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VALORIZATION OF WATERMELON FRUIT (CITRULLUS LANATUS) BYPRODUCTS: PHYTOCHEMICAL AND BIOFUNCTIONAL PROPERTIES WITH EMPHASIS ON RECENT TRENDS AND ADVANCES

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ABSTRACT

Watermelon (*Citrullus lanatus*) a fruit crop, is an herbaceous creeping plant belonging to the family Cucurbitaceae. It is a tropical plant, mainly propagated by seeds and thrives best in warm areas. While the fruit pulp is consumed, seeds are often discarded. The continuously growing global market for the main tropical fruits is currently estimated at ~85 million tons, of which approximately half is lost or wasted throughout the whole processing chain. Developing novel processes for the conversion of these byproducts into value-added products could provide a viable way to manage this waste problem, aiming at the same time to create a sustainable economic growth within a bio-economy perspective. Given the ever-increasing concern about sustainability, complete valorization through a bio-refinery approach, that is, zero waste concepts is therefore most important. This paper aims to report the status on the valorization of tropical fruit byproducts, more specifically in watermelon seeds and their content in bioactive compounds, such as phenolic acids, flavonoids, carotenoids, alkaloids. Moreover, the bioactivity of the different types of phytochemicals and their possible application as a resource for different sectors (food, pharmaceutical, and environmental sciences) is discussed. Consequently, this review presents the concepts of tropical fruit byproducts recovery, and the potential applications of the isolated fractions.

KEYWORDS: *Citrullus lanatus*, byproducts, bioactive compounds, biological activities, toxicity, functional food.

1. INTRODUCTION

The Cucurbitaceae family is recognized as numerous and heterogeneous, covering about 115 genera.[1] Among the ~115 genera belonging to the Cucurbitaceae family, four are of great economic importance: Citrullus, Cucumis, Cucurbita and Lagenaria. Watermelon (Citrullus lanatus) is the main world crop in the Cucurbitaceae family (~ 40%), followed by cucumber (Cucumis sativus) (~ 27%), melon (Cucumis melo) (~ 20%) and pumpkin (Cucurbita) (~ 13%), respectively.[2] According to the United Nations Food and Agriculture Organization (FAO), the global production of watermelon is, approximately 118 million tonnes and China is the World's leading Watermelon producer.[3] However, the Middle East, the USA, Africa, India, Japan, and Europe are the most important watermelon producing areas. According to bibliographic data, the watermelon was first cultivated in Africa, from where it spread to Europe, the Near East and India. Later on, it was introduced in China and America. Nevertheless, there are two hypotheses on the origin of watermelons. The first states that this species comes from wild populations of Africa, whereas different research claims that it is original from a species of Cucurbitaceae that grows wild in the valley of the Nile. It was first cultivated, most probably, in Africa, from where it spread to the Mediterranean, the Near East and India. There are few registries of this species until the XVIth century, but from that time onwards it begins to be popular.[4]

Cultivated watermelon has three species *Citrullus lanatus* var. *lanatus*, *C. lanatus* var. *citroides* and *C. mucusospermus*. *Citrullus colocynthis* and *Citrullus*

eccirrhosus are two perennial wild species. *Praecitrullus fistulosus* (Stocks) Pangalo usuaaly called 'Tinda' from India and Pakistan is a related species. Watermelon is an annual plant with long angular trailing vines bearing lobed leaves, branched tendrils and separate solitary male and female flowers.[5] Watermelons require a long, warm growing season and are usually grown for the consumption of their fresh, edible fruit flesh. Unlike melons and pumpkins, for instance, the part consumed is the placental region, or endocarp. In some regions, consumption of the seeds is important, too.

In morphological terms, watermelon consists of pericarp (peel), mesocarp (white part) and endocarp (pulp). This fruit is recognized by for its large proportions and shapes, varying from round to cylindrical. Its bark presents different colors and is usually solid green or green with lighter streaks. The pulp is usually pink and contains several seeds dispersed inside.[6] The black or dark brown seeds are in the endocarp, presenting an oval shape with small dimensions. Usually, the most consumed part of the watermelon is the pulp. However, it has been reported that the consumption of seeds can bring health benefits.[7]

2. Nutritional and Chemical Composition

Despide this study focuses on the by-products of this fruit and due to the nutritional richness of the edible part, it becomes necessary to highlighted. Regarding nutritional composition, all fruits belonging to Cucurbitaceae family are particularly nutritious. For instance, carotenes (precursors of vitamin A) are present in pumpkin and melon cultivars in high quantity. Also, lycopene is reported in watermelon and has been recognized for its biological properties. The sugar content and sweetness are the critical factors in determining the quality of many watermelon varieties. It is known to be low in calories but highly nutritious and thirst quenching. It is also high in fibre and citrulline; an amino acid the body uses to make arginine.[8-10] As a matter of fact, watermelon can be used as fresh salad, dessert, snack, and for decorations. Drinks can also be made from the juice. In Namibia, the juice is fermented into a refreshing, lightly alcoholic drink. In several parts of Africa the rind is sliced, dried, cooked and eaten. Also, pickled watermelon rind is widely eaten in some parts of USA.

Although there are more studies on the nutritional and phytochemical composition of the edible parts of these fruits (pulp), some seeds from Cucurbits are usually consumed in several countries (e.g., roasted seeds in the Middle East, watermelon seed as snacks after salting and roasting in Arabian and Asian regions), for its high levels of fat and protein.[11] However, the ingesting of Cucurbitaceae seeds has not yet become a common eating habit, which implies that the consumption of these fruits can lead to high organic waste, causing environmental damage. Thus, when it comes to environmental sustainability, it is impossible not to relate with economics. First, it is necessary to consider that many of the environmental problems of the 21st century stem from the lack of industrial strategies for the balanced use of natural resources.[12,13]

Fruit and vegetable industries generate large amounts of by-products with a great economic potential. The processing by-products account from 25 up to 60% of the weight of the fruit and would be mainly made of skin, pulp and seeds. Functional molecules obtained from these by-products using environmentally friendly processes could have novel applications in the food, pharmaceutical and cosmetic industries.[14] Therefore, Cucurbitaceae seeds can be used for the development of medicines and cosmetics.[14,15] Cucurbit seeds oils are also rich in essential active ingredients. So, cucurbit seeds oil can be produced in large-scale in food industry and dietary supplement industry in paramedical sector.[16] Jorge et al. reported that the amount of oil content in watermelon seeds is about 27.1%.[17] Triglycerides, saturated fatty acids and omega-6 are present in watermelon seeds composition, representing a great importance for cooking, cosmetic, and therapeutic oil needs.[18] Also, according to Rezig et al.[19] watermelon seeds can be an alternative source of edible oil in food applications. Watermelon seeds are known to be highly nutritional; they are rich sources of protein, vitamins B, minerals (such as magnesium, potassium, phosphorous, sodium, iron, zinc, manganese and copper) and fat among others as well phytochemicals.[20] The seeds of watermelons are known by having economic benefits, especially in countries where cultivation is on the increase. In spite of the several potential applications, the watermelon seeds are often discarded while the fruit is eaten. There is also limited literature on the effect of variety on the nutritional, phytochemical and antioxidant properties of the watermelon seeds.

Given the above, watermelon seeds may provide considerable medicinal, health and economic benefits if freshly consumed or utilized in food products. According to Avinash and Rai,[15] considering the nutritional and chemical composition of these seeds, they may be useful in the treatment of various pathologies, such as, bronchitis, diabetes, nephritis, asthma, sinusitis, syphilis, psychiatric diseases, among others. Therefore, its nutritional and pharmacological potential must be evaluated, emphasizing the biological properties and health benefits.[21]

2.1. Watermelon seeds: nutritional composition

Each watermelon seed possesses a length ~8.01 mm and a width ~0.32 mm, and 100 g correspond to approximately 2000 seeds. These seeds have a high nutritional and energy value, in which a comparison with the pulp of the watermelon is established.

The approximate composition of 100 g of watermelon seeds reveals an energy value of 619 Kcal, while the pulp presents higher nutritional value and lower energy value.

Unlike pulp, seeds have low moisture content (~4.9 g), which prevents their rapid degradation through biological contamination.[7] Watermelon seeds are rich in vitamins B and minerals,[5,20] while fruit pulp is a source of vitamins A, B1, B2, B3, B6 and, mostly, C.[22] The most abundant minerals in the seeds are magnesium and potassium,[19] ranging values between 86.67-109.63 mg/100 g and 55.15-82.63 mg/100 g, respectively, according to the location where they are found: whole seed, peeled seed or seed husk.[23] *Citrullus lanatus* seeds also present high amounts of crude fibre (48.26%).[19] The high iodine values of seed oils (135.39 ± 12.84 g I_2/ 100 g oil) were related with their abundance in unsaturated fatty acids, indicating that these oils are appropriate for edible and/or drying oil purposes.[19] There are hundreds of underexplored plant seeds rich in oil suitable for edible or industrial purposes, and watermelon seeds are considered to be a good source of oil that can be used in food, pharmaceutical and cosmetic industries.[24] Seed oils showed high amounts of total unsaturated fatty acids (~82.32%), mainly oleic (C18:1) and linoleic (C18:2) acids.[19] These two acids, in addition to being essential, offer nutritional advantages, and when mixed with other edible oils, can originate oils with modified nutritional values. Palmitic and stearic acids are also present in high concentrations, and although they are saturated fatty acids, they can be useful in cosmetic applications, namely in the manufacture of shaving creams.[21,25] Also, watermelon seed oil can be a potential source of antioxidant compounds (total phenol, α-tocopherol and vitamin-E). According to most of the researches the values of the physicochemical characteristics of watermelon seed oil are within the recommended limits and therefore it could be a good source of cooking and frying oil, as well as an ingredient in cosmetic formulations. Rai et al.,[26] watermelon seed oil has high antioxidant activity, helping to prevent certain chronic diseases such as diabetes, cardiovascular disease, and obesity. However, it is important to note that the centesimal composition of watermelon seeds can vary widely and is influenced by several factors, including origin, plant species and edaphoclimatic conditions, among others.[17]

2.2. Bioactive compounds in watermelon seeds

Phenolic compounds, commonly known as bioactive compounds, are secondary metabolites present in plants and widely distributed in the plant kingdom. They are found in different parts of the plants (edible and non-edible), such as pulp, seeds, leaves, bark and roots.[27] They range from simple molecules to others with a high degree of polymerization and can be present in free form, linked to sugars (glycosides) and/or proteins. Currently, more than 8,000 chemical structures are known, whose organic origins are associated with the pathway of shikimic acid and with the pathway of phenylpropanoids.[28,29]

Currently, watermelon already plays an important role in human nutrition, and can be eaten fresh, packaged, in frozen juices and pulps. In fact, due to the high-water content and low-calorie values, the watermelon consumption and consequent production are increasing. Fruit pulp contains bioactive compounds, mostly citrulline and lycopene.[30,31] Citrulline exerts antioxidant activity and has a beneficial effect on atherosclerosis and improves endothelium-dependent vasorelaxation. It is endogenously converted to arginine, and the oxidation of arginine forms NO, a molecule involved in vasodilation.[32] Lycopene, responsible for the red color of watermelon, is known for its antioxidant properties and its consumption has been associated to a prevention of cancer and degenerative diseases.[33] Lycopene is the carotenoid with the greatest antioxidant capacity, due to the presence of two unconjugated double bonds in its acyclic structure, which offers it greater reactivity acting as a sequestering agent for singlet oxygen.[30] Lycopene in watermelon is 40% higher than in tomato and it does not need to be heat treated to become available, like in tomatoes.[34] Other compounds present in the pulp comprise phenolic compounds, hydroxycinnamic acids, hydroxybenzoic acids, flavonoids, stilbenes vitamins, and flavonoids, which can protect cellular constituents against oxidative damage and therefore limit the risk of various degenerative diseases associated with oxidative stress.[35]

Watermelon fruit pulp also contains vitamins and other bioactive compounds, but the most representative are phenolic acids, lignans, coumarins and stilbenes.[36] Among the phenolic acids, Stafussa et al.[35] reported hydroxycinnamic acids as the most significant bioactive compounds in watermelon pulp. In general, the presence of these compounds is common in all parts of the same plant species, including pulp and seeds, and may differ in quantitative terms.

Several authors reported phenolic acids, flavonoids, terpenoids, alkaloids, steroids, carotenoids, and saponins in considerable amounts in watermelon seeds.[5,37,38] α-spinasterol is the predominant phytosterol found in watermelon seeds (~57,7%), is a component of natural food ingredients. e.g., argan oil is used as a traditional food ingredient in the 'Amazigh diet' and provides about 25% of the total diet fat intake to the indigenous consumers.[39] This phytosterol differs from cholesterol by (i) an additional ethyl group and double bond in the aliphatic side chain; and (ii) the position of the double bond in the tetracyclic ring system and is one of the main mediator to reduce the ability for the plasma LDL-cholesterol level. Investigating the physiological effect(s) of α-spinasterol, several studies showed that it modulates mitochondrial activity and gene expression of nuclear receptors exhibits antitumor, antioxidative, and anti-inflammatory activities,[40,41] and influences serum concentrations and metabolism of cholesterol in rats. *Citrullus lanatus* seeds contain a high content of total phenolic (215 mg gallic acid equivalents/100 g) and of

total flavonoid (73 mg catechin equivalents/100 g) contents.[41] Phenolic compounds present anticancer, anti-inflammatory, antiviral, and antioxidant effects. Eight phenolic acids were identified from watermelon seeds: syringic acid, caffeic acid, sinapic acid, ferrulic acid, vanilic acid, *p*-coumaric acid, gallic acid, and 4-hydroxy benzoic acid.[42] Rutin and quercetin were also described.[36] Braide et al.[20] referred saponins, alkaloids and terpenoids (cucurbitacins) as the major compounds present in watermelon seeds. Pectin, although a polysaccharide, has also been described as a bioactive compound present in seeds. In fact, although it is not a secondary metabolite, pectin acts at intestinal level, controlling the absorption of carbohydrates and cholesterol and feeding the beneficial intestinal flora as a prebiotic agent.[43]

2.3. Biological activity

Bioactive compounds are defined as components of food that have an impact on physiological or cellular activities in the humans or animals that consume such compounds. They include flavonoids, anthocyanins, tannins, betalains, carotenoids, plant sterols, and glucosinolates. They have antioxidant, anti-inflammatory, and anti-carcinogenic effects; and can be protective against various diseases and metabolic disorders. Such beneficial effects make them good candidates for development of new functional food with potential protective and preservative properties. Watermelon, although recognized as food, is used as a medicinal plant, particularly in African and Asian cultures, due to its richness in bioactive compounds with biological activities. Of the many biological activities described, the anti-diabetic,[44] hypoglycemic, hypolipidemic, hypocholesterolemic,[45] diuretic, anti-urolithiatic,[46] and anthelmintic,[47] properties can be mentioned. Some studies have shown that watermelon seed extracts contain antimicrobial activity, which can be incorporated into pharmacological formulations against some pathogenic microorganisms. For example, Sola et al.[48] reported antibacterial activity against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterococcus faecalis* and *Bacilus subtilis*. The ethanol extract of *C. lanatus* seeds showed significant analgesic and anti-inflammatory activity between 3 to 24 hours as compared to standard drugs, presumably due to the presence of cucurbitacins, which are thought to inhibit COX 2 (Cyclooxygenase 2).[49] The ethyl acetate extract of *C. lanatus* seeds seems to be active against some bacteria and fungi associated with respiratory, gastrointestinal and urinary tract infections.[50] Thus, the watermelon seeds may also have direct application in herbal medicine.

The antioxidant activity of the seeds is one of the most described biological properties in literature, being active against DPPH, H_2O_2 and NO.[5,15,51,52] Wen et al.[52] identified five novel watermelon seed peptides, that showed DPPH and ABTS radical scavenging capacity, and oxygen radical absorbance capacity. One of these five peptides may protect HepG2 cells from H_2O_2-induced oxidative damage by inhibiting reactive oxygen species, intracellular free [Ca^{2+}], malondialdehyde levels and increasing antioxidative enzyme activities. A list of different pharmacological activities of *C. lanatus* seeds are described in Table 1.

Table 1: Different pharmacological activities of *C. lanatus* seeds.

Pharmacological Activity	Effects
Anti-inflammatory	Cox2 inhibition[49]
Sexual enhancement	Increases serum testosterone and luteinizing hormone[53]
Antimicrobial	Activity against *S. aureus, E. coli, B. stubtilis*and *P. aeruginosa*[50]
Weight loss and haematological benefits	Reduction of weight in Wistar rats; treatment of anaemia; depressing effects on platelet activity and leucocyte function[54]
Anti-hepatotoxicactivity	Seed extract inhibited the elevations of hepatic enzymes in serum, and ameliorated the histopathological changes induced by CCl_4 in mice[55]
Anti-diabetic	Methanolic seed extract caused a reduction in the blood glucose concentrations in rats[56]
Antiulcer and gastroprotective	Gastric ulcer inhibition in rats[57]
Cardiovascular benefits	Reduced body weight gain, decreased plasma cholesterol concentrations, improved homeostasis of pro- and anti-inflammatory cytokines, and attenuated development of atherosclerosis in hypercholesterolemic mice[58]

Some of the watermelon seeds components are related to some specific biological actions. Poduri et al.[58] attributed the cardiovascular benefits of *C. lanatus* consumption to citrulline, which can be found in watermelon skin, pulp and seeds. Rats fed with an extract containing 20–30 mg/g of citrulline, presented a reduction in cholesterol concentrations plasma (LDL-cholesterol) and a decrease in atherosclerosis in both arch and thoracic regions of aortas.[58] Citrulline relaxes and dilates blood vessels, thus justifying the consumption of this fruit as an aphrodisiac. This amino acid (citrulline) can also contribute positively to atherosclerosis and hypertension reduction, thus preventing cardiovascular diseases.[59] Also,

cucurbitacin, a terpenoid present only in the Cucurbitaceae family, may present therapeutic potential in the treatment of a variety of diseases diseases related with inflammatory processes. The anti-inflammatory activity of cucurbitacin E isolated from watermelon seeds has been studied. This biological activity is due to the inhibition of nitric oxide production in macrophages.[59]

Lycopene, the major carotene in watermelon pulp and seeds is a recognized antioxidant and antineoplastic compound.[43] Watermelon seeds, being rich in magnesium and calcium, presents ability to regulate blood pressure and carbohydrate metabolism. Accordingly, these minerals show beneficial effect on blood glucose regulation and, consequently, prevent diabetes.[43] The sodium/potassium ratio ingested is especially important for the prevention and control of high blood pressure, being recommended a value below 1. Watermelon seeds showed a Na/K ratio of 0.06 to 0.29, depending on whether the values refer to the whole, peeled or skin seed, respectively. Therefore, and since the seeds have a Na/K ratio less than 1, they can help to reduce blood pressure and prevent cardiovascular diseases, such as hypertension.[59] Oelschlägel et al.[61] and Rezig et al.[19] described the presence of phytosterols in watermelon seed oil, such as β-sitosterol, campesterol and stigmasterol. The use of phytosterols for therapeutic purposes, to prevention the development of cardiovascular diseases, has been known since the 1950s and many technological advances have been proposed so that the efficacy of pharmaceutical or food products developed with these compounds is increasingly effective.

2.4. Toxicity in watermelon seeds

Antinutrients are substances that interfere with digestibility, absorption and use of nutrients and non-nutrients, blocking metabolic pathways and decreasing their bioavailability.[62] Therefore, antinutrients must be determined to ensure nutritional security. The most common antinutritional factors present in watermelon seeds include tannins, phytates and oxalates, but also saponins, alkaloids, hydrocyanic acid, and phenols.[6] Tannins are a group of polyphenols that bind and form complexes with proteins, minerals, digestive enzymes, and vitamins, and inhibit their metabolism in the body. Phytic acid or phytate binds minerals, such as calcium, magnesium, iron, copper and zinc, inhibiting its absorption by the intestine. Oxalate forms a complex with calcium and makes it unavailable for absorption. This precipitates in the form of insoluble salts, which accumulate in the renal glomeruli thus contributing to the development of renal dysfunction.[62,63] Thus, in order to reduce or to eliminate antinutritional composition in foods, there are several methods, including their immersion at high temperatures, fermentation, extrusion, roasting, bleaching and germination.[6] Addo et al.[6] reported contents of oxalate, phytate and tannin (0.43-0.48 g/100 g, 0.23-0.30 g/100 g and 5.06-6.45 g/100 g, respectively) in watermelon seeds. Those authors showed that thermal processing allowed the decrease of oxalate (~92-96%), phytate (~73-82%) and tannin (~23-38%) contents. Another study described saponin (2.31mg/100 g), alkaloid (0.36 mg/100 g), and tannins (0.61 mg/100 g) as the major antinutrients in watermelon seeds.[64] Atolani et al.[65] have concluded that watermelon seeds oil showed a relatively moderate cytotoxicity. Since these antinutrients may be found in low amounts in watermelon seeds, these by-product shows pharmacologic and dietary benefits with low toxic risk.[18,66]

2.5. Watermelon seeds as potential functional foods

Watermelon seeds are usually discarded as by-products of food processing, but they contain a rich stock of nutrientes, such as proteins, unsaturated fatty acids, phenolic acids, carotenoids, among others, exerting biological activity, and do not contain any major anti-nutrient,[18] which indicate their potential uses as dietary supplement in relevant applications, namellyto formulate nutraceuticals.[21]

Since seed extracts possess antioxidative, anticancer, antihypertensive, cardioprotective, antimicrobial, among others, this by-product shows good functional properties and contains a high content of several nutrients, so that it can be used as a dietary supplement or a food additive.[21,23] The watermelon seeds proved to be very versatile and, in economic terms, the use of this by-product is quite beneficial, since they can be used in a wide variety of ways, for instance, snacks, oil and grounds in flours.[21,37] Also, the addition of watermelon seed flour increases the thickness, nutrition and flavor, ultimately enriching food.[7,21] Watermelon seeds oil contains several fatty acids, mainly mono- and polyunsaturated, showing up as a potential functional food.[67] Thus, seeds oil can be used in cooking, as well as in pharmaceutical and cosmetic industries.[18,24]

Still from a functional food perspective, watermelon seeds contain high amount of nutritional proteins, usefull to produce cereal based products due to their health promoting benefits.[5] Protein malnutrition affects many developing countries, as large numbers of people do not have access to a cheap source of protein. Watermelon seeds present a high protein content, so they could be used as a food supplement to solve this worldwide problem.[23] Also, plant seed proteins provide several beneficial properties like antimicrobial, antihypertensive, antiviral and antioxidant.[18,24] Taking this into account, Sonawane and Arya,[68] prepared cookies with wheat flour fortified with watermelon seeds, improving their protein quality. Those cookies improved with watermelon seeds protein, presented a lower carbohydrates content. Lakshmi and Kaul,[66] prepared a defatted flour and a protein isolate from watermelon seeds meal. These authors concluded that watermelon seeds are a good protein source, with a moderate quality with methionine and cysteine as limiting amino acids.

The protein isolated presented good digestibility *in vitro*, higher than wheat flour. Bioaccessible zinc and iron was higher in protein isolate than in defatted flour, and the latter is superior to that of the whole meal. So, protein isolate was a good source of iron and zinc contents. The functional properties of the watermelon seeds proteins were good, suggesting their chemical composition its suitability as a matrix for mineral fortification, suitable for food formulations. Functional molecules could be produced by environmentally friendly methods from watermelon seeds, with potential applications in industry.[14]

3. CONCLUSION

The emergence of sustainable development has promoted the orientation of efforts towards finding ways for environmental protection. In view of the above, in recent years, there has been an increase in interest on the part of industries and research centers in reusing food by-products, valuing their potential as future ingredients and / or foods.

Watermelon (*Citrullus lanatus*) is one of the most consumed fruits and the second most produced worldwide. Its composition has a large percentage of water, an extremely high nutritional value, and a low energy value. Watermelon seeds, despite having a high nutritional and energy value, are usually discarded as a food by-product. However, it was found that these seeds contain high levels of protein, unsaturated fatty acids, vitamins and minerals. In addition to these nutrients, they also contain some phytochemicals such as phenolic acids (hydroxybenzoic and hydroxycinnamic), flavonoids, alkaloids and saponins, which give watermelon seeds biological properties: antioxidant, antineoplastic, hypoglycemic, antihypertensive, antilipidemic, antibacterial, cardioprotective, among others. Considering the scarcity of information about these seeds, their possible toxicity was investigated, and some articles were found that reported the presence of tannin, phytate and oxalate that inhibit the absorption of proteins, vitamins and minerals. Despite the presence of these antinutrients, it was found that it is possible to reduce their concentration through cooking methods, and the best method is to dry the seeds in a boiling oven.

It has also been proven that these seeds can be used in various ways in food: toast, in flour, oil, sauces, broths and as a seasoning. Due to their nutritional and pharmacological richness, they can also be used in nutritional supplements, in the incorporation of drugs with therapeutic effects in the treatment and prevention of various pathologies and in cosmetics.

REFERENCES

1. Schaefer H, Renner SS. (Phylogenetic relationships in the order Cucurbitales and a new classification of the gourd family (Cucurbitaceae)). Taxon, 2011; 60(1): 122-138.
2. Bomfim IGA, Cruz DO, Freitas BM, Aragão F.AS. Polinização em melancia com e sem semente. 1st ed. Embrapa Agroindústria Tropical, Fortaleza, 2013.
3. FAO, Food and Agriculture Organization of the United Nations. Moving forward on food loss and waste reduction food and agriculture, Rome, 2019. http://www.fao.org/3/ca6030en/ca6030en.pdf.
4. Dube J, Ddamulira G, Maphosa M. (Watermelon production in Africa: challenges and opportunities). Int J Veg Sci, *in press*, 2020.
5. Tabiri B, Agbenorhevi J, Wireko-Manu FD, Ompouma EL. (Watermelon seeds as food: nutrient composition, phytochemicals and antioxidant activity). Int J Nutr Food Sci, 2016; 5(2): 139-144.
6. Addo PW, Agbenorhevi JK, Poku DA. (Antinutrient contents of watermelon seeds). MOJ Food Process Technol, 2018; 6(2): 237-239.
7. Tak J, Jain S. (Nutrient potential of watermelon (*Citrullus lanatus*) seeds and its incorporation in product preparation). Food Sci Res, 2016; 7(2): 202-206.
8. Hodges D, Lester GE. Cucurbits [Cucumber, melon, pumpkin and squash]. In: Terry, L., editor. Health-Promoting Properties of Fruit and Vegetables. Wallingford, UK: CABI Publishing, 2011; 118-134.
9. Nollet LML, Toldra F. Handbook of Analysis of Active Compounds in Functional Foods. CRC Press, 2012. ISBN 9781439815885.
10. Naz A, Butt MS, Sultan MT, Qayyum MMN, Niaz RS. (Watermelon lycopene and allied health claims). EXCLI Journal, 2014; 13: 650-660.
11. Raihana ARN, Marikkar JMN, Amin I, Shuhaimi M. (A review on food values of selected tropical fruits' seeds). Int J Food Prop, 2015; 18(11): 2380-2392.
12. Sousa C, Vinha A, Nunes A. Desperdícios da vinicultura: potenciais aplicações e sustentabilidade – Subprodutos da produção vinícola, Alemanha, Novas Edições Acadêmicas (OmniScriptumAraPersGmbH), 2017. ISBN: 978-3-330-20104-0.
13. Vinha AF, Sousa C, Oliveira MBPP. Food waste and by-producs recovery: nutraceutical and health potential of carotenoids as natural pigments. Lambert Academic Publishing, 2020; 1st ed.
14. Rico X, Gullón B, Alonso JL, Yáñez R. (Recovery of high value-added compounds from pineapple, melon, watermelon and pumpkin processing by-products: An overview). Food Res Int, 2020; 132: 109086.
15. Avinash TS, Rai VR. (An ethanobotanical investigation of cucurbitaceae from South India: A review). J Med Plants Stud, 2017; 5(3): 250-254.
16. Karrar E, Sheth S, Navicha WB, Wei W, Hassanin H, Abdalla M, Wang X. A potential new source: nutritional and antioxidant properties of edible oils from cucurbit seeds and their impact on human health). J Food Biochem, 2019; 43(2): e12733.
17. Jorge N, Silva AC, Malacrida CR. (Physicochemical characterization and radical-scavenging activity of

Cucurbitaceae seed oils). Nat Prod Res, 2015; 29(24): 2313-2317.
18. Logaraj TV. Watermelon (*Citrullus lanatus* (Thunb.) Matsumura and Nakai) seed oils and their use in health. *In*: Nuts and Seeds in Health and Disease Prevention, 2011; 136: 1149-1157.
19. 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.
20. Braide W, Odiong IJ, Oranusi S. (Phytochemical and antibacterial properties of the seed of watermelon (*Citrullus lanatus*)). Prime J Microbiol Res, 2012; 2(3): 99-104.
21. Patel S, Rauf A. (Edible seeds from Cucurbitaceae family as potential functional foods: immense promises, few concerns). Biomed Pharmacother, 2017; 91: 330-337.
22. Olayinka BU, Etejere EO. (Proximate and chemical compositions of watermelon (*Citrullus lanatus* (Thunb.) Matsum and Nakai cv Red and Cucumber (Cucumis sativus L. cv Pipino). Int Food Res J, 2018; 25(3): 1060-1066.
23. Otutu OL, Seidu KT, Muibi BO, Oladokun F, Oyalowo MR. (Potential food value of watermelon (*Citrulluslanatus*) seed constituents). Int J Sci Technol, 2015; 3(7): 222-231.
24. Ajuru M, Nmom F. (A review on the economic uses of species of Cucurbitaceae and their sustainability in Nigeria). Am J Plant Biol, 2017; 2(1): 17-24.
25. Pereira TA, Guerreiro CM, Maruno M, Ferrari M, Rocha-Filho PA. (Exotic vegetable oils for cosmetic O/W nanoemulsions: in vivo evaluation). Molecules, 2016; 21(3): 248-264.
26. Rai A, Mohanty B, Bhargava R. (2015). (Modeling and response surface analysis of supercritical extraction of watermelon seed oil using carbon dioxide). Sep PurificTechnol, 2015; 141: 354-365.
27. Tungmunnithum D, Thongboonyou A, Pholboon A, Yangsabai A. (Flavonoids and other phenolic compounds from medicinal plants for pharmaceutical and medical aspects: an overview). Medicines, 2018; 5(3): 93.
28. Lin D, Xiao M, Zhao J, Li Z, Xing B, Li X, Kong M, Li L, Zhang Q, Liu Y, Chen, H, Qin W, Wu H, Chen S. (An overview of plant phenolic compounds and their importance in human nutrition and management of type 2 diabetes). Molecules, 2016; 21(10): 1374-1392.
29. Sales PM, Souza PM, Simeoni LA, Magalhães PO, Silveira D. (α-Amylase inhibitors: a review of raw material and isolated compounds from plant source). J Pharm Sci, 2012; 15(1): 141-183.
30. Tarazona-Díaz MP, Aguayo E. (Influence of acidification, pasteurization, centrifugation and storage time and temperature on watermelon juice quality). J Sci Food Agric, 2013; 93(15): 3863-3869.
31. Tarazona-Díaz MP, Ascensión MS, Aguayo E. (Preservation of bioactive compounds and quality parameters of watermelon juice enriched with L-citrulline through short thermal treatment). J Food Qual, 2017. Article ID 3283054.
32. Rogers JM, Gills J, Gray M. (Acute effects of Nitrosigine® and citrulline malate on vasodilation in young adults). J Int Soc of Sports Nutr, 2020; 17: 12.
33. Sampaio GLA, Pacheco S, Ribeiro APO, Galdeano MC, Gomes FS, Tonon RV. (Encapsulation of a lycopene-rich watermelon concentrate in alginate and pectin beads: Characterization and stability). LWT - Food Sci Technol, 2019; 116: 108589.
34. Becraft AR, Sturm ML, Mendez RL, Park SH, Lee SI, Shay NF. (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(3): 434-442.
35. Stafussa A, Maciel G, Rampazzo V, Bona E, Makara C, Junior B, Haminiuk C. (Bioactive compounds of 44 traditional and exotic Brazilian fruit pulps: phenolic compounds and antioxidant activity). Int J Food Prop, 2018; 21(1): 106-118.
36. Abu-Reidah IM, 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(1): 354-362.
37. Maoto MM, Beswa D, Jideani AIO. (Watermelon as a potential fruit snack). Int J Food Prop, 2019; 22(1): 355-370.
38. Deshmukh CD, Jain A, Tambe MS. (Phytochemical and pharmacological profile of *Citrullus lanatus* (Thunb)). Biolife, 2015; 3(2): 483-488.
39. Wang M, Zhang L, Wu X, Zhao Y, Wu L, Lu B. (Quantitative determination of free and esterified phytosterol profile in nuts and seeds commonly consumed in China by SPE/GC–MS). LWT - Food Sci Technol, 2019; 100: 355-361.
40. Jeong GS, Li B, Lee DS, Kim KH, Lee IK, Lee KR, Kim YC. (Cytoprotective and anti-inflammatory effects of spinasterol via the induction of heme oxygenase-1 in murine hippocampal and microglial cell lines). Int. Immunopharmacol, 2010; 10: 1587-1594.
41. Bhatt MZ, Saeed A, Marwat MS, Shah AH, Naz R, Abidin SZU, Akbar S, Khan R, Navid MT, Saeed, A. (Assessment of total phenolic and flavonoid contents of selected fruits and vegetables). Indian J Tradit Knowl, 2019; 18(4): 686-693.
42. Fadimu GJ, Ghafoor K, Babiker EE, Al‐Juhaimi F, Abdulraheem RA, Adenekan MK. (Ultrasound-assisted process for optimal recovery of phenolic compounds from watermelon (*Citrullus lanatus*) seed and peel). J Food Meas Charact, 2020; 14: 1784-1793.
43. Rajasree RS, Sibi PI, Francis F, William H. Phytochemicals of Cucurbitaceae family – A review.

Int J Pharmacogn Phytochem Res, 2016; 8(1): 113-123.
44. Simpson R, Morris GA. (The anti-diabetic potential of polysaccharides extracted from members of the cucurbit family: A review). Bioact Carbohydr Diet Fibre, 2014; 3(2): 106-114.
45. Biswas R, Chattopadhyay A, De SD. (Hypoglycemic and hypolipidemic effects of watermelon (*Citrullus vulgaris*) seed kernels on male albino rats). Curr Res Nutr Food Sci, 2017; 5(3): 368-373.
46. Siddiqui WA, 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.
47. Okpo SO, Nnajekwu OC. (In vitro anthelmintic activity of the seed extracts of three plants of the Cucurbitaceae family on Lumbricusterrestres). J Pharm Biores, 2012; 9(2): 92-98.
48. Sola AO, Ogunmefun OTO, Olufunke FS. (Chemical composition, nutritional values and antibacterial activities of watermelon seed (*Citrullus lanatus*). Int J Biochem Res Rev, 2019; 27(1): 1-9.
49. Wahid S, Khan RA, 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(3): 1049-1055.
50. Babaiwa, UF, Erharuyi O, Falodun AO, Akerele J. (Antimicrobial activity of ethyl acetate extract of *Citrullus lanatus* seeds). Trop J Pharm Res, 2017; 16(7): 1631-1636.
51. Acar R, Ozcan MM, Kanbur G, Dursun N. (Some physico-chemical properties of edible and forage watermelon seeds). Iran J Chem Eng, 2012; 31(4): 41-47.
52. Wen C, Zhang J, Feng Y, Duan Y, Ma H, Zhang H. (2020). (Purification and identification of novel antioxidant peptides from watermelon seed protein hydrolysates and their cytoprotective effects on H_2O_2-induced oxidative stress). Food Chem, 2020; 327: 127059.
53. Onyinye AV, Emeka AG. (*Citrullus lanatus* ethanolic seed extract improved male sexual behavior in rats via enhancement of sexual hormone and hypothalamic-pituitary-gonadal pathway). J Krishna Inst Medical Sci Univ, 2019; 8(3): 96-107.
54. Adedeji GT, Bamidele O, Ogunbiyi A. (Haematological and biochemical properties of methanolic extract of *Citrullus lanatus* seeds). Brit J Pharm Res, 2017; 15(6): 1-10.
55. Zhan YY, Wang JH, Tian X, Feng SX, Xue L, Tian LP. (Protective effects of seed melon extract on CCl4-induced hepatic fibrosis in mice). J Ethnopharmacol, 2016; 193: 531-537.
56. Omigie I, Agoreyo F. (Effects of watermelon (*Citrullus lanatus*) seed on blood glucose and electrolyte parameters in diabetic wistar rats). Journal of Applied Sciences and Environmental Management, 2014; 18(2): 231-233.
57. Lucky OO, John UO, Kate IE, Peter OO, Jude OE. (2012). (Quantitative determination, metal analysis and antiulcer evaluation of methanol seeds extract of *Citrullus lanatus* Thunb (Cucurbitaceae) in rats). Asian Pac J Trop Dis, 2012; 2(3): S1261-S1265.
58. Poduri A, Rateri DL, Saha SK, Saha S, Daugherty A. (*Citrullus lanatus* `sentinel' (watermelon) extract reduces atherosclerosis in LDL receptor deficient mice). J Nutr Biochem, 2013; 24(5): 882-886.
59. 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(7): 1679.
60. Danlami U, Machan BD, Joshua M, Galadanchi KM, Dare OS. (Proximate, mineral composition, phytochemical constituents and characterization of oil of *Citrullus lanatus* seeds). Am J Biosci Bioeng, 2015; 3(5): 72-75.
61. Oelschlägel S, Menzel C, Speer K. (Phytosterols and steryl esters in diverse *Cucurbita*, *Cucumis* and *Citrullus* seed oils). Lipid Technol, 2012; 24(8): 181-184.
62. Popova A, Mihaylova D. (Antinutrients in plant-based foods: a review). Open Biotechnol J, 2019; 13: 68-76.
63. García-Fernández AJ, Espín S, Gómez-Ramírez P, Martínez-López E. Oxalates. In: Encyclopedia of Toxicology. 3rd Ed., 2014; 730-734.
64. Egbuonu ACC. (Assessment of some antinutrient properties of the watermelon (*Citrullus lanatus*) rind and seed). Res J Environ Sci, 2015; 9(5): 225-232.
65. Atolani O, Omere J, Otuechere CA, Adewuyi A. (Antioxidant and cytotoxicity effects of seed oils from edible fruits). J Acute Dis, 2012; 1(2): 130-134.
66. Lakshmi AJ, Kaul P. (Nutritional potential, bioaccessibility of minerals and functionality of watermelon (*Citrullus vulgaris*) seeds). LWT - Food Sci Technol, 2011; 44: 1821-1826.
67. Mahla HR, Rathore SS, Venkatesan K, Sharma R. (Analysis of fatty acid methyl esters and oxidative stability of seed purpose watermelon (*Citrullus lanatus*) genotypes for edible oil). J Food SciTechnol, 2018; 55(4): 1552–1561.
68. Sonawane SK, Arya SS. (Plant seed proteins: chemistry, technology, and applications). Curr Res Nutr Food Sci, 2018; 6(2): 461-469.