopene administration has also potential in reducing the negative effect of cancer radiotherapy [204].

Furthermore, watermelon seeds also contain β-carotene, which has strong anticancer properties like lycopene [207]. The plethora of' phytochemicals found in watermelon seeds, including tannins, are effective against cancer, whereas alkaloids show anti-diarrheal effects [34]. More specifically, watermelon seeds contain around 8 phenolic compounds (caffeic acid, syringic acid, ferulic acid, sinapic acid, p-coumaric acid, vanillic acid, 4-hydroxy benzoic acid, and gallic acid) which also possess anti-cancer, anti-viral, anti-inflammatory, and antioxidant activities [208]. The extracts of watermelon seeds have also been linked with anticancer effects [209].

3.4. Anti-diabetic health promoting effects

Watermelon is a rich in bioactive compounds with several biological activities such as antidiabetic [210]. The anti-diabetic properties of watermelon and WJ were presented in an *in-vivo* study in alloxan-induced diabetic male Wistar albino rats [211]. Vincellette et al., reported that supplementation with WJ, contributed to decrease in Macrovascular and microvascular dysfunction caused by hyperglycemia in healthy adult individuals [212]. Moreover, another *in vivo* study also presented the anti-diabetic effect of watermelon, as its consumption improved the control of pancreatic cells death [213].

Zia et al. reported that watermelon by-products have excellent therapeutic properties including anti-diabetic activity, too [214]. It was observed that watermelon rind exhibited anti-diabetic activity by increasing the level of serum insulin and decreasing in level of blood glucose as recommended hypoglycaemic drug in Wistar rats [215,216]. Some studies have also reported a decrease in blood glucose by the consumption of the extracts of watermelon seed and peel [217–219], while methanol extract of watermelon seeds decrease blood glucose level in rats [66]. In addition, administration of a watermelon peel methanol extract in diabetic rats improved blood glucose concentration, serum lipid profile, enzymes in the liver, creatinine, urea, and other plod biomarkers, suggesting a strong anti-diabetic activity [193]. Jibril et al., Adebayo et al. and Arise et al. have also evaluated the anti-diabetic effects of watermelon pulp, rind, and seed extracts, which showed noteworthy inhibition of alpha-amylase and alpha-glucosidase activities [72,180,220].

Watermelon pulp containing lycopene that possess high antioxidant activity, has also exhibited a notable anti-diabetic effect [57]. Watermelon curcubitacins that possess many therapeutic activities, have also shown anti-diabetic properties [221–223].

3.5. Other health promoting effects

3.5.1. Hepatoprotective properties

The rich content of watermelon and its by-products in phytochemicals and lycopene seems to also prevent liver-related disorders [63,83,181]. Oyenihi et al. reported that WJ had an antioxidant and hepatoprotective effect in ethanol-induced oxidation in the liver of rats [224]. Watermelon seed and seed oil also showed hepatoprotective activity in CCl_4 induced hepatotoxicity in rats, as it improved the serum enzymatic activities of hepatic enzymes and the histopathology of liver tissues [64,155].

3.5.1. Antimicrobial properties

Several studies have shown that watermelon extracts have antimicrobial activities against bacteria as well as fungi [67,225–227]. Ethanol extract of watermelon seeds showed great potential of antimicrobial activities against four bacterial strains (2 Gram-negative and 2 Gram-positive) were studied for their limited direct anti-fungal effects against four fungal species, primarily influencing bacterial-fungal interactions and susceptibility patterns in specific contexts [228]. Moreover, crude extracts of watermelon seeds, using cold and hot water, ethanol, and methanol showed antimicrobial activities against bacteria and fungi [94,229,230]. The observed antimicrobial activities of chloroform extracts were attributed to watermelon secondary metabolites such as flavonoids, tannins, and saponins [67], while lycopene also seem to possess antimicrobial activity [67].

3.5.1. Analgesic properties

Watermelon rich content in lycopene has an analgesic effect [63]. Moreover, Wahid, et al. observed analgesic activities of ethanol extracts from watermelon seeds in an *in vivo* study in rats

[184], while aqueous extracts of watermelon peel showed *in vivo* analgesic properties too [231]. Thus, extracts of watermelon by-products have the potential to be used as a functional ingredient for the development of analgesics [179,184]. The highest concentration of alkaloids found in seeds, in comparison to all the other parts of watermelon, have also showed several therapeutic effects as secondary metabolites, including analgesic properties, as well as anti-bacterial, and antispasmodic effects [232].

Table 3. Health promoting properties of watermelon and its by-products.

Heath Promoting Properties	**Watermelon Part**	**Compound/ component**	**Study type**	**Specific effects**	**References**
Antioxidant	Seed	Aqueous extract	*In-vivo*		[179]
	Seed	Extract	*In-vitro*		[182]
	Seed	Extract (chloroform, ethyl acetate, and methanol)	*In-vitro*		[178]
	Seed	Extract	*In-vitro*		[182]
	Rind& Seed	Extract	*In-vivo*		[183][191][194][188]
	Peel	Extract	*In-vitro*		[192]
	Pulp & Seed	Lycopene	*In-vitro*		[233]
	Seed	Extract	*In-vitro*		[234]
	Whole watermelon powder		*In-vivo*	Ingestion	[186]
	Fruit	Bioactive compounds	*In-vitro*		[10]
Cardioprotective	Pulp	Extract	*In-vivo*	Anti-atherosclerotic activity	[174]
	Seeds	Phytochemicals	*In-vivo*	Anti-hypertensive	[40]
	Rind	Extract of polysaccharides	*In-vivo*	Anti-hypertensive	[14]
	Seeds	Extract	*In-vivo*	Decrease serum Cholesterol	[235]
	Pulp	Carotene	*In-vitro*	Heart health	[236]
	Pulp	Lycopene	*In-vitro*	heart health	[74]
	Rind	Phytochemicals	*In-vitro* *In-vivo*	Hypocholesterolemic effect	[215]

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Seed	Extract,	*In-vitro* *In-vivo*	Hypolipidemic effect anti-inflammatory and antioxidant properties	[182] [235]
Seeds	Kernel	*In-vivo*	Hypolipidemic efficiency	[83]
Whole watermelon powder		*In-vivo*	Improvement of lipid profiles	[186]
Rind and peel	Powder	*In-vivo*	LDL Control anti-inflammatory reduces atherosclerosis	[174]
Pulp	Juice; L-Citrulline	*In-vivo* *In-vitro*	Recovery heart rate and muscle soreness	[201]
Seeds	Extract	*In-vivo*	Reduction in creatine kinase, triglycerides, LDL, and sodium	[161]
Flesh, Seeds, Rind	L-citrulline and Arginine	*In-vivo*	Regulation of blood pressure and vascular health	[237]
Seeds	Extract	*In-vivo*	Cardioprotective potential	[203]
Seeds	Extract	*In-vivo*	Cardiovascular benefits, Anti-hypertension, reduce blood pressure	[174,200]
Seed	Sitosterol, campesterol, and stigmasterol in seed oil.	*In-vitro*	Cardiovascular health	[238,239]
Rind	Citrulline	*In-vitro*	Cardiovascular health	[75]
Rind	l-citrulline and l-arginine	*In-vivo*	Cardiovascular health	[240]

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	Pulp		*In-vivo*	Cardiovascular Protective	[187,241]
	Pulp	Juice	*In-vivo*	Control serum lipid profile	[242]
Antidiabetic	Flesh, seed, rind	Extract and Juice	*In-vivo*		[72,93,180,220,243,244]
	Rind	Citrulline	*In-vitro*		[215,216,245,246]
	Seeds	Extract	*In-vivo*		[218]
	Flesh and Rind	Extract and powder	*In-vivo*		[213]
	Pulp	Juice	*In-vivo*	Inhibitory activity against - glucosidase and - amylase that is dosage dependent.	[242]
	Pulp	Juice, extract (containing alkaloids, flavonoids, and saponins)	*In-vivo*	Stimulate insulin release during pancreatic-cell regeneration and hinder intestinal glucose absorption.	[247]
	Rind	Extract	*In-vivo*		[211,248]
	Rind and Peel	Pomace	*In-vivo*		[171]
Gastrointestinal tract diseases	Seed	Seed extract	*In-vivo*	Anti-ulcer activity	[65]
	Pulp	Juice	*In-vino*	Anti-secretary activity	[249]
	Pulp	Juice	*In-vivo*	Anti-secretory effects	[249]
	Rind	Hydro-methanolic extracts	*In-vivo*	Anti-ulcer	[193]
	Seeds	Extract	*In-vivo*	Antiulcer and gastroprotective	[66]
	Seed	Seed extract	*In-vivo*	Anti-ulcer action in pyloric ligated and water immersion stress generated ulcer models.	[65,66]

	Seeds	Methanolic extract	*In-vivo*	Anti-ulcerogenic	[65]
	Pulp	Pulp extract	*In-vivo*	Gastroprotective Laxative Activity in Indomethacin-Induced Ulcer Model	[250]
	Pulp	Pulp extract	*In-vivo*	Loperamide-induced constipation decreases in a dose-dependent manner by laxative activity.	[250]
	Pulp	Extract	*In-vivo*	Laxative Activity	[250]
	Pulp		*In-vivo*	Ameliorate the gastrointestinal discomforts	[171]
Hepatoprotective	Pulp	Juice	*In-vivo*		[251]
	Seeds	Extract	*In-vivo*		[252]
	Seed	Seed oil	*In-Vivo*	Oral, estimate serum hepatic enzyme level	[64]
	Seeds	Oil	*In-vivo*		[64]
	Seeds	Extract	*In-vivo*		[155] [253]
Anti-inflammatory	Seed	Seed Oil	*In-vivo & In-Vitro*		[64]
	Seed	Aqueous extract	*In-vivo*		[179]
	Seeds	Extract	*In-vivo*		[184]
	Seed	Oil, extract	*In-vitro*		[254–256]
	Rind	Methanolic extract	*In-vivo*		[184,193]
	Pulp	Juice	*In-vivo*	α-glucosidase and α-amylase inhibitory action in a dose-dependent manner	[242]
	Seed	Seed oil	*In-vivo & In-vitro*	Carrageenan-induced paw	[64,257]

				edema in a rat model	
	Seed	Seed Oil,	*In-vitro and In-vivo*		[64]
	Whole watermelon powder		*In-vivo*	Ingestion	[186]
	Pulp	l-citrulline and l-arginine	*In-vivo*		[258]
Antimicrobial	Seed	Seed extract	*In-vitro*	cup-plate and disc diffusion method	[229,230]
	Rind	Extract	*In-vitro*		[259]
	Seed	Extract	*In-vitro*		[99,228,260]
	Seed	Oil, extract	*In-vitro*		[254–256]
	Seed	Seed extract	*In-vitro*		[94,261]
	Seeds	Extract	*In-vitro*		[229]
	Pulp	Extract	*In-vitro*		[67]
	Seeds	Extract	*In-vitro*		[229]
	Seed	Seed extract	*In-vitro*		[225]
	Pulp	Juice	*In-vivo*		[8,224]
Role in oxidative stress	Pulp	l-citrulline & l-arginine	*In-vivo*		[258]
	Peel	Extract	*In-vivo*		[231]
Analgesic and antipyretic	Seed	Aqueous extract	*In-vivo*		[179]
	Rind	Methanolic extract	*In-vivo*		[184,193]
	Pulp	Lycopene	*In-vitro*		[74]
Anticancer	Rind	Extract	*In-vivo*		[262]
	Rind	Extracted polysaccharides	*In-vivo*		[262]
	Pulp	Extract	*In-vivo In-vitro*	U Anti- urolithiatic and diuretic activities	[71]
Urinary tract disorders	Fruit	Aqueous extract	*In-vivo*	U Kidney health	[263]
	Flesh and Rind	Extract	*In-vivo*	Uterine Contractility	[264]

	Seeds	Extract	*In-vivo*	Anti-Prostatic Hyperplasia activity	[265]
Miscellaneous Effects	Seeds	Methanolic extract	*In-vivo*	Nephroprotective effects	[253,266]
	Seeds	Extract	*In-vivo*	Neuroprotective	[267,268]
	Seeds	Extract		Male Sexual enhancement	[252]
	Seeds	Extract	*In-vivo*	Weight loss and hematological benefits	[269]

4. Potential applications of watermelon by-products that improve bio-functionality and health promoting effects of food and cosmetics products

The most well-established food and cosmetics applications of ingredients from watermelon and its by-products in other food products and cosmetics are the antimicrobial and antioxidant preservative properties they possess. For example, watermelon derived lycopene is used as a "natural preservative" to retard the oxidation of products during processing and storage [270]. Due to its low cost, cooking convenience, and palatable taste, watermelon and its by-products can be applied in some food products such as cookies, dairy, and meat products, and can be considered environment-friendly for food packaging systems. Moreover, the chemical composition of watermelon by-products (rind and seeds) exhibits a potential source of nutrients and bioactives to be utilized as functional ingredients for developing novel valuable products in several applications with a relevant impact on the food and cosmetic sectors.

4.1. Applications in bakery and other staple-based products

Addition of watermelon by-products-based flour and ingredients in wheat flour enhanced the functional properties of bread. For example, Badr suggested that incorporation of watermelon rind flour at 6-12% showed the potential increase in antioxidants and shelf life of pan bread [32]. Moreover, sensory properties were also improved. Shivapour et al. developed toast bread with the incorporation of watermelon rind flour at 9.06% using RSM methodology [271]. It was concluded that the watermelon rind showed potential anti-stalling properties. Imoisi et al. reported the enhancement of nutritional composition, and functional and chemical properties of bread developed with the addition of different ratios of watermelon rind flour [272]. To fabricate bread, Anang et al. fortified the wheat flour with WMS flour at 15 and 25% [273]. Particularly, the total microbial count findings were below the recommended limits and the sensory features did not display any modification between all fortification concentrations.

Supplementation of watermelon rind in cakes improves health promoting effect and enhances shelf life [57]. Adegunwa et al. and Ashoka et al. developed sponge cake by substituting watermelon rind flour which results increase in protein content [274,275]. Ho et al. developed cupcakes from oven-dried and freeze-dried watermelon rind flour [276]. The first method showed significantly higher fat, ash, and fiber while the second method showed outstanding physical properties. Hassan et al. developed cake with different ratios of watermelon rind flour i.e., 0, 10, 20, 30, and 40% which significant ($p<0.05$) increased the carbohydrate content, fiber, fat, K, Mg, and volume of cake [277]. 40% incorporated cake was accepted by sensory panelists. Hoque & Iqbal reported that the incorporation of 10% watermelon rind flour for the development of cake was found acceptable overall [31].

The increasing ratio of watermelon rind powder incorporation in bakery products like cookies increased the total phenolic content, dietary fiber, and antioxidant activity while decreasing glycemic

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index (GI). Naknaen et al. and Olaitan et al. developed cookies with the incorporation of watermelon rind flour at different ratios which improved the antioxidants and functional properties [278,279]. A substitution of 20% rind powder showed the highest sensory scores [278]. Omobolanle et al. assessed the ability of WMS flour, as a partial substitute for wheat in cookies production [280]. Results showed an enhancement of the minerals (Ca, Na, Zn, Cu, and Mg), fiber, ash, and protein contents. In the same way, a reduction of anti-nutrient levels has been also observed. Ogo et al. found that wheat flour substituted with watermelon rind and pomace of orange at a level of 10% showed good sensory quality of biscuits and improved nutritional quality [281]. Peter-Ikechukwu et al. produced biscuits made from wheat flour and toasted WMS meal at 10, 20, 30, 40 and 50% (w/w), respectively [282]. Till 50% of WMS meal, the protein, ash, and fiber content were increased; however, the carbohydrates and fat levels were reduced. Physical properties viz. bulk density, water, and oil absorption capacity were increased and wettability was decreased. Based on sensory scores, 30% of the WMS meal substation level was acceptable. Franca et al. employed WMS flour as a margarine substitute in a cookie [283]. With increasing the level of WMS flour (20 and 30 g/100g of margarine), a rise in the protein content and a decrease in carbohydrates and fat was detected. In addition, 20 g of WMS with 10% margarine was the most acceptable based on sensory analysis.

Chakrabarty et al. found that noodles prepared with the addition of pale green watermelon rind flour at a level of 10% were acceptable as compared to control [42]. Ho and Che Dahri developed noodles with the substitution of watermelon rind flour and found a significant increase in fat, fiber, carbohydrates, and phenolic contents [284].

4.2. Applications in meat-based products

Badr et al. prepared beef burgers with the addition of watermelon rind powder at different ratios which increased fiber, carbohydrates, and polyphenols [37]. Kumar et al. prepared pork patties with the addition of watermelon rind extract (ethanolic) [285]. It increased oxidative stability, and sensory and microbiological properties of pork patties due to having antimicrobial and antioxidant potential hence it can be utilized as a natural preservative.

4.3. Applications in dairy products and dairy alternatives

Shahein et al. investigated several levels of WMS milk (0.0, 25, 50, and 75%) to prepare new yogurt [286]. Sensorial features viz. flavor, texture, appearance, and overall acceptability confirmed that the blended treatment (50% cow's milk and 50% WMS milk) was the most acceptable. In albino rats, WMS milk was revealed to confer effective protection against hyperuricemia. During two months of storage, Qayyum et al. proved that 10% of WMS flour had a strong impact on physicochemical (pH, melting resistance, and acidity) and sensory (surface appearance, ice crystals, body and texture, and overall acceptability) properties of ice cream [287]. Ice creams established from soy milk, WMS milk, and guava pulp have been prepared by Bisla et al. [288]. The results showed that ice creams made from a mixture of 50% soy milk and 50% WMS milk as well as guava pulp were the most acceptable on the 9-point hedonic scale. Lipid, protein, iron, and vitamin C levels were improved compared to the control ice cream (100% cow's milk).

4.4. Applications in other food-based products

Nasir et al. prepared watermelon rind-based candy with the addition of pectin and citric acid in 1.5%, respectively [289]. It showed the great acceptability of candies as compared to control. Thapa et al. developed candy from watermelon rind with the addition of sugar and honey syrup [290]. Sensory characteristics showed that the development of candy with the addition of honey is more acceptable. Dhakal & Pradhananga reported that watermelon rind is wasted which can be utilized for the development of functional candy [291]. However, watermelon rind treated with sucrose and honey in a ratio of 75:25 was recorded with acceptable sensory properties. Hani et al. prepared candy from watermelon rind through an osmotic dehydration process [292]. Moreover, stickiness and hardness were increased with the increase in dehydration time.

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Islam prepared watermelon rind jam with different ratios of sugar and strawberry flavor [293]. Watermelon rind and sugar in a ratio of 50:50 with flavor was considered a promising level. Watermelon rind, due to its favorable pectin content, the rind can be turned into jam or candy-like in Turkish cuisine [294]. Zia et al. prepared watermelon rind-based fruit butter by incorporating pulp, powder, and extract as functional ingredients [214]. It was found that the addition of watermelon rind at a level of 6% significantly increased microbial safety and shelf life.

Prabha et al. developed watermelon rind-based dietary chips mixed with composite pulse flour [295]. As a result, developed dietary chips showed increased dietary fiber with low fat.

Adding 6% watermelon rind powder to reduced-fat mayonnaise enhanced its antioxidant capacity while practically matching its viscosity to the original (full-fat) mayonnaise [296].

Saavedra et al. prepared a therapeutic sports drink from the by-product (rind) of watermelon [297]. It was found that the rind part is rich in electrolytes for body requirements hence it can be consumed as a sports drink. Kumar et al. prepared a functional drink by blending watermelon flesh and rind to assess the quality parameters influenced by different treatments at storage conditions [298]. Also, Gunawan and Basoeki enriched the jackfruit seed drink with watermelon rind as a functional ingredient [299]. Moreover, it was found that the incorporation of watermelon rind significantly increased the antioxidant potential, nutrition value, and health benefits of the drink.

4.5. Alternetive applications related to food industry

By casting technique, Todhanakasem et al. developed a biodegradable active film composed of polyvinyl alcohol, corn starch, and WMR [300]. At 10% of WMR extract, the mechanical and physical properties were improved compared to control films (without active fraction). In addition, the established film can inhibit foodborne B. cereus ATCC 11778, E. coli ATCC 8739, and S. enterica subsp. enterica serovar Typhimurium ATCC 13311, and displayed an antioxidant potential. These authors examined the potential of packed WVMRE in fresh-cut purple cabbage. Findings revealed that WVMRE extends its shelf live without sensory change. In another study, from WMS, Łopusiewicz et al. isolated melanin and employed it as a modifier for whey protein concentrate-producing films at 0.1 and 0.5% [301]. These authors concluded that melanin from WMS can be used as a functional modifier to develop bioactive biopolymer films with good mechanical, antioxidant, and antibacterial properties potential and can be utilized in food packaging applications Later, Łopusiewicz et al. developed films of alginate coated with melanin from watermelon at 0.10%, 0.25% and 0.50% w/w blended with Ag and ZnO nanoparticle [302]. Results demonstrated that melanin had an apparent impact on mechanical and barrier (thickness, tensile strength, and water vapor transmission rate), antioxidant (ABTS+, DPPH, and superoxide), and hydrodynamic properties. These authors suggested that the prepared film can be useful for food packaging. Wang et al. experienced the potency of a film matrix containing chitosan, guar gum, and WMR to preserve fresh-cut bananas [303]. Remarkably, developed films at 4 wt% of WRE, successfully inhibited the changes in appearance, firmness, weight, color, and total soluble solids content of the studied food product during storage.

WMR is a good source of pectin and therefore, could be possibly utilized to extract pectin. Han and Song developed ecofriendly WMR pectin (WRP) films including 0.5, 1.0, and 1.5 % kiwifruit peel extract (KPE) [304]. The obtained WRP films showed excellent mechanical properties and with the increase of KPE level, the opacity, EAB, and WVP of the films augmented. Additionally, after 9 days of storage, the lipid oxidation parameters (peroxide value) and TBARS in the chicken thigh wrapped with the WRP/1.5 % KPE film were lower than those in the unwrapped ones. A pH indicator film was developed using pectin from watermelon peel and beetroot extract to store chilled beef. The pectin from watermelon peel was found to possess good film-forming capacity [305]. Guo et al. investigated a pH-sensitive indicator film incorporating beetroot extract at 1, 2, and 3%, w/w, encapsulated in pectin from watermelon peel (WMP) and controlled the quality parameters of chilled beef during storage [90]. The WMP/BTE2 film exhibited a colorimetric response at a pH ranging between 3 and 10. The WMP/BTE2 film color changed from pink to brown on days 0 and 8, respectively. The results reported that WMP/BTE film is favorable to sustainable pH change sensing

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and could be used to detect changes in the pH of packaged meat. Xie et al. fabricated and characterized a potato starch (Pst)/watermelon peel pectin (Wpp) composite film encapsulated with the flavonoid isolated from Lycium barbarum leaf (MLF) and nano-TiO_2 (Pst/Wpp/MLF/TiO_2) [306]. The established film was used to preserve Tan mutton. MLF and TiO2 successfully improved the mechanical properties, thermal stability, and antioxidant and antimicrobial potential. Packaged samples inhibited the development of microorganisms and the chemical oxidation of mutton samples. Colivet et al. extracted watermelon seed oil (WSO) by pressurized ethanol and via emulsions, these authors produced film by using crosslinked cassava starch/WSO [WSOE] [307]. Remarkably, the structure of the films was affected by increasing WSOE levels (between 0.1 and 0.5 g/100 g of filmogenic solution). The WSOE incorporation increased the elongation capacity of the films and reduced the strain at break. Guo et al. explored the impact of active packaging films prepared by pectin and polyphenols (WMP-WME) of watermelon peel on chilled mutton quality during super-chilled storage [308]. The evaluation of the meat quality showed that the instrumental color (L* and b*), protein oxidation parameters (TBARs and TVB-N), and microorganisms' deterioration of samples were expressively lower. To preserve mutton freshness, Guo et al. produced a novel colorimetric indicator film derived from watermelon peel pectin (WVP) and anthocyanins from purple cabbage [309]. The film had exceptional color stability and pH response properties. The WMP/PCE1.5% film color varied from mauve to baby blue according to the quality of the mutton (fresh to spoil).

4.6. Applications in cosmetics

Dried watermelon seeds are a rich source of minerals and protein and they can be implemented in cosmetic products for stimulation and revitalization. Fatty acids are widely used in the cosmetics industry [310]. Watermelon seeds and peels are a great source of such fatty acids [185]. According to Omoniyi watermelon seed oil (WSO), can be used as a source of oil/fat in cosmetics [311]. WSO's antioxidative properties can help in the reduction and prevention of skin cellular damage, by scavenging free radicals resulting from sun damage or pollutants [185]. Thus, the application of WSO in cosmetics, can result in products which combat skin aging. The humectant properties and the great skin absorbance of WSO, makes it suitable for skin care products and especially moisturizers [256]. Watermelon white rind can be utilized in cosmetic products as a cheap and safe whitening and anti-browning agent [312]. Simamora et al., used watermelon rind ethanol extract to prepare a skin moisturizing gel in concentrations of 0, 2.5%, 5 % and 10% [313]. They then tested it on the skin of male mice in a span of 4 weeks, which resulted in increasing the elasticity, sebum and hydration of the skin of the mice. Patra et al., produced silver nanoparticles from aqueous extract of watermelon rind [314]. The silver nanoparticles when mixed with kanamycin and rifampicin presented antibacterial activity, while when mixed with amphotericin b they had significant antioxidative properties. Thus, these silver nanoparticles have potential applications in cosmetics. According to Cefali et al. lycopene extract from watermelon pulp can be implemented in skin care products as an antioxidant agent for limiting skin aging [315]. Kamble and Kamble prepared a herbal lipstick using watermelon sourced lycopene as a coloring agent, replacing synthetic ones [316]. The product presented acceptable results, shining the lips and improving their smoothness and spreading.

5. Limitations – Future Perspectives

The limitations of this study may include the need for further research to fully understand the bioavailability and interactions of nutrients in watermelon by-products when incorporated into different food products. Additionally, exploring the long-term effects and optimal consumption levels would strengthen the findings. Future prospects could involve focusing on practical applications in rural areas, optimizing extraction methods for maximum nutrient retention, and conducting clinical trials to validate the health benefits in diverse populations. Integrating sustainability aspects, such as addressing environmental impacts and economic viability, could further enhance the feasibility of utilizing watermelon by-products on a larger scale.

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6. Conclusions

Watermelon and its by-products are rich sources of bioactive compounds and phytochemicals, particularly lycopene in the pulp portion. It contributes potential health benefits to prevent several chronic diseases. In all aspects, watermelon, and its by-products have nutraceutical properties reported by several researchers and hence considered as a functional food. Moreover, by-products are potential sources of macro-nutrients and micro-nutrients with several therapeutic properties such as antioxidants, cardiovascular diseases, anti-diabetic, anti-cancer, gastrointestinal tract disease, hepatoprotective, anti-inflammatory, anti-microbial, reduced oxidative stress, analgesic, anti-pyretic and urinary tract disease. Properly utilizing watermelon and its by-products, especially in rural areas, can be helpful to prevent rising issues, including malnutrition, environmental pollution, and landfilling of agro-waste. Moreover, it recommends developing functional and nutraceutical food and pharmaceutical products by incorporating their by-products. Further, research studies should be conducted to evaluate nutrients' bioavailability and their interaction with food products when combined; therefore, nutrient-rich by-product utilization through staple foods would be an excellent strategy to improve the nutritional requirements of all age groups.

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References

1. WHO, A. World Health Statistics 2016: Monitoring Health for the SDGs Sustainable Development Goals. *World Health Organ.* **2016**.
2. Tsoupras, A.B.; Iatrou, C.; Frangia, C.; Demopoulos, C.A. The Implication of Platelet Activating Factor in Cancer Growth and Metastasis: Potent Beneficial Role of PAF-Inhibitors and Antioxidants. *Infect. Disord. - Drug TargetsDisorders* **2009**, *9*, 390–399, doi:10.2174/187152609788922555.
3. Tsoupras, A.; Lordan, R.; Zabetakis, I. Inflammation, Not Cholesterol, Is a Cause of Chronic Disease. *Nutrients* **2018**, *10*, doi:10.3390/nu10050604.
4. Zabetakis, I.; Lordan, R.; Tsoupras, A. Chapter 9 - Nutrition Versus Statins in Primary Prevention: Where Do We Stand Now? In *The Impact of Nutrition and Statins on Cardiovascular Diseases*; Zabetakis, I., Lordan, R., Tsoupras, A., Eds.; Academic Press, 2019; pp. 289–317 ISBN 978-0-12-813792-5.
5. Tsoupras, A. The Anti-Inflammatory and Antithrombotic Properties of Bioactives from Orange, Sanguine and Clementine Juices and from Their Remaining By-Products. *Beverages* **2022**, *8*, 39.
6. Zabetakis, I.; Lordan, R.; Tsoupras, A.; Ramji, D. *Functional Foods and Their Implications for Health Promotion*; Academic Press, 2022; ISBN 0-12-823812-7.
7. Karasawa, M.M.G.; Mohan, C. Fruits as Prospective Reserves of Bioactive Compounds: A Review. *Nat. Prod. Bioprospecting* **2018**, *8*, 335–346.
8. Naz, A.; Butt, M.S.; Sultan, M.T.; Qayyum, M.M.N.; Niaz, R.S. Watermelon Lycopene and Allied Health Claims. *EXCLI J.* **2014**, *13*, 650.
9. Kyriacou, M.C.; Leskovar, D.I.; Colla, G.; Rouphael, Y. Watermelon and Melon Fruit Quality: The Genotypic and Agro-Environmental Factors Implicated. *Sci. Hortic.* **2018**, *234*, 393–408.

10. Tlili, I.; Hdider, C.; Lenucci, M.S.; Ilahy, R.; Jebari, H.; Dalessandro, G. Bioactive Compounds and Antioxidant Activities during Fruit Ripening of Watermelon Cultivars. *J. Food Compos. Anal.* **2011**, *24*, 923–928.
11. Abourashed, E.A. Bioavailability of Plant-Derived Antioxidants. *Antioxidants* **2013**, *2*, 309–325.
12. Sa'id, M. A Study in the Variability of Some Nutrient Contents of Watermelon (Citrullus Lanatus) before and after Ripening Consumed within Kano Metropolis, Nigeria. *Int. J. Sci. Res. IJSR* **2014**, *3*, 1365–1368.
13. Jumde, A.; Shukla, R.; Gousoddin DEVELOPMENT AND CHEMICAL ANALYSIS OF WATERMELON BLENDS WITH BEETROOT JUICE DURING STORAGE. *Int. J. Sci. Eng. Technol.* **2015**, *3*, 960–964, doi:10.2348/ijset07150960.
14. Romdhane, M.B.; Haddar, A.; Ghazala, I.; Jeddou, K.B.; Helbert, C.B.; Ellouz-Chaabouni, S. Optimization of Polysaccharides Extraction from Watermelon Rinds: Structure, Functional and Biological Activities. *Food Chem.* **2017**, *216*, 355–364.
15. Choudhary, B.; Haldhar, S.; Maheshwari, S.; Bhargava, R.; Sharma, S. Phytochemicals and Antioxidants in Watermelon (Citrullus Lanatus) Genotypes under Hot Arid Region. **2015**.
16. Ijah, U.; Auta, H.; Aransiola, S. Microbiological and Some Sensory Attributes of Water Melon Juice and Watermelon-Orange Juice Mix. **2015**.
17. Bianchi, G.; Rizzolo, A.; Grassi, M.; Provenzi, L.; Scalzo, R.L. External Maturity Indicators, Carotenoid and Sugar Compositions and Volatile Patterns in 'Cuoredolce®'and 'Rugby'Mini-Watermelon (Citrullus Lanatus (Thunb) Matsumura & Nakai) Varieties in Relation of Ripening Degree at Harvest. *Postharvest Biol. Technol.* **2018**, *136*, 1–11.
18. Chidambara Murthy, K.; Vanitha, A.; Mahadeva Swamy, M.; Ravishankar, G. Antioxidant and Antimicrobial Activity of Cissus Quadrangularis L. *J. Med. Food* **2003**, *6*, 99–105.
19. Sharififar, F.; Dehghn-Nudeh, G.; Mirtajaldini, M. Major Flavonoids with Antioxidant Activity from Teucrium Polium L. *Food Chem.* **2009**, *112*, 885–888.
20. Suhail, N.; Bilal, N.; Khan, H.; Hasan, S.; Sharma, S.; Khan, F.; Mansoor, T.; Banu, N. Effect of Vitamins C and E on Antioxidant Status of Breast-cancer Patients Undergoing Chemotherapy. *J. Clin. Pharm. Ther.* **2012**, *37*, 22–26.
21. Mehra, M.; Pasricha, V.; Gupta, R.K. Estimation of Nutritional, Phytochemical and Antioxidant Activity of Seeds of Musk Melon (Cucumis Melo) and Water Melon (Citrullus Lanatus) and Nutritional Analysis of Their Respective Oils. *J. Pharmacogn. Phytochem.* **2015**, *3*, 98–102.
22. Castro-López, C.; Ventura-Sobrevilla, J.M.; González-Hernández, M.D.; Rojas, R.; Ascacio-Valdés, J.A.; Aguilar, C.N.; Martínez-Ávila, G.C. Impact of Extraction Techniques on Antioxidant Capacities and Phytochemical Composition of Polyphenol-Rich Extracts. *Food Chem.* **2017**, *237*, 1139–1148.
23. Hasanin, M.S.; Hashem, A.H. Eco-Friendly, Economic Fungal Universal Medium from Watermelon Peel Waste. *J. Microbiol. Methods* **2020**, *168*, 105802.
24. Zamuz, S.; Munekata, P.E.; Gullón, B.; Rocchetti, G.; Montesano, D.; Lorenzo, J.M. Citrullus Lanatus as Source of Bioactive Components: An up-to-Date Review. *Trends Food Sci. Technol.* **2021**, *111*, 208–222.
25. Johnson, J.; Lennox, J.; Ujong, U.; Odey, M.; Fila, W.; Edem, P.; Dasofunjo, K. Comparative Vitamins Content of Pulp, Seed and Rind of Fresh and Dried Watermelon (Citrullus Lanatus). *Int. J. Sci. Technol.* **2013**, *2*, 99–103.
26. Oberoi, D.P.S.; Sogi, D.S. Utilization of Watermelon Pulp for Lycopene Extraction by Response Surface Methodology. *Food Chem.* **2017**, *232*, 316–321.

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27. Oyeleke, G.; Ojo, A.; Ajao, F.; Adetoro, R. Development and Analysis of Blended Pineapple-Watermelon Ready-to-Drink (RTD) Juice. *J. Environ. Sci. Toxicol. Food Technol.* **2013**, *4*, 22–24.
28. Al-Sayed, H.M.; Ahmed, A.R. Utilization of Watermelon Rinds and Sharlyn Melon Peels as a Natural Source of Dietary Fiber and Antioxidants in Cake. *Ann. Agric. Sci.* **2013**, *58*, 83–95.
29. Kiin-Kabari, D.; Akusu, O. Effect of Processing on the Proximate Composition, Functional Properties and Storage Stability of Water Melon (Citrullus Lanatus) Seed Flour. *Int J Biotechnol Food Sci* **2014**, *2*, 143–148.
30. Egbuonu, A.C.C. Comparative Investigation of the Proximate and Functional Properties of Watermelon (Citrullus Lanatus) Rind and Seed. *Res. J. Environ. Toxicol.* **2015**, *9*, 160–167.
31. Hoque, M.M.; Iqbal, A. Drying of Watermelon Rind and Development of Cakes from Rind Powder. *Int. J. Nov. Res. Life Sci.* **2015**, *2*, 14–21.
32. Badr, S. Quality and Antioxidant Properties of Pan Bread Enriched with Watermelon Rind Powder. *Curr. Sci. Int.* **2015**, *4*, 117–126.
33. Omoboyowa, D.A.; Otuchristian, G.; Danladi, G.J.; Igara, C.; Ngobidi, K.; Okon, M.U.; Agbo, F.A. Evaluation of Chemical Compositions of Citrulus Lanatus Seed and Cocos Nucifera Stem Bark. *Afr. J. Food Sci. Technol.* **2015**, *6*, 75–83.
34. Tabiri, B.; Agbenorhevi, J.K.; Wireko-Manu, F.D.; Ompouma, E.I. Watermelon Seeds as Food: Nutrient Composition, Phytochemicals and Antioxidant Activity. **2016**.
35. Romelle, F.D.; Rani, A.; Manohar, R.S. Chemical Composition of Some Selected Fruit Peels. *Eur. J. Food Sci. Technol.* **2016**, *4*, 12–21.
36. Abu-Hiamed, H.A. Research Article Chemical Composition, Flavonoids and $-Sitosterol Contents of Pulp and Rind of Watermelon (Citrullus Lanatus) Fruit. **2017**.
37. Badr, S.; El-Waseif, M.; Ghaly, M. Effect of Addition Watermelon Rind Powder on Quality Criteria and Microbial Aspects of Beef Burger Patties during Frozen Storage Periods. *J. Food Dairy Sci.* **2018**, *9*, 177–187.
38. Milala, M.; Luther, A.; Burah, B. Nutritional Comparison of Processed and Unprocessed Citrillus Lanatus (Watermelon) Seeds for Possible Use in Feed Formulation. *Am. J. Food Nutr.* **2018**, *6*, 33–36.
39. United States Department of Agriculture National Nutrient Database for Standard Reference Release 28. *USDA Agric Res Serv* **2016**.
40. Sajjad, S.; Israr, B.; Ali, F.; Pasha, I. INVESTIGATING THE EFFECT OF PHYTOCHEMICALS RICH WATERMELON SEEDS AGAINST HYPERTENSION. *Pak. J. Agric. Sci.* **2020**, *57*.
41. Kausar, T.; Hassan, M.T.; ud Din, G.M. 21. Utilization of Watermelon Seed Flour as Protein Supplement in Cookies. *Pure Appl. Biol. PAB* **2020**, *9*, 202–206.
42. Chakrabarty, N.; Mourin, M.M.; Islam, N.; Haque, A.R.; Akter, S.; Siddique, A.A.; Sarker, M. Assessment of the Potential of Watermelon Rind Powder for the Value Addition of Noodles. *J. Biosyst. Eng.* **2020**, *45*, 223–231.
43. Sadiq, I.; Saminu, M.; Zainab, L.; Adeleye, A.; Sanni, L.; Dandalma, Z. Proximate Analysis and Phytochemical Screening of Watermelon (Citrullus Lanatus) Pulp, Peels and Seeds. **2021**.
44. Burton-Freeman, B.; Freeman, M.; Zhang, X.; Sandhu, A.; Edirisinghe, I. Watermelon and L-Citrulline in Cardio-Metabolic Health: Review of the Evidence 2000–2020. *Curr. Atheroscler. Rep.* **2021**, *23*, 81.
45. Adedeji, T.; Oluwalana, I. Physico-Chemical, Sensory and Microbial Analysis of Wine Produced from Watermelon (Citrullus Lanatus) and Pawpaw (Carica Papaya) Blend. *Food Sci. Qual. Manag.* **2013**, *19*, 41–50.

46. Sivudu, S.N.; Umamahesh, K.; Reddy, O. A Comparative Study on Probiotication of Mixed Watermelon and Tomato Juice by Using Probiotic Strains of Lactobacilli. *Int. J. Curr. Microbiol. Appl. Sci.* **2014**, *3*, 977–984.
47. Soteriou, G.; Kyriacou, M.; Siomos, A.; Gerasopoulos, D. Evolution of Watermelon Fruit Physicochemical and Phytochemical Composition during Ripening as Affected by Grafting. *Food Chem.* **2014**, *165*, 282–289.
48. Jebir, R.M.; Mustafa, Y.F. Natural Coumarin-Lead Compounds: A Review of Their Medicinal Potentials. *Iraqi J. Pharm.* **2022**, *18*, 139–161.
49. Okonmah, L. Effects of Different Types of Staking and Their Cost Effectiveness on the Growth, Yield and Yield Components of Cucumber (Cucumis Sativa L.). *Int. J. AgriScience* **2011**, *1*, 290–295.
50. Campbell, I. Macronutrients, Minerals, Vitamins and Energy. *Anaesth. Intensive Care Med.* **2017**, *18*, 141–146.
51. Shao, P.; Qiu, Q.; Xiao, J.; Zhu, Y.; Sun, P. Chemical Stability and in Vitro Release Properties of β-Carotene in Emulsions Stabilized by Ulva Fasciata Polysaccharide. *Int. J. Biol. Macromol.* **2017**, *102*, 225–231.
52. Gao, L.; Zhao, S.; Lu, X.; He, N.; Zhu, H.; Dou, J.; Liu, W. Comparative Transcriptome Analysis Reveals Key Genes Potentially Related to Soluble Sugar and Organic Acid Accumulation in Watermelon. *PloS One* **2018**, *13*, e0190096.
53. King, S. Lycopene and Citrulline Contents in Watermelon (Citrullus Lanatus) Fruit with Different Ploidy and Changes during Fruit Development.; 2009; pp. 543–550.
54. Perkins-Veazie, P.; Collins, J.K.; Davis, A.R.; Roberts, W. Carotenoid Content of 50 Watermelon Cultivars. *J. Agric. Food Chem.* **2006**, *54*, 2593–2597.
55. Perkins-Veazie, P.; Davis, A.; Collins, J.K. Watermelon: From Dessert to Functional Food. *Isr. J. Plant Sci.* **2012**, *60*, 395–402.
56. Liu, J.; Guo, S.; He, H.; Zhang, H.; Gong, G.; Ren, Y.; Xu, Y. Dynamic Characteristics of Sugar Accumulation and Related Enzyme Activities in Sweet and Non-Sweet Watermelon Fruits. *Acta Physiol. Plant.* **2013**, *35*, 3213–3222.
57. Casacchia, T.; Sofo, A.; CRINATOMA, C.; DRĂGĂNESCU, D.; TIȚA, B.; Statti, G.A. NUTRACEUTICAL PROPERTIES AND HEALTH-PROMOTING BIOLOGICAL ACTIVITIES OF FRUITS OF WATERMELON CULTIVARS WITH DIFFERENT ORIGINS. *Farmacia* **2020**, *68*.
58. Lemos, Á.T.; Ribeiro, A.C.; Fidalgo, L.G.; Delgadillo, I.; Saraiva, J.A. Extension of Raw Watermelon Juice Shelf-Life up to 58 Days by Hyperbaric Storage. *Food Chem.* **2017**, *231*, 61–69.
59. Kehili, M.; Kammlott, M.; Choura, S.; Zammel, A.; Zetzl, C.; Smirnova, I.; Allouche, N.; Sayadi, S. Supercritical CO2 Extraction and Antioxidant Activity of Lycopene and β-Carotene-Enriched Oleoresin from Tomato (Lycopersicum Esculentum L.) Peels by-Product of a Tunisian Industry. *Food Bioprod. Process.* **2017**, *102*, 340–349.
60. Leong, L.; Shui, G. An Investigation of Antioxidant Capacity of Fruits in Singapore Markets. *Food Chem.* **2002**, *76*, 69–75.
61. Lewinsohn, E.; Sitrit, Y.; Bar, E.; Azulay, Y.; Meir, A.; Zamir, D.; Tadmor, Y. Carotenoid Pigmentation Affects the Volatile Composition of Tomato and Watermelon Fruits, as Revealed by Comparative Genetic Analyses. *J. Agric. Food Chem.* **2005**, *53*, 3142–3148.
62. Charoensiri, R.; Kongkachuichai, R.; Suknicom, S.; Sungpuag, P. Beta-Carotene, Lycopene, and Alpha-Tocopherol Contents of Selected Thai Fruits. *Food Chem.* **2009**, *113*, 202–207.
63. Rimando, A.M.; Perkins-Veazie, P.M. Determination of Citrulline in Watermelon Rind. *J. Chromatogr. A* **2005**, *1078*, 196–200.

64. Madhavi, P.; Vakati, K.; Rahman, H. Evaluation of Anti-Inflammatory Activity of Citrullus Lanatus Seed Oil by in-Vivo and in-Vitro Models. *Int. Res. J. Pharm. Appl. Sci.* **2012**, *2*, 104–108.
65. Bhardwaj, A.; Kumar, R.; Dabasa, V.; Alam, N. Evaluation of Anti-Ulcer Activity of Citrullus Lanatus Seed Extract in Wistar Albino Rats. *Int. J. Pharm. Pharm. Sci.* **2012**, *4*, 135–139.
66. Lucky, O.O.; John, U.O.; Kate, I.E.; Peter, O.O.; Jude, O.E. Quantitative Determination, Metal Analysis and Antiulcer Evaluation of Methanol Seeds Extract of Citrullus Lanatus Thunb (Cucurbitaceae) in Rats. *Asian Pac. J. Trop. Biomed.* **2012**, *2*, S1261–S1265.
67. Hassan, L.E.A.; Sirat, H.M.; Yagi, S.M.A.; Koko, W.S.; Abdelwahab, S.I. In Vitro Antimicrobial Activities of Chloroformic, Hexane and Ethanolic Extracts of Citrullus Lanatus Var. Citroides (Wild Melon). *J. Med. Plants Res.* **2011**, *5*, 1338–1344.
68. Naz, A.; Butt, M.S.; Pasha, I.; Nawaz, H. Antioxidant Indices of Watermelon Juice and Lycopene Extract. *Pak. J. Nutr.* **2013**, *12*, 255.
69. Kim, C.; Park, M.; Kim, S.; Cho, Y. Antioxidant Capacity and Anti-inflammatory Activity of Lycopene in Watermelon. *Int. J. Food Sci. Technol.* **2014**, *49*, 2083–2091.
70. Alemika, T.; Ojerinde, O.S.; Samali, A.; Mustapha, B.K.; Gamaniel, K.S. Nutriceutical Potentials of Nigerian Grown Citrullus Lanatus (Watermelon) Seed. *J. Pharm. Bioresour.* **2017**, *14*, 253–259.
71. Siddiqui, W.A.; Shahzad, M.; Shabbir, A.; Ahmad, A. Evaluation of Anti-Urolithiatic and Diuretic Activities of Watermelon (Citrullus Lanatus) Using in Vivo and in Vitro Experiments. *Biomed. Pharmacother.* **2018**, *97*, 1212–1221.
72. Jibril, M.M.; Abdul-Hamid, A.; Ghazali, H.M.; Dek, M.S.P.; Ramli, N.S.; Jaafar, A.H.; Karrupan, J.; Mohammed, A.S. Antidiabetic Antioxidant and Phytochemical Profile of Yellow-Fleshed Seeded Watermelon (Citrullus Lanatus) Extracts. *J Food Nutr Res* **2019**, *7*, 82–95.
73. Bailey, S.J.; Blackwell, J.R.; Williams, E.; Vanhatalo, A.; Wylie, L.J.; Winyard, P.G.; Jones, A.M. Two Weeks of Watermelon Juice Supplementation Improves Nitric Oxide Bioavailability but Not Endurance Exercise Performance in Humans. *Nitric Oxide* **2016**, *59*, 10–20.
74. Rao, A.V.; Agarwal, S. Role of Antioxidant Lycopene in Cancer and Heart Disease. *J. Am. Coll. Nutr.* **2000**, *19*, 563–569.
75. Romero, M.J.; Platt, D.H.; Caldwell, R.B.; Caldwell, R.W. Therapeutic Use of Citrulline in Cardiovascular Disease. *Cardiovasc. Drug Rev.* **2006**, *24*, 275–290.
76. Wan, X.; Liu, W.; Yan, Z.; Zhao, S.; He, N.; Liu, P. Changes of the Contents of Functional Substances Including Lycopene, Citrulline and Ascorbic Acid during Watermelon Fruits Development. *Sci. Agric. Sin.* **2011**, *44*, 2738–2747.
77. Tarazona-Díaz, M.P.; Viegas, J.; Moldao-Martins, M.; Aguayo, E. Bioactive Compounds from Flesh and By-product of Fresh-cut Watermelon Cultivars. *J. Sci. Food Agric.* **2011**, *91*, 805–812.
78. Sultana, B.; Ashraf, R. Watermelon (Citrullus Lanatus) Oil. *Fruit Oils Chem. Funct.* **2019**, 741–756.
79. Abu-Reidah, I.M.; Arráez-Román, D.; Segura-Carretero, A.; Fernández-Gutiérrez, A. Profiling of Phenolic and Other Polar Constituents from Hydro-Methanolic Extract of Watermelon (Citrullus Lanatus) by Means of Accurate-Mass Spectrometry (HPLC–ESI–QTOF–MS). *Food Res. Int.* **2013**, *51*, 354–362.
80. Mushtaq, M.; Sultana, B.; Bhatti, H.N.; Asghar, M. RSM Based Optimized Enzyme-Assisted Extraction of Antioxidant Phenolics from Underutilized Watermelon (Citrullus Lanatus Thunb.) Rind. *J. Food Sci. Technol.* **2015**, *52*, 5048–5056.

 doi:10.20944/preprints202312.1677.v1

81. Jimoh, T.O.; Ademiluyi, A.O.; Oboh, G.; Boligon, A.A. Phenolic Extracts and Amino Acids Content from Cucumeropsis Mannii Naudin and Citrullus Lanatus Inhibit Relevant Enzymes of Erectile Dysfunction in Rat's Penile Tissue. *Biochem. Biophys. Rep.* **2017**, *12*, 5.
82. Nkoana, D.K.; Mashilo, J.; Shimelis, H.; Ngwepe, R.M. Nutritional, Phytochemical Compositions and Natural Therapeutic Values of Citron Watermelon (Citrullus Lanatus Var. Citroides): A Review. *South Afr. J. Bot.* **2022**, *145*, 65–77.
83. Biswas, R.; Ghosal, S.; Chattopadhyay, A.; Datta, S. A Comprehensive Review on Watermelon Seed Oil–An Underutilized Product. *IOSR J Pharm* **2017**, *7*, 01–07.
84. Maoto, M.M.; Beswa, D.; Jideani, A.I. Watermelon as a Potential Fruit Snack. *Int. J. Food Prop.* **2019**, *22*, 355–370.
85. Banureka, V.; Mahendran, T. Formulation of Wheat-Soybean Biscuits and Their Quality Characteristics. **2009**.
86. Ubbor, S.; Akobundu, E. Quality Characteristics of Cookies from Composite Flours of Watermelon Seed, Cassava and Wheat. *Pak. J. Nutr.* **2009**, *8*, 1097–1102.
87. Jiang, G.; Wu, Z.; Ameer, K.; Li, S.; Ramachandraiah, K. Particle Size of Ginseng (Panax Ginseng Meyer) Insoluble Dietary Fiber and Its Effect on Physicochemical Properties and Antioxidant Activities. *Appl. Biol. Chem.* **2020**, *63*, 1–10.
88. Zhao, C.-C.; Ameer, K.; Eun, J.-B. Effects of Various Drying Conditions and Methods on Drying Kinetics and Retention of Bioactive Compounds in Sliced Persimmon. *Lwt* **2021**, *143*, 111149.
89. Kulczyński, B.; Gramza-Michałowska, A.; Kobus-Cisowska, J.; Kmiecik, D. The Role of Carotenoids in the Prevention and Treatment of Cardiovascular Disease–Current State of Knowledge. *J. Funct. Foods* **2017**, *38*, 45–65.
90. Guo, Z.; Ge, X.; Yang, L.; Gou, Q.; Han, L.; Yu, Q. Utilization of Watermelon Peel as a Pectin Source and the Effect of Ultrasound Treatment on Pectin Film Properties. *LWT* **2021**, *147*, 111569.
91. Morais, D.R.; Rotta, E.M.; Sargi, S.C.; Bonafe, E.G.; Suzuki, R.M.; Souza, N.E.; Matsushita, M.; Visentainer, J.V. Proximate Composition, Mineral Contents and Fatty Acid Composition of the Different Parts and Dried Peels of Tropical Fruits Cultivated in Brazil. *J. Braz. Chem. Soc.* **2017**, *28*, 308–318.
92. Gladvin, G.; Sudhaakr, G.; Swathi, V.; Santhisri, K. Mineral and Vitamin Compositions Contents in Watermelon Peel (Rind). *Int. J. Curr. Microbiol. Appl. Sci.* **2017**, *5*, 129–133.
93. Rezq, A.A. Antidiabetic Activity and Antioxidant Role of Watermelon (Citrullus Lanatus) Peels in Streptozotocine-Induced Diabetic Rats. *Egypt. J. Nutr.* **2017**, *32*, 1–36.
94. Braide, W.; Odiong, I.; Oranusi, S. Phytochemical and Antibacterial Properties of the Seed of Watermelon (Citrullus Lanatus). *Prime J. Microbiol. Res.* **2012**, *2*, 99–104.
95. Khan, M.A.; Amir, R.M.; Ameer, K.; Rakha, A.; Faiz, F.; Hayat, I.; Nadeem, M.; Ahmed, Z.; Riaz, A.; Ashraf, I. Characterization of Oat Bran β-Glucan with Special Reference to Efficacy Study to Elucidate Its Health Claims for Diabetic Patients. *Food Sci. Technol.* **2020**, *41*, 105–112.
96. Kaul, P. Nutritional Potential, Bioaccessibility of Minerals and Functionality of Watermelon (Citrullus Vulgaris) Seeds. *LWT-Food Sci. Technol.* **2011**, *44*, 1821–1826.
97. Coburn, L.A.; Gong, X.; Singh, K.; Asim, M.; Scull, B.P.; Allaman, M.M.; Williams, C.S.; Rosen, M.J.; Washington, M.K.; Barry, D.P. L-Arginine Supplementation Improves Responses to Injury and Inflammation in Dextran Sulfate Sodium Colitis. *PloS One* **2012**, *7*, e33546.

98. Ren, W.; Yin, J.; Wu, M.; Liu, G.; Yang, G.; Xion, Y.; Su, D.; Wu, L.; Li, T.; Chen, S. Serum Amino Acids Profile and the Beneficial Effects of L-Arginine or L-Glutamine Supplementation in Dextran Sulfate Sodium Colitis. *PloS One* **2014**, *9*, e88335.
99. Sola, A.O.; Temitayo, O.O.; Olufunke, A.; Shittu, F. Chemical Composition, Nutritional Values and Antibacterial Activities of Watermelon Seed (Citrullus Lanatus). *Int. J. Biochem. Res. Rev.* **2019**, *27*, 1–9.
100. Metcalf, R.L.; Metcalf, R.A.; Rhodes, A. Cucurbitacins as Kairomones for Diabroticite Beetles. *Proc. Natl. Acad. Sci.* **1980**, *77*, 3769–3772.
101. Panosyan, A.; Nikishchenko, M.; Avetisyan, G. Structure of 22-Deoxocucurbitacins Isolated from Bryonia Alba and Ecbalium Elaterium. *Chem. Nat. Compd.* **1985**, *21*, 638–645.
102. Elfattah, H.; Zaghloul, A.; Halim, A.; Waight, E. CUCURBITACINS AND STEROIDS FROM CUCUMIS-CALLOSUS (ROTTL) CONG. *ACTA Pharm. Jugosl.* **1989**, *39*, 137–141.
103. Karawya, M.; El-Gengaihi, S.; Selim, M.; Motawe, H.; Ibrahim, N. Major Cucurbitacins of Momordica Balsamina L. *Pharmazie* **1996**, *51*, 434–435.
104. Arisawa, M.; Pezzuto, J.M.; Cordell, G.A.; Farnsworth, N.R.; Kinghorn, A.D. Plant Anticancer Agents XXX: Cucurbitacins from Ipomopsis Aggregata (Polemoniaceae). *J. Pharm. Sci.* **1984**, *73*, 411–413.
105. Stuppner, H.; Moller, E. Cucurbitacins with Unusual Side Chains from Picrorhiza Kurroa. *Phytochemistry* **1993**, *33*, 1139–1145.
106. Fuller, R.W.; Cardellina, J.H.; Cragg, G.M.; Boyd, M.R. Cucurbitacins: Differential Cytotoxicity, Dereplication and First Isolation from Gonystylus Keithii. *J. Nat. Prod.* **1994**, *57*, 1442–1445.
107. Miro, M. Cucurbitacins and Their Pharmacological Effects. *Phytother. Res.* **1995**, *9*, 159–168.
108. Chen, J.C.; Chiu, M.H.; Nie, R.L.; Cordell, G.A.; Qiu, S.X. Cucurbitacins and Cucurbitane Glycosides: Structures and Biological Activities. *Nat. Prod. Rep.* **2005**, *22*.
109. Jayaprakasam, B.; Seeram, N.P.; Nair, M.G. Anticancer and Antiinflammatory Activities of Cucurbitacins from Cucurbita Andreana. *Cancer Lett.* **2003**, *189*, 11–16.
110. Tannin-Spitz, T.; Grossman, S.; Dovrat, S.; Gottlieb, H.E.; Bergman, M. Growth Inhibitory Activity of Cucurbitacin Glucosides Isolated from Citrullus Colocynthis on Human Breast Cancer Cells. *Biochem. Pharmacol.* **2007**, *73*, 56–67.
111. Lee, D.H.; Iwanski, G.B.; Thoennissen, N.H. Cucurbitacin: Ancient Compound Shedding New Light on Cancer Treatment. *Sci. World J.* **2010**, *10*, 413–418.
112. Park, C.S.; Lim, H.; Han, K.J.; Baek, S.H.; Sohn, H.O.; Lee, D.W.; Kim, Y.-G.; Yun, H.-Y.; Baek, K.J.; Kwon, N.S. Inhibition of Nitric Oxide Generation by 23, 24-Dihydrocucurbitacin D in Mouse Peritoneal Macrophages. *J. Pharmacol. Exp. Ther.* **2004**, *309*, 705–710.
113. Escandell, J.M.; Recio, M.-C.; Máñez, S.; Giner, R.-M.; Cerdá-Nicolás, M.; Ríos, J.-L. Dihydrocucurbitacin B, Isolated from Cayaponia Tayuya, Reduces Damage in Adjuvant-Induced Arthritis. *Eur. J. Pharmacol.* **2006**, *532*, 145–154.
114. Escandell, J.M.; Recio, M.C.; Máñez, S.; Giner, R.M.; Cerdá-Nicolás, M.; Ríos, J.L. Cucurbitacin R Reduces the Inflammation and Bone Damage Associated with Adjuvant Arthritis in Lewis Rats by Suppression of Tumor Necrosis Factor-α in T Lymphocytes and Macrophages. *J. Pharmacol. Exp. Ther.* **2007**, *320*, 581–590.
115. Escandell, J.M.; Kaler, P.; Recio, M.C.; Sasazuki, T.; Shirasawa, S.; Augenlicht, L.; Ríos, J.-L.; Klampfer, L. Activated kRas Protects Colon Cancer Cells from Cucurbitacin-Induced Apoptosis: The Role of P53 and P21. *Biochem. Pharmacol.* **2008**, *76*, 198–207.

 doi:10.20944/preprints202312.1677.v1

116. Siqueira Jr, J.M.; Peters, R.R.; Gazola, A.C.; Krepsky, P.B.; Farias, M.R.; Rae, G.A.; de Brum-Fernandes, A.J.; Ribeiro-do-Valle, R.M. Anti-Inflammatory Effects of a Triterpenoid Isolated from Wilbrandia Ebracteata Cogn. *Life Sci.* **2007**, *80*, 1382–1387.
117. Bartalis, J.; Halaweish, F.T. Relationship between Cucurbitacins Reversed-Phase High-Performance Liquid Chromatography Hydrophobicity Index and Basal Cytotoxicity on HepG2 Cells. *J. Chromatogr. B* **2005**, *818*, 159–166.
118. Sun, J.; Blaskovich, M.A.; Jove, R.; Livingston, S.K.; Coppola, D.; Sebti, S.M. Cucurbitacin Q: A Selective STAT3 Activation Inhibitor with Potent Antitumor Activity. *Oncogene* **2005**, *24*, 3236–3245.
119. L Rios, J.; Andújar, I.; M Escandell, J.; M Giner, R.; C Recio, M. Cucurbitacins as Inducers of Cell Death and a Rich Source of Potential Anticancer Compounds. *Curr. Pharm. Des.* **2012**, *18*, 1663–1676.
120. Recio, M.C.; Prieto, M.; Bonucelli, M.; Orsi, C.; Máñez, S.; Giner, R.M.; Cerda-Nicolas, M.; Ríos, J.-L. Anti-Inflammatory Activity of Two Cucurbitacins Isolated from Cayaponia Tayuya Roots. *Planta Med.* **2004**, *70*, 414–420.
121. Sadzuka, Y.; Hatakeyama, H.; Daimon, T.; Sonobe, T. Screening of Biochemical Modulator by Tumor Cell Permeability of Doxorubicin. *Int. J. Pharm.* **2008**, *354*, 63–69.
122. Liu, T.; Zhang, M.; Zhang, H.; Sun, C.; Yang, X.; Deng, Y.; Ji, W. Combined Antitumor Activity of Cucurbitacin B and Docetaxel in Laryngeal Cancer. *Eur. J. Pharmacol.* **2008**, *587*, 78–84.
123. Agati, G.; Azzarello, E.; Pollastri, S.; Tattini, M. Flavonoids as Antioxidants in Plants: Location and Functional Significance. *Plant Sci.* **2012**, *196*, 67–76.
124. Mahomoodally, M.F.; Gurib-Fakim, A.; Subratty, A.H. Antimicrobial Activities and Phytochemical Profiles of Endemic Medicinal Plants of Mauritius. *Pharm. Biol.* **2005**, *43*, 237–242.
125. Pandey, A.K. Anti-Staphylococcal Activity of a Pan-Tropical Aggressive and Obnoxious Weed Parthenium Histerophorus: An in Vitro Study. *Natl. Acad. Sci. Lett.* **2007**, *30*, 383–386.
126. Chiou, A.; Panagopoulou, E.A.; Gatzali, F.; De Marchi, S.; Karathanos, V.T. Anthocyanins Content and Antioxidant Capacity of Corinthian Currants (Vitis Vinifera L., Var. Apyrena). *Food Chem.* **2014**, *146*, 157–165.
127. Chiou, A. *Handbook of Anthocyanins: Food Sources, Chemical Applications and Health Benefits*; Nova Publishers, 2015; ISBN 1-63321-795-7.
128. Panagopoulou, E.A.; Chiou, A.; Bismpikis, M.; Mouraka, P.; Mangiorou, E.; Karathanos, V.T. Dried Fruits: Phytochemicals and Their Fate during in Vitro Digestion. *Int. J. Food Sci. Technol.* **2021**, *56*, 4506–4515.
129. Leopoldini, M.; Russo, N.; Chiodo, S.; Toscano, M. Iron Chelation by the Powerful Antioxidant Flavonoid Quercetin. *J. Agric. Food Chem.* **2006**, *54*, 6343–6351.
130. Dixon, R.; Dey, P.; Lamb, C. Phytoalexins: Enzymology and Molecular Biology. *Adv. Enzymol. Relat. Areas Mol. Biol.* **1983**, *55*, 69.
131. Kumar, S.; Gupta, A.; Pandey, A.K. Calotropis Procera Root Extract Has the Capability to Combat Free Radical Mediated Damage. *Int. Sch. Res. Not.* **2013**, *2013*.
132. Heim, K.E.; Tagliaferro, A.R.; Bobilya, D.J. Flavonoid Antioxidants: Chemistry, Metabolism and Structure-Activity Relationships. *J. Nutr. Biochem.* **2002**, *13*, 572–584.
133. Mishra, A.; Sharma, A.K.; Kumar, S.; Saxena, A.K.; Pandey, A.K. Bauhinia Variegata Leaf Extracts Exhibit Considerable Antibacterial, Antioxidant, and Anticancer Activities. *BioMed Res. Int.* **2013**, *2013*.
134. Hollman, P.C.; Bijsman, M.N.; Van Gameren, Y.; Cnossen, E.P.; De Vries, J.H.; Katan, M.B. The Sugar Moiety Is a Major Determinant of the Absorption of Dietary Flavonoid Glycosides in Man. *Free Radic. Res.* **1999**, *31*, 569–573.

135. Halliwell, B. Antioxidant Defence Mechanisms: From the Beginning to the End (of the Beginning). *Free Radic. Res.* **1999**, *31*, 261–272.
136. BROWN, E.J.; Khodr, H.; HIDER, C.R.; RICE-EVANS, C.A. Structural Dependence of Flavonoid Interactions with Cu2+ Ions: Implications for Their Antioxidant Properties. *Biochem. J.* **1998**, *330*, 1173–1178.
137. Kumar, S.; Pandey, A. Antioxidant, Lipo-Protective and Antibacterial Activities of Phytoconstituents Present in Solanum Xanthocarpum Root. *Int. Rev. Biophys. Chem.* **2012**, *3*, 42–47.
138. Kerry, N.L.; Abbey, M. Red Wine and Fractionated Phenolic Compounds Prepared from Red Wine Inhibit Low Density Lipoprotein Oxidation in Vitro. *Atherosclerosis* **1997**, *135*, 93–102.
139. Van Acker, S.; van den Berg, D.; Tromp, M. Structural Aspects of Antioxidant Activity of Flavanoids. **1996**.
140. Choleva, M.; Boulougouri, V.; Panara, A.; Panagopoulou, E.; Chiou, A.; Thomaidis, N.S.; Antonopoulou, S.; Fragopoulou, E. Evaluation of Anti-Platelet Activity of Grape Pomace Extracts. *Food Funct.* **2019**, *10*, 8069–8080.
141. Pannala, A.S.; Chan, T.S.; O'Brien, P.J.; Rice-Evans, C.A. Flavonoid B-Ring Chemistry and Antioxidant Activity: Fast Reaction Kinetics. *Biochem. Biophys. Res. Commun.* **2001**, *282*, 1161–1168.
142. Tsoupras, A.; Ni, V.L.J.; O'Mahony, É.; Karali, M. Wine-Making;"with One Stone Two Birds"? A Holistic Review of the Bio-Functional Compounds, Applications and Health Benefits of Wine and Wineries' By-Products. **2023**.
143. Tsoupras, A.; Moran, D.; Byrne, T.; Ryan, J.; Barrett, L.; Traas, C.; Zabetakis, I. Anti-Inflammatory and Anti-Platelet Properties of Lipid Bioactives from Apple Cider by-Products. *Molecules* **2021**, *26*, 2869.
144. Tsoupras, A.B.; Fragopoulou, E.; Nomikos, T.; Iatrou, C.; Antonopoulou, S.; Demopoulos, C.A. Characterization of the de Novo Biosynthetic Enzyme of Platelet Activating Factor, DDT-Insensitive Cholinephosphotransferase, of Human Mesangial Cells. *Mediators Inflamm.* **2007**, *2007*.
145. Vlachogianni, I.C.; Fragopoulou, E.; Stamatakis, G.M.; Kostakis, I.K.; Antonopoulou, S. Platelet Activating Factor (PAF) Biosynthesis Is Inhibited by Phenolic Compounds in U-937 Cells under Inflammatory Conditions. *Prostaglandins Other Lipid Mediat.* **2015**, *121*, 176–183.
146. Aderiye, B.; David, O.; Fagbohun, E.; Faleye, J.; Olajide, O. Immunomodulatory and Phytomedicinal Properties of Watermelon Juice and Pulp (Citrullus Lanatus Linn): A Review. *GSC Biol. Pharm. Sci.* **2020**, *11*, 153–165.
147. Dahan, K.; Fennal, M.; Kumar, N.B. Lycopene in the Prevention of Prostate Cancer. *J. Soc. Integr. Oncol.* **2008**, *6*.
148. Erdman Jr, J.W.; Ford, N.A.; Lindshield, B.L. Are the Health Attributes of Lycopene Related to Its Antioxidant Function? *Arch. Biochem. Biophys.* **2009**, *483*, 229–235.
149. Alim-un-Nisa, J.A.; Firdous, S.; Saeed, M.; Hina, S.; Ejaz, N. Nutritional Aspects and Acceptability of Watermelon Juice Syrup. *Pak J Food Sci* **2012**, *22*, 32–35.
150. Elumalai, M.; Karthika, B.; Usha, V. Lycopene-Role in Cancer Prevention. *Int J Pharma Bio Sci* **2013**, *4*, 371–378.
151. Hayashi, T.; Juliet, P.A.; Matsui-Hirai, H.; Miyazaki, A.; Fukatsu, A.; Funami, J.; Iguchi, A.; Ignarro, L.J. L-Citrulline and l-Arginine Supplementation Retards the Progression of High-Cholesterol-Diet-Induced Atherosclerosis in Rabbits. *Proc. Natl. Acad. Sci.* **2005**, *102*, 13681–13686.
152. Aguirre, V.; Uchida, T.; Yenush, L.; Davis, R.; White, M.F. The C-Jun NH2-Terminal Kinase Promotes Insulin Resistance during Association with Insulin Receptor Substrate-1 and Phosphorylation of Ser307. *J. Biol. Chem.* **2000**, *275*, 9047–9054.

153. Ilahy, R.; Tlili, I.; Siddiqui, M.W.; Hdider, C.; Lenucci, M.S. Inside and beyond Color: Comparative Overview of Functional Quality of Tomato and Watermelon Fruits. *Front. Plant Sci.* **2019**, *10*, 769.
154. Hong, M.Y.; Beidler, J.; Hooshmand, S.; Figueroa, A.; Kern, M. Watermelon and L-Arginine Consumption Improve Serum Lipid Profile and Reduce Inflammation and Oxidative Stress by Altering Gene Expression in Rats Fed an Atherogenic Diet. *Nutr. Res.* **2018**, *58*, 46–54.
155. Bazabang, S.A.; Monday, N.; Adebisi, S.S.; Makena, W.; Iliya, I.A. Hepatoprotective Effects of Aqueous Extract of Watermelon (Citrullus Lanatus) Seeds on Ethanol-Induced Oxidative Damage in Wister Rats. *Sub-Sahar. Afr. J. Med.* **2018**, *5*, 129.
156. DeWeese, R.S.; Ohri-Vachaspati, P. Cost of Children's Healthy vs Unhealthy Snacks Does Not Differ at Convenience Stores. *J. Nutr. Educ. Behav.* **2017**, *49*, 241–243.
157. Milind, P.; Kulwant, S. Musk Melon Is Eat-Must Melon. *IRJP* **2011**, *2*, 52–57.
158. Stahl, W.; Sies, H. Lycopene: A Biologically Important Carotenoid for Humans? *Arch. Biochem. Biophys.* **1996**, *336*, 1–9.
159. Shi, J.; Maguer, M.L. Lycopene in Tomatoes: Chemical and Physical Properties Affected by Food Processing. *Crit. Rev. Food Sci. Nutr.* **2000**, *40*, 1–42.
160. Holzapfel, N.P.; Holzapfel, B.M.; Champ, S.; Feldthusen, J.; Clements, J.; Hutmacher, D.W. The Potential Role of Lycopene for the Prevention and Therapy of Prostate Cancer: From Molecular Mechanisms to Clinical Evidence. *Int. J. Mol. Sci.* **2013**, *14*, 14620–14646.
161. Ibrahim, A.; Babaye, H.; Ya'u, M.; Babagana, K.; Abubakar, S.; Ahmad, J. Nigerian Citrullus Lanatus Fruit and Seed Juice Reduces Cardiovascular Diseases Modifiable Risk Biomarkers in Normal Experimental Rats. *J Hypertens Manag* **2018**, *4*, 1–7.
162. Nadeem, M.; Navida, M.; Ameer, K.; Iqbal, A.; Malik, F.; Nadeem, M.A.; Fatima, H.; Ahmed, A.; Din, A. A Comprehensive Review on the Watermelon Phytochemical Profile and Their Bioactive and Therapeutic Effects. *Korean J. Food Preserv.* **2022**, *29*, 546–576.
163. Saini, R.K.; Nile, S.H.; Park, S.W. Carotenoids from Fruits and Vegetables: Chemistry, Analysis, Occurrence, Bioavailability and Biological Activities. *Food Res. Int.* **2015**, *76*, 735–750.
164. Rai, C.; Rai, P.; Majumdar, G.; De, S.; DasGupta, S. Mechanism of Permeate Flux Decline during Microfiltration of Watermelon (Citrullus Lanatus) Juice. *Food Bioprocess Technol.* **2010**, *3*, 545–553.
165. Montesano, D.; Fallarino, F.; Cossignani, L.; Bosi, A.; Simonetti, M.S.; Puccetti, P.; Damiani, P. Innovative Extraction Procedure for Obtaining High Pure Lycopene from Tomato. *Eur. Food Res. Technol.* **2008**, *226*, 327–335.
166. Story, E.N.; Kopec, R.E.; Schwartz, S.J.; Harris, G.K. An Update on the Health Effects of Tomato Lycopene. *Annu. Rev. Food Sci. Technol.* **2010**, *1*, 189–210.
167. Fattore, M.; Montesano, D.; Pagano, E.; Teta, R.; Borrelli, F.; Mangoni, A.; Seccia, S.; Albrizio, S. Carotenoid and Flavonoid Profile and Antioxidant Activity in "Pomodorino Vesuviano" Tomatoes. *J. Food Compos. Anal.* **2016**, *53*, 61–68.
168. Suwanaruang, T. Analyzing Lycopene Content in Fruits. *Agric. Agric. Sci. Procedia* **2016**, *11*, 46–48.
169. Manivannan, A.; Lee, E.-S.; Han, K.; Lee, H.-E.; Kim, D.-S. Versatile Nutraceutical Potentials of Watermelon—A Modest Fruit Loaded with Pharmaceutically Valuable Phytochemicals. *Molecules* **2020**, *25*, 5258.
170. Bhattacharjee, C.; Saxena, V.; Dutta, S. Novel Thermal and Non-Thermal Processing of Watermelon Juice. *Trends Food Sci. Technol.* **2019**, *93*, 234–243.

171. Wu, G.; Collins, J.K.; Perkins-Veazie, P.; Siddiq, M.; Dolan, K.D.; Kelly, K.A.; Heaps, C.L.; Meininger, C.J. Dietary Supplementation with Watermelon Pomace Juice Enhances Arginine Availability and Ameliorates the Metabolic Syndrome in Zucker Diabetic Fatty Rats. *J. Nutr.* **2007**, *137*, 2680–2685.
172. Collins, J.K.; Wu, G.; Perkins-Veazie, P.; Spears, K.; Claypool, P.L.; Baker, R.A.; Clevidence, B.A. Watermelon Consumption Increases Plasma Arginine Concentrations in Adults. *Nutrition* **2007**, *23*, 261–266.
173. El-Razek, F.; Sadeek, E.A. Dietary Supplementation with Watermelon (Citrullus Ianatus) Juice Enhances Arginine Availability and Modifies Hyperglycemia, Hyperlipidemia, and Oxidative Stress in Diabetic Rats. *Aust J Basic Appl Sci* **2011**, *5*, 1284–1295.
174. Poduri, A.; Rateri, D.L.; Saha, S.K.; Saha, S.; Daugherty, A. Citrullus Lanatus 'Sentinel'(Watermelon) Extract Reduces Atherosclerosis in LDL Receptor-Deficient Mice. *J. Nutr. Biochem.* **2013**, *24*, 882–886.
175. Deshmukh, A.S.; Long, Y.; de Castro Barbosa, T.; Karlsson, H.; Glund, S.; Zavadoski, W.; Gibbs, E.; Koistinen, H.; Wallberg-Henriksson, H.; Zierath, J.R. Nitric Oxide Increases Cyclic GMP Levels, AMP-Activated Protein Kinase (AMPK) A1-Specific Activity and Glucose Transport in Human Skeletal Muscle. *Diabetologia* **2010**, *53*, 1142–1150.
176. Lira, V.A.; Soltow, Q.A.; Long, J.H.; Betters, J.L.; Sellman, J.E.; Criswell, D.S. Nitric Oxide Increases GLUT4 Expression and Regulates AMPK Signaling in Skeletal Muscle. *Am. J. Physiol.-Endocrinol. Metab.* **2007**, *293*, E1062–E1068.
177. Rains, J.L.; Jain, S.K. Oxidative Stress, Insulin Signaling, and Diabetes. *Free Radic. Biol. Med.* **2011**, *50*, 567–575.
178. Singh Gill, N.; Sood, S.; Muthuraman, A.; Bali, M.; Dev Sharma, P. Evaluation of Antioxidant and Anti-Ulcerative Potential of Citrullus Lanatus Seed Extract in Rats. *Lat. Am. J. Pharm.* **2011**, *30*.
179. Gill, N.; Bansal, R.; Manju, G.; Shailja, S.; Arunachalam, M.; Manoj, B. Evaluation of Antioxidant, Anti-Inflammatory and Analgesic Potential of Citrullus Lanatus Seed Extract in Rodent Model. *Internet J. Nutr. Wellness* **2010**, *9*.
180. Adebayo, A.O.; Alozie, I.; somtochi Olivia, C.-O. Evaluating the Influence of Citrullus Lanatus Seed Extracts on Electrolytes, Urea and Creatinine in Streptozotocin Induced Diabetic Albino Rats. *2663-1040* **2018**, *2*, 87–94.
181. Deshmukh, C.D.; Jain, A.; Tambe, M.S. Phytochemical and Pharmacological Profile of Citrullus Lanatus (THUNB). *Biolife* **2015**, *3*, 483–488.
182. Rahman, H.; Manjula, K.; Anoosha, T.; Nagaveni, K.; Eswaraiah, M.C.; Bardalai, D. In-Vitro Antioxidant Activity of Citrullus Lanatus Seed Extracts. *Asian J Pharm Clin Res* **2013**, *6*, 152–157.
183. Ikpeme, E.; Udensi, O.; Ekerette, E.; Okon, U. Potential of Ginger (Zingiber Officinale) Rhizome and Watermelon (Citrullus Lanatus) Seeds in Mitigating Aspartame-Induced Oxidative Stress in Rat Model. *Res J Med Plant* **2016**, *10*, 55–66.
184. Wahid, S.; Khan, R.A.; Feroz, Z.; Ikram, R. Analgesic, Anti-Inflammatory and Toxic Effects of Ethanol Extracts of Cucumis Melo and Citrullus Lanatus Seeds. *Pak. J. Pharm. Sci.* **2020**, *33*.
185. Petchsomrit, A.; McDermott, M.I.; Chanroj, S.; Choksawangkarn, W. Watermelon Seeds and Peels: Fatty Acid Composition and Cosmeceutical Potential. *OCL* **2020**, *27*, 54.
186. Hong, M.Y.; Hartig, N.; Kaufman, K.; Hooshmand, S.; Figueroa, A.; Kern, M. Watermelon Consumption Improves Inflammation and Antioxidant Capacity in Rats Fed an Atherogenic Diet. *Nutr. Res.* **2015**, *35*, 251–258.

187. Connolly, M.; Lum, T.; Marx, A.; Hooshmand, S.; Kern, M.; Liu, C.; Hong, M.Y. Effect of Fresh Watermelon Consumption on Risk Factors for Cardiovascular Disease in Overweight and Obese Adults (P06-102-19). *Curr. Dev. Nutr.* **2019**, *3*, nzz031-P06.
188. Wen, C.; Zhang, J.; Feng, Y.; Duan, Y.; Ma, H.; Zhang, H. Purification and Identification of Novel Antioxidant Peptides from Watermelon Seed Protein Hydrolysates and Their Cytoprotective Effects on H2O2-Induced Oxidative Stress. *Food Chem.* **2020**, *327*, 127059.
189. Dash, P.; Rath, G.; Ghosh, G. In Vivo Antioxidant Potential of Protein Hydrolysates of Some Cucurbitaceae Seed. *J. Drug Deliv. Ther.* **2020**, *10*, 128–132.
190. Wen, C.; Zhang, J.; Zhang, H.; Duan, Y.; Ma, H. Effects of Divergent Ultrasound Pretreatment on the Structure of Watermelon Seed Protein and the Antioxidant Activity of Its Hydrolysates. *Food Chem.* **2019**, *299*, 125165.
191. Sonawane, S.K.; Arya, S.S. Citrullus Lanatus Protein Hydrolysate Optimization for Antioxidant Potential. *J. Food Meas. Charact.* **2017**, *11*, 1834–1843.
192. Asghar, M.N.; Shahzad, M.T.; Nadeem, I.; Ashraf, C.M. Phytochemical and in Vitro Total Antioxidant Capacity Analyses of Peel Extracts of Different Cultivars of Cucumis Melo and Citrullus Lanatus. *Pharm. Biol.* **2013**, *51*, 226–232.
193. Kolawole, T.; Ojeka, S.; Dapper, D. Anti-Diabetic Effects of the Methanolic Extract of the Rind of Citrullus Lanatus (Watermelon) in Alloxan Induced Diabetes in Male Albino Wistar Rats. *J. Med. Med. Sci.* **2016**, *7*, 023–029.
194. Kolawole, A.; Dapper, V.; Eziuzo, C. Effects of the Methanolic Extract of the Rind of Citrullus Lanatus (Watermelon) on Some Erythrocyte Parameters and Indices of Oxidative Status in Phenylhydrazine-Treated Male Wistar Rats. *J. Afr. Assoc. Physiol. Sci.* **2017**, *5*, 22–28.
195. Alamsyah, N.; Djamil, R.; Rahmat, D. Antioxidant Activity of Combination Banana Peel (Musa Paradisiaca) and Watermelon Rind (Citrullus Vulgaris) Extract in Lotion Dosage Form. *Asian J Pharm Clin Res* **2016**, *9*, 300–304.
196. Figueroa, A.; Wong, A.; Kalfon, R. Effects of Watermelon Supplementation on Aortic Hemodynamic Responses to the Cold Pressor Test in Obese Hypertensive Adults. *Am. J. Hypertens.* **2014**, *27*, 899–906.
197. Sultan, S.; D'Souza, A.; Zabetakis, I.; Lordan, R.; Tsoupras, A.; Kavanagh, E.P.; Hynes, N. Chapter 6 - Statins: Rationale, Mode of Action, and Side Effects. In *The Impact of Nutrition and Statins on Cardiovascular Diseases*; Zabetakis, I., Lordan, R., Tsoupras, A., Eds.; Academic Press, 2019; pp. 171–200 ISBN 978-0-12-813792-5.
198. Figueroa, A.; Sanchez-Gonzalez, M.A.; Wong, A.; Arjmandi, B.H. Watermelon Extract Supplementation Reduces Ankle Blood Pressure and Carotid Augmentation Index in Obese Adults with Prehypertension or Hypertension. *Am. J. Hypertens.* **2012**, *25*, 640–643.
199. Ellis, A.C.; Dudenbostel, T.; Crowe-White, K. Watermelon Juice: A Novel Functional Food to Increase Circulating Lycopene in Older Adult Women. *Plant Foods Hum. Nutr.* **2019**, *74*, 200–203.
200. Khalaf, D.; Krüger, M.; Wehland, M.; Infanger, M.; Grimm, D. The Effects of Oral L-Arginine and L-Citrulline Supplementation on Blood Pressure. *Nutrients* **2019**, *11*, 1679.
201. Tarazona-Díaz, M.P.; Alacid, F.; Carrasco, M.; Martínez, I.; Aguayo, E. Watermelon Juice: Potential Functional Drink for Sore Muscle Relief in Athletes. *J. Agric. Food Chem.* **2013**, *61*, 7522–7528.
202. Jorge, N.; da Silva, A.C.; Malacrida, C.R. Physicochemical Characterisation and Radical-Scavenging Activity of Cucurbitaceae Seed Oils. *Nat. Prod. Res.* **2015**, *29*, 2313–2317.

203. Karikpo, C.; Bartimaeus, E.; Holy, B. Evaluation of the Cardioprotective Effect of Citrullus Lanatus (Watermelon) Seeds in Streptozotocin Induced Diabetic Albino Rats. *Asian J. Biochem. Genet. Mol. Biol.* **2019**, *1*, 1–6.
204. Gajowik, A.; Dobrzynska, M. Lycopene-Antioxidant with Radioprotective and Anticancer Properties. A Review. *Rocz. Państw. Zakładu Hig.* **2014**, *65*.
205. Nahum, A.; Hirsch, K.; Danilenko, M.; Watts, C.K.; Prall, O.W.; Levy, J.; Sharoni, Y. Lycopene Inhibition of Cell Cycle Progression in Breast and Endometrial Cancer Cells Is Associated with Reduction in Cyclin D Levels and Retention of p27Kip1 in the Cyclin E–Cdk2 Complexes. *Oncogene* **2001**, *20*, 3428–3436.
206. Butt, M.S.; Sultan, M.T. Selected Functional Foods for Potential in Disease Treatment and Their Regulatory Issues. *Int. J. Food Prop.* **2013**, *16*, 397–415.
207. Barkur, S.; Bankapur, A.; Chidangil, S.; Mathur, D. Effect of Infrared Light on Live Blood Cells: Role of β-Carotene. *J. Photochem. Photobiol. B* **2017**, *171*, 104–116, doi:10.1016/j.jphotobiol.2017.04.034.
208. Fadimu, G.J.; Ghafoor, K.; Babiker, E.E.; Al-Juhaimi, F.; Abdulraheem, R.A.; Adenekan, M.K. Ultrasound-Assisted Process for Optimal Recovery of Phenolic Compounds from Watermelon (Citrullus Lanatus) Seed and Peel. *J. Food Meas. Charact.* **2020**, *14*, 1784–1793.
209. Patel, S.; Rauf, A. Edible Seeds from Cucurbitaceae Family as Potential Functional Foods: Immense Promises, Few Concerns. *Biomed. Pharmacother.* **2017**, *91*, 330–337.
210. Simpson, R.; Morris, G.A. The Anti-Diabetic Potential of Polysaccharides Extracted from Members of the Cucurbit Family: A Review. *Bioact. Carbohydr. Diet. Fibre* **2014**, *3*, 106–114.
211. Oseni, O.; Odesanmi, O.; Oladele, F. Antioxidative and Antidiabetic Activities of Watermelon (Citrullus Lanatus) Juice on Oxidative Stress in Alloxan-Induced Diabetic Male Wistar Albino Rats. *Niger. Med. J. J. Niger. Med. Assoc.* **2015**, *56*, 272.
212. Vincellette, C.M.; Losso, J.; Early, K.; Spielmann, G.; Irving, B.A.; Allerton, T.D. Supplemental Watermelon Juice Attenuates Acute Hyperglycemia-Induced Macro-and Microvascular Dysfunction in Healthy Adults. *J. Nutr.* **2021**, *151*, 3450–3458, doi:10.1093/jn/nxab279.
213. Ahn, J.; Choi, W.; Kim, S.; Ha, T. Anti-Diabetic Effect of Watermelon (Citrullus Vulgaris Schrad) on Streptozotocin-Induced Diabetic Mice. *Food Sci. Biotechnol.* **2011**, *20*, 251–254.
214. Zia, S.; Khan, M.R.; Aadil, R.M.; Shahid, M. Development and Storage Stability of Value-added Watermelon Fruit Butter by Incorporating Watermelon Rind Byproduct. *J. Food Process. Preserv.* **2022**, *46*, e17031.
215. Abu-Hiamed, H. Hypocholesterolemic Effects of Watermelon Fruit Rind on Rats. *Nutr. Food Sci.* **2018**, *48*, 836–845.
216. Owo, J.; Beresford, S. Blood Sugar Lowering Potentials of Aqueous and Ethanol Extracts of the Mixture of Rinds of Citrullus Vulgaris Schrad (Watermelon) and Chrysophyllum Albidum G.(Udara) Fruits on Alloxan-Induced Diabetic Wistar Rats. *J. Pharm. Res. Int.* **2020**, *32*, 86–90.
217. Parmar, H.S.; Kar, A. Possible Amelioration of Atherogenic Diet Induced Dyslipidemia, Hypothyroidism and Hyperglycemia by the Peel Extracts of Mangifera Indica, Cucumis Melo and Citrullus Vulgaris Fruits in Rats. *Biofactors* **2008**, *33*, 13–24.
218. Omigie, I.; Agoreyo, F. Effects of Watermelon (Citrullus Lanatus) Seed on Blood Glucose and Electrolyte Parameters in Diabetic Wistar Rats. *J. Appl. Sci. Environ. Manag.* **2014**, *18*, 231–233.
219. Belemkar, S.; Shendge, P.N. Toxicity Profiling of the Ethanolic Extract of Citrullus Lanatus Seed in Rats: Behavioral, Biochemical and Histopathological Aspects. *Biosci. Rep.* **2021**, *41*, BSR20202345.
220. Arise, R.O.; Yekeen, A.A.; Ekun, O.E. In Vitro Antioxidant and α-Amylase Inhibitory Properties of Watermelon Seed Protein Hydrolysates. *Environ. Exp. Biol.* **2016**, *14*.

221. Montesano, D.; Rocchetti, G.; Putnik, P.; Lucini, L. Bioactive Profile of Pumpkin: An Overview on Terpenoids and Their Health-Promoting Properties. *Curr. Opin. Food Sci.* **2018**, *22*, 81–87.
222. Liang, J.; Zhang, X.; Yuan, J.; Zhang, H.; Liu, D.; Hao, J.; Ji, W.; Wu, X.; Chen, D. Cucurbitacin B Inhibits the Migration and Invasion of Breast Cancer Cells by Altering the Biomechanical Properties of Cells. *Phytother. Res.* **2019**, *33*, 618–630.
223. Kaushik, U.; Aeri, V.; Mir, S.R. Cucurbitacins–an Insight into Medicinal Leads from Nature. *Pharmacogn. Rev.* **2015**, *9*, 12.
224. Oyenihi, O.R.; Afolabi, B.A.; Oyenihi, A.B.; Ogunmokun, O.J.; Oguntibeju, O.O. Hepato-and Neuro-Protective Effects of Watermelon Juice on Acute Ethanol-Induced Oxidative Stress in Rats. *Toxicol. Rep.* **2016**, *3*, 288–294.
225. Sathya, J.; Shoba, F.G. Assessment of Antimicrobial Efficacy of Citrullus Lanatus Methanolic Seed Extract. *J Chem Pharm Res* **2014**, *6*, 640–643.
226. Dash, P.; Ghosh, G. Fractionation, Amino Acid Profiles, Antimicrobial and Free Radical Scavenging Activities of Citrullus Lanatus Seed Protein. *Nat. Prod. Res.* **2017**, *31*, 2945–2947.
227. Sonawane, S.K.; Bhagwat, A.N.; Arya, S. Limonia Acidissima and Citrullus Lanatus Fruit Seeds: Antimicrobial, Thermal, Structural, Functional and Protein Identification Study. *Food Biosci.* **2018**, *26*, 8–14.
228. Hameed, B.; Ali, Q.; Hafeez, M.; Malik, A. Antibacterial and Antifungal Activity of Fruit, Seed and Root Extracts of Citrullus Colocynthis Plant. *Biol. Clin. Sci. Res. J.* **2020**, *2020*.
229. Loiy, E.; Hassan, A.; Hasnah, M.; Ahmed, Y.; Asking, M.; Koko, W.; Siddig, A. In Vitro Anti-Microbial Activities of Chloroformic, Hexane & Ethanolic Extracts of C. Lanatus Var. Citroides. *J Med Plants Res* **2011**, *5*, 1338–1344.
230. Adunola, A.; Chidimma, A.L.; Olatunde, D.S.; Peter, O.A. Antibacterial Activity of Watermelon (Citrullus Lanatus) Seed against Selected Microorganisms. *Afr. J. Biotechnol.* **2015**, *14*, 1224–1229.
231. Kumari, A.; Rao, J.; Kumari, J.; Sharma, N.; Jain, P.; Dave, V.; Sharma, S. Analgesic Activity of Aqueous Extract of Citrullus Lanatus Peels. *Adv. Pharmacol. Pharm.* **2013**, *1*, 135–138.
232. Akshaya, M.; Sasikala, S.; Nithyalakshmi, V.; Meenakshi, N.; Dhivya Kiruthika, K.; Pavithra, M. Effect of Pre-Treatments on the Phytochemical Composition of Watermelon (Citrullus Lanatus) Rind. *Int. Food Res. J.* **2018**, *25*.
233. Rajasree, R.; Sibi, P.; Francis, F.; William, H. Phytochemicals of Cucurbitaceae Family—A Review. *Int. J. Pharmacogn. Phytochem. Res.* **2016**, *8*, 113–123.
234. Yadav, S.; Bhargav, M.; Ramya, R.; Nowfal, H. In-Vitro Antioxidant and Immunomodulatory Activity of Citrullus Lanatus Seed. *Int. J. Eng. Sci. Res. Technol.* **2016**, *5*, 679–685.
235. Messaoudi, S.; Tebibel, S.; Beladjila, A.K.; Touhami, F.K.; Kabouche, Z. Anti-Hyperlipidemic, Anti-Inflammatory and Antioxidant Activities of Citrullus Lanatus. *World J. Environ. Biosci.* **2019**, *8*, 100–106.
236. Tomes, M.; Johnson, K.; Hess, M. The Carotene Pigment Content of Certain Red Fleshed Watermelons.; 1963; Vol. 82, pp. 460–464.
237. Fan, J.; Park, E.; Zhang, L.; Edirisinghe, I.; Burton-Freeman, B.; Sandhu, A.K. Pharmacokinetic Parameters of Watermelon (Rind, Flesh, and Seeds) Bioactive Components in Human Plasma: A Pilot Study to Investigate the Relationship to Endothelial Function. *J. Agric. Food Chem.* **2020**, *68*, 7393–7403.
238. Rezig, L.; Chouaibi, M.; Meddeb, W.; Msaada, K.; Hamdi, S. Chemical Composition and Bioactive Compounds of Cucurbitaceae Seeds: Potential Sources for New Trends of Plant Oils. *Process Saf. Environ. Prot.* **2019**, *127*, 73–81.

239. Oelschlägel, S.; Menzel, C.; Speer, K. Phytosterols and Steryl Esters in Diverse Cucurbita, Cucumis and Citrullus Seed Oils. *Lipid Technol.* **2012**, *24*, 181–184.
240. Suliburska, J.; Bogdanski, P.; Krejpcio, Z.; Pupek-Musialik, D.; Jablecka, A. The Effects of L-Arginine, Alone and Combined with Vitamin C, on Mineral Status in Relation to Its Antidiabetic, Anti-Inflammatory, and Antioxidant Properties in Male Rats on a High-Fat Diet. *Biol. Trace Elem. Res.* **2014**, *157*, 67–74.
241. Shanely, R.A.; Zwetsloot, J.J.; Jurrissen, T.J.; Hannan, L.C.; Zwetsloot, K.A.; Needle, A.R.; Bishop, A.E.; Wu, G.; Perkins-Veazie, P. Daily Watermelon Consumption Decreases Plasma sVCAM-1 Levels in Overweight and Obese Postmenopausal Women. *Nutr. Res.* **2020**, *76*, 9–19.
242. Ajiboye, B.O.; Shonibare, M.T.; Oyinloye, B.E. Antidiabetic Activity of Watermelon (Citrullus Lanatus) Juice in Alloxan-Induced Diabetic Rats. *J. Diabetes Metab. Disord.* **2020**, *19*, 343–352.
243. Onyeso, G.; Nkpaa, K.; Omenihu, S. Co-Administration of Caffeine and Hydromethanolic Fraction of Citrullus Lanatus Seeds Improved Testicular Functions in Alloxan-Induced Diabetic Male Wistar Rats. *Asian Pac. J. Reprod.* **2016**, *5*, 105–110.
244. Sorour, H.; Selim, M.; Almoselhy, L.; Gouda, S. Ameliorative Effect of Watermelon Rind Ingestion on the Pancreas of Diabetic Female Albino Rat (Histological, Immunohistochemical and Morphometric Study). *Egypt. J. Histol.* **2019**, *42*, 10–22.
245. Azizi, S.; Mahdavi, R.; Vaghef-Mehrabany, E.; Maleki, V.; Karamzad, N.; Ebrahimi-Mameghani, M. Potential Roles of Citrulline and Watermelon Extract on Metabolic and Inflammatory Variables in Diabetes Mellitus, Current Evidence and Future Directions: A Systematic Review. *Clin. Exp. Pharmacol. Physiol.* **2020**, *47*, 187–198.
246. Becraft, A.R.; Sturm, M.L.; Mendez, R.L.; Park, S.H.; Lee, S.I.; Shay, N.F. Intake of Watermelon or Its Byproducts Alters Glucose Metabolism, the Microbiome, and Hepatic Proinflammatory Metabolites in High-Fat–Fed Male C57BL/6 J Mice. *J. Nutr.* **2020**, *150*, 434–442.
247. Gad-Elkareem, M.A.; Abdelgadir, E.H.; Badawy, O.M.; Kadri, A. Potential Antidiabetic Effect of Ethanolic and Aqueous-Ethanolic Extracts of Ricinus Communis Leaves on Streptozotocin-Induced Diabetes in Rats. *PeerJ* **2019**, *7*, e6441.
248. Okechukwu, H.; Ihentuge, C.; Ugochukwu, C.; Anibeze, C. Histological Changes in the Pancreas of Streptozotocin Induced Diabetic Rats Fed with Rind of Citrullus Lanatus. *FASEB J.* **2015**, *29*, 544–548.
249. Oluwole, F.S.; Balogun, M.E.; Temitope, A.G. Antisecretory Effects of Watermelon (Citrullus Lanatus) Juice in Male Albino Rats. *Annu. Res. Rev. Biol.* **2013**, 358–366.
250. Sharma, S.; Sarvesh, P.; Dwivedi, J.; Amita, T. First Report on Laxative Activity of Citrullus Lanatus. *Pharmacologyonline* **2011**, *2*, 790–797.
251. Altaş, S.; Kızıl, G.; Kızıl, M.; Ketani, A.; Haris, P.I. Protective Effect of Diyarbakır Watermelon Juice on Carbon Tetrachloride-Induced Toxicity in Rats. *Food Chem. Toxicol.* **2011**, *49*, 2433–2438.
252. Zhan, Y.-Y.; Wang, J.-H.; Tian, X.; Feng, S.-X.; Xue, L.; Tian, L.-P. Protective Effects of Seed Melon Extract on CCl4-Induced Hepatic Fibrosis in Mice. *J. Ethnopharmacol.* **2016**, *193*, 531–537.
253. Ogbeifun, H.; Peters, D.; Monanu, M. Ameliorative Effect of Citrullus Lanatus (Water Melon) Seeds on Alloxan Induced Hepato and Nephro Toxicity. *Asian J. Adv. Res. Rep.* **2020**, *9*, 1–10.
254. Iswariya, S.; Uma, T. Evaluation of in Vitro Anti-Inflammatory and Antimicrobial Activity of Aqueous and Methanolic Seed Extracts of Citrullus Lanatus. *Int J Pharm Pharm Sci* **2017**, *9*, 29–33.
255. Gabriel, A.; Igwemmar, N.; Sadam, A.; Babalola, S. Characterization of Seed Oil from Citrullus Lanatus (Watermelon). *Direct Res J Public Health Env. Technol* **2018**, *3*, 34–40.

256. Athar, S.; Ghazi, A.; Chourasiya, O.; Karadbhajne, V.Y. „Watermelon Seed Oil: Its Extraction, Analytical Studies, Modification and Utilization in Cosmetic Industries". *Int. Res. J. Eng.* **2020**.
257. Deng, J.; Wang, S.; Guo, L.; Fan, L. Anti-Inflammatory and Analgesic Effects of Extract from Roots and Leaves of Citrullus Lanatus. *Chin Herb Med* **2010**, *2*, 231–235.
258. Alam, M.A.; Kauter, K.; Withers, K.; Sernia, C.; Brown, L. Chronic L-Arginine Treatment Improves Metabolic, Cardiovascular and Liver Complications in Diet-Induced Obesity in Rats. *Food Funct.* **2013**, *4*, 83–91.
259. Soliman, W. Fabrication of Electrospun Nanofibers Made of Watermelon Peel Extract and PVA and Investigating Their Antioxidant and Antibacterial Activities. **2019**.
260. Hassan, R.; Amira, E.; Odeyemi, O.; Omorinoye, J. Phytochemicals and Antimicrobial Potential of Citrullus Vulgaris Seed and Pod Extracts. *Int. J. Innov. Res. Adv. Stud.* **2020**, *7*, 103–106.
261. Thirunavukkarasu, P.; Ramanathan, T.; Ravichandran, N.; Ramkumar, L. Screening of Anti-Microbial Effect in Watermelon (Citrullus Sp.). *J. Biol. Sci.* **2010**, *10*, 682–685.
262. Dammak, M.I.; Salem, Y.B.; Belaid, A.; Mansour, H.B.; Hammami, S.; Le Cerf, D.; Majdoub, H. Partial Characterization and Antitumor Activity of a Polysaccharide Isolated from Watermelon Rinds. *Int. J. Biol. Macromol.* **2019**, *136*, 632–641.
263. Oyewo, O.; Onyije, F.; Akintunde, O.; Ashamu, E. Effects of Aqueous Extract of Citrullus Lanatus on the Histology of the Kidney of Adult Wistar Rats. *World Appl. Sci. J.* **2012**, *17*, 1178–1181.
264. Munglue, P.; Eumkep, G.; Wray, S.; Kupittayanant, S. The Effects of Watermelon (Citrullus Lanatus) Extracts and L-Citrulline on Rat Uterine Contractility. *Reprod. Sci.* **2013**, *20*, 437–448.
265. Olamide, A.A.; Olayemi, O.O.; Demetrius, O.O.; Olatoye, O.J.; Kehinde, A.A. Effects of Methanolic Extract of Citrullus Lanatus Seed on Experimentally Induced Prostatic Hyperplasia. *Eur. J. Med. Plants* **2011**, *1*, 171–179.
266. Omotoso, O.; Osadiaye, A. The Regenerative Efficacy of Aqueous and Methanolic Extracts of Watermelon, Citrullus Lanatus Seeds on Physiological Saline and Acetaminophen-Induced Kidney Damage in Female Albino Rats. *Br. J. Multidiscip. Adv. Stud.* **2018**, *2*, 98–108.
267. Owoeye, O.; Akinbami, R.; Thomas, M. Neuroprotective Potential of Citrullus Lanatus Seed Extract and Vitamin E against Mercury Chloride Intoxication in Male Rat Brain. *Afr. J. Biomed. Res.* **2018**, *21*, 43–49.
268. Finbarrs, E.; Chinedu, F.; Ojo, O.P. Effect of Ethanolic Seed Extract of Citrus Lanatus (Watermelon) on Immunoreactivity of Hippocampal Neurofilament of Adult Wistar Rats. *Eras J. Med. Res.* **2018**, *5*, 1–5.
269. Adedeji, G.; Bamidele, O.; Ogunbiyi, A. Haematological and Biochemical Properties of Methanolic Extract of Citrullus Lanatus Seeds. *Br. J. Pharm. Res.* **2017**, *15*, 1–10.
270. Ferreira, J.; Rodriguez-Amaya, D. Degradation of Lycopene and Β-carotene in Model Systems and in Lyophilized Guava during Ambient Storage: Kinetics, Structure, and Matrix Effects. *J. Food Sci.* **2008**, *73*, C589–C594.
271. Shivapour, M.; Yousefi, S.; Ardabili, S.M.S.; Weisany, W. Optimization and Quality Attributes of Novel Toast Breads Developed Based on the Antistaling Watermelon Rind Powder. *J. Agric. Food Res.* **2020**, *2*, 100073.
272. Imoisi, C.; Iyasele, J.; Michael, U.; Imhontu, E. The Effects of Watermelon Rind Flour on the Functional and Proximate Properties of Wheat Bread. *J. Chem. Soc. Niger.* **2020**, *45*.
273. Anang, D.A.; Pobee, R.A.; Antwi, E.; Obeng, E.M.; Atter, A.; Ayittey, F.K.; Boateng, J.T. Nutritional, Microbial and Sensory Attributes of Bread Fortified with Defatted Watermelon Seed Flour. *Int. J. Food Sci. Technol.* **2018**, *53*, 1468–1475.

274. Adegunwa, M.; Oloyede, I.; Adebanjo, L.; Alamu, E. Quality Attribute of Plantain (Musa Paradisiaca) Sponge-Cake Supplemented with Watermelon (Citrullus Lanatus) Rind Flour. *Cogent Food Agric.* **2019**, *5*, 1631582.
275. ASHOKA, S.; BEGUM, S.S.; RAY, B.R.M. Effect of Watermelon (Citrullus Lanatus) Rind Flour Incorporation on Nutritional and Organoleptic Attributes of Cakes. **2021**.
276. Ho, L.-H.; Paet, M.; Suhaimi, M.A. The Physicochemical and Sensory Attributes of Watermelon Rind Flour Incorporated Steamed Cupcake. *J. Agrobiotechnology* **2018**, *9*, 31–42.
277. HASSAN, N.S.; MAHMOUD, A.H.; EL-KHOLAN, E.A. Quality Enhancing of Cake Using White Watermelon Rinds. *Egypt. J. Agric. Res.* **2017**, *95*, 1653–1667.
278. Naknaen, P.; Itthisoponkul, T.; Sondee, A.; Angsombat, N. Utilization of Watermelon Rind Waste as a Potential Source of Dietary Fiber to Improve Health Promoting Properties and Reduce Glycemic Index for Cookie Making. *Food Sci. Biotechnol.* **2016**, *25*, 415–424.
279. Olaitan, N.; Eke, M.; Agudu, S. Effect of Watermelon (Citrullus Lanatus) Rind Flour Supplementation on the Quality of Wheat Based Cookies. *Int J Eng Sci* **2017**, *6*, 59–66.
280. Omobolanle, O.; Oluwatoyin, A.; Michael, I.; Adefunke, B.; Olamiji, A. Evaluation of Potentials of Some Selected Seeds' Flours as Partial Substitute for Wheat in Cookies Production. *Intl J Sci Eng Res* **2017**, *8*, 739–752.
281. Ogo, A.; Ajekwe, D.; Enenche, D.; Obochi, G. Quality Evaluation of Novel Biscuits Made from Wheat Supplemented with Watermelon Rinds and Orange Pomace Flour Blends. *Food Nutr. Sci.* **2021**, *12*, 332–341.
282. Peter-Ikechukwu, A.; Omeire, G.; Kabuo, N.; Eluchie, C.; Amandikwa, C.; Odoemenam, G. Production and Evaluation of Biscuits Made from Wheat Flour and Toasted Watermelon Seed Meal as Fat Substitute. *J Food Res* **2018**, *7*, 112.
283. Franca, E. CHEMICAL PROPERTIES OF WATERMELON SEED AND THE UTILIZATION OF DEHULLED SEED IN COOKIES PRODUCTION. *Carpathian J. Food Sci. Technol.* **2017**, *9*.
284. Ho, L.-H.; Che Dahri, N. Effect of Watermelon Rind Powder on Physicochemical, Textural, and Sensory Properties of Wet Yellow Noodles. *CyTA-J. Food* **2016**, *14*, 465–472.
285. Kumar, P.; Mehta, N.; Malav, O.; Kumar Chatli, M.; Rathour, M.; Kumar Verma, A. Antioxidant and Antimicrobial Efficacy of Watermelon Rind Extract (WMRE) in Aerobically Packaged Pork Patties Stored under Refrigeration Temperature (4±1 C). *J. Food Process. Preserv.* **2018**, *42*.
286. Shahein, M.R.; Atwaa, E.S.H.; El-Zahar, K.M.; Elmaadawy, A.A.; Hijazy, H.H.A.; Sitohy, M.Z.; Albrakati, A.; Elmahallawy, E.K. Remedial Action of Yoghurt Enriched with Watermelon Seed Milk on Renal Injured Hyperuricemic Rats. *Fermentation* **2022**, *8*, 41.
287. Qayyum, A.; Huma, N.; Sameen, A.; Siddiq, A.; Munir, M. I Mpact of Watermelon Seed Flour on the Physico-chemical and Sensory Characteristics of Ice Cream. *J. Food Process. Preserv.* **2017**, *41*, e13297.
288. Bisla, G.; Archana, P.V.; Sharma, S. Development of Ice Creams from Soybean Milk & Watermelon Seeds Milk and Evaluation of Their Acceptability and Nourishing Potential. *Adv Appl Sci Res* **2012**, *3*, 371–376.
289. Nasir, H.; Allai, F.; Gull, A.; Ganaie, T.; Azad, Z. Effect of Pre-Treatments on Desirable Qualities Attributes of Watermelon Rind Based Candy. *J. Postharvest Technol.* **2020**, *8*, 38–52.
290. Thapa, P.; Pahari, A.; Thagunna, B.; Kusma, R. Preparation and Quality Evaluation of Sugar and Honey-Based Watermelon Rind (By-Product) Candies.
291. Dhakal, D.; Pradhananga, M.L. Utilization of Watermelon Rind (Byproduct) in Preparation of Candy and Its Quality Evaluation. *Int. J. Multidiscip. Pap.* **2017**, *2*, 1–6.

292. Hani, M.N.F.; Zahidah, W.; Saniah, K.; Irwani, H. Effects of Drying on the Physical Characteristics of Dehydrated Watermelon Rind Candies. *J Trop Agric Fd Sc* **2014**, *42*, 115–123.
293. Islam, M. Value Addition to Watermelon Rind through Jam Preparation. **2017**.
294. Petkowicz, C.; Vriesmann, L.; Williams, P. Pectins from Food Waste: Extraction, Characterization and Properties of Watermelon Rind Pectin. *Food Hydrocoll.* **2017**, *65*, 57–67.
295. Prabha, H.P.; Deva Pavithra, B.; Ishwariya, S.; Jashwanthi, P.; Shendhura Devi, M. Valorization of Watermelon Rind as Dietary Chips Fortified with Composite Flour. *Int. J. Creat. Res. Thoughts* **2021**, *9*, 591–596.
296. Evanuarini, H.; Amertaningtyas, D.; Utama, D. Viscosity, Fat Content, Total Acidity, and Antioxidant Capacity of Reduced-Fat Mayonnaise Made with Watermelon (Citrullus Lanatus) Rind Flour as Stabilizer.; IOP Publishing, 2021; Vol. 788, p. 012100.
297. Saavedra, G.; Maternal, J.A.E.; Comahig, M.C.; Pimentel, J. Nutrient Analysis and Shelf Life Study of Watermelon Rind Sports Drink.
298. Kumar, V.; Jain, S.K.; Amitabh, A.; Chavan, S.M. Effect of Ohmic Heating on Physicochemical, Bioactive Compounds, and Shelf Life of Watermelon Flesh-rind Drinks. *J. Food Process Eng.* **2022**, *45*, e13818.
299. Gunawan, W.B.; Basoeki, L.E.A.S. Incorporating Watermelon Rind into Jackfruit Seed Drink: A Functional Drink Rich in Antioxidant and Phenolic Compounds. *EDUFORTECH* **2022**, *7*.
300. Todhanakasem, T.; Jaiprayat, C.; Sroysuwan, T.; Suksermsakul, S.; Suwapanich, R.; Maleenont, K.K.; Koombhongse, P.; Young, B.M. Active Thermoplastic Starch Film with Watermelon Rind Extract for Future Biodegradable Food Packaging. *Polymers* **2022**, *14*, 3232.
301. Łopusiewicz, Ł.; Drozłowska, E.; Trocer, P.; Kostek, M.; Śliwiński, M.; Henriques, M.H.; Bartkowiak, A.; Sobolewski, P. Whey Protein Concentrate/Isolate Biofunctional Films Modified with Melanin from Watermelon (Citrullus Lanatus) Seeds. *Materials* **2020**, *13*, 3876.
302. Łopusiewicz, Ł.; Macieja, S.; Śliwiński, M.; Bartkowiak, A.; Roy, S.; Sobolewski, P. Alginate Biofunctional Films Modified with Melanin from Watermelon Seeds and Zinc Oxide/Silver Nanoparticles. *Materials* **2022**, *15*, 2381.
303. Wang, F.; Xie, C.; Ye, R.; Tang, H.; Jiang, L.; Liu, Y. Development of Active Packaging with Chitosan, Guar Gum and Watermelon Rind Extract: Characterization, Application and Performance Improvement Mechanism. *Int. J. Biol. Macromol.* **2023**, *227*, 711–725.
304. Han, H.-S.; Song, K.B. Antioxidant Properties of Watermelon (Citrullus Lanatus) Rind Pectin Films Containing Kiwifruit (Actinidia Chinensis) Peel Extract and Their Application as Chicken Thigh Packaging. *Food Packag. Shelf Life* **2021**, *28*, 100636.
305. Guo, Z.; Ge, X.; Li, W.; Yang, L.; Han, L.; Yu, Q. Active-Intelligent Film Based on Pectin from Watermelon Peel Containing Beetroot Extract to Monitor the Freshness of Packaged Chilled Beef. *Food Hydrocoll.* **2021**, *119*, 106751.
306. Xie, Q.; Liu, X.; Zhang, Y.; Liu, G. Development and Characterization of a New Potato Starch/Watermelon Peel Pectin Composite Film Loaded with TiO2 Nanoparticles and Microencapsulated Lycium Barbarum Leaf Flavonoids and Its Use in the Tan Mutton Packaging. *Int. J. Biol. Macromol.* **2023**, *252*, 126532.
307. Colivet, J.; Garcia, V.A. dos S.; Lourenço, R.V.; Yoshida, C.M.P.; Oliveira, A.L. de; Vanin, F.M.; Carvalho, R.A. de Characterization of Films Produced with Cross-Linked Cassava Starch and Emulsions of Watermelon Seed Oils. *Foods* **2022**, *11*, 3803.

 doi:10.20944/preprints202312.1677.v1

308. Guo, Z.; Wu, S.; Lin, J.; Zheng, H.; Lei, H.; Yu, Q.; Jiang, W. Active Film Preparation Using Pectin and Polyphenols of Watermelon Peel and Its Applications for Super-Chilled Storage of Chilled Mutton. *Food Chem.* **2023**, *417*, 135838.
309. Guo, Z.; Zuo, H.; Ling, H.; Yu, Q.; Gou, Q.; Yang, L. A Novel Colorimetric Indicator Film Based on Watermelon Peel Pectin and Anthocyanins from Purple Cabbage for Monitoring Mutton Freshness. *Food Chem.* **2022**, *383*, 131915.
310. Kelm, G.R.; Wickett, R.R. The Role of Fatty Acids in Cosmetic Technology. In *Fatty Acids*; Elsevier, 2017; pp. 385–404.
311. Omoniyi, S. Nutrient and Anti-Nutritional Composition of Watermelon (Citrullus Lanatus) Seed: A Review. *FUW Trends Sci. Technol.* **2020**, *5*, 048–051.
312. Baeeri, M.; Sarkhail, P.; Hashemi, G.; Marefatoddin, R.; Shahabi, Z. Data Showing the Optimal Conditions of Pre-Extraction and Extraction of Citrullus Lanatus (Watermelon) White Rind to Increase the Amount of Bioactive Compounds, DPPH Radical Scavenging and Anti-Tyrosinase Activity. *Data Brief* **2018**, *20*, 1683–1685, doi:10.1016/j.dib.2018.09.024.
313. Simamora, F.S.; Janice, J.; Amir, W.P. Effectiveness Test of White Skin Extract Cream from Red Watermelon (Citrullus Lanatus) on Increasing Elasticity, Sebum and Hydration in White Mice (Mus Musculus) Skin. *Int. J. Health Pharm. IJHP* **2023**, *3*, 322–330.
314. Patra, J.K.; Das, G.; Baek, K.-H. Phyto-Mediated Biosynthesis of Silver Nanoparticles Using the Rind Extract of Watermelon (Citrullus Lanatus) under Photo-Catalyzed Condition and Investigation of Its Antibacterial, Anticandidal and Antioxidant Efficacy. *J. Photochem. Photobiol. B* **2016**, *161*, 200–210, doi:10.1016/j.jphotobiol.2016.05.021.
315. Cefali, L.C.; Ataide, J.A.; Donegá, R.T.; Godoy, K. de M.S.; de AraÃºjo, F.G.; Mazzola, P.G. Development of Emulsion Containing Watermelon Extract for Skin Aging. *J. Med. Plants Res.* **2017**, *11*, 749–754.
316. Kamble, C.; Kamble, V. Formulation and Evaluation of Herbal Lipstick Using Lycopene Extracted from Citrullus Lanatus. Research & Reviews: A Journal of Pharmaceutical Science. 2021; 12 (3): 50–55p. *Formul. Eval. Herb. Lipstick Kamble Al STM J.* 2021, 2.