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Review

Horned Melon (*Cucumis metuliferus* E. Meyer Ex. Naudin)—Current Knowledge on Its Phytochemicals, Biological Benefits, and Potential Applications

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Abstract: Recent studies reveal that numerous non-edible parts of fruits and vegetables, as well as food wastes, are a good source of phytochemicals that can be extracted and reintroduced into the food chain as natural food additives. Horned melon or kiwano (*Cucumis metuliferus* E. Mey. Ex. Naudin) is a fruit rich in various phytochemical components important in the daily diet. After primary processing, horned melon non-edible parts (e.g., peels and seeds) can represent raw materials that can be utilized in numerous applications. Among under-researched fruits, this study aims to present the potential of using horned melon edible and non-edible parts based on current knowledge on nutritional value, phytochemicals, biological activity, as well as biological benefits. Overall, this review concluded that the biological properties of horned melon are associated with the phytochemicals present in this fruit and its waste parts. Further studies should be conducted to identify phytochemicals and valorize all horned melon parts, assess their biological efficacy, and promote their potential uses in different health purposes.

Keywords: horned melon; kiwano; phytochemicals; antifungal potential; medicine plant with prospective benefits

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1. Introduction

Current trends in the food industry refer to the continuous search for healthy products since the worldwide health crisis redirected the consumer attitude, perception, and awareness to a diet rich in natural and high-quality products [1]. The phytochemicals derived from different plants, fruits, and vegetables have been extensively studied through numerous applications to maintain food quality, food safety, and appeal, or as food additives or nutraceuticals to improve nutritional quality and support physiological functions [2]. Phytochemicals refer to all compounds which are naturally present in foods that exert a specified biological effect on the human body. Recent studies reveal that numerous food wastes and non-edible parts are a good source of phytochemicals that can be extracted and reintroduced into the food chain as natural food additives [3]. This approach is supported by a circular economy that encompasses the valorization of waste, allowing for the extraction of novel ingredients by returning them to the supply chain and boosting the economy while reducing the environmental impact [4].

Cucumbers (Cucumis) were previously grown in the area of Ancient Egypt, while today they are a food that is consumed daily all over the world, especially in Africa, Asia, Australia, and some islands in the Pacific. This genus contains over 30 species, among which the two most famous commercial products are *Cucumis sativus* and *Cucumis melo*, better known as cucumber and melon. However, the use of *Cucumis anguria* (gherkin) and *Cucumis metuliferus* (horned melon) is on the rise due to their ability to grow very

successfully outside the characteristic geographical area of growth, which is primarily Africa [5].

Horned melon or kiwano (*Cucumis metuliferus* E. Mey. Ex. Naudin) is a fruit rich in various phytochemical components important in the daily diet. As a spiky orange oddity crammed with green jelly and white seeds, the horned melon has become a global fruit in recent decades. Due to the remarkable ease of expansion of this fruit, horned melon could represent an economically advantageous nutritional source to alleviate malnutrition or provide phytochemicals to the food and pharmaceutical industries [6]. In addition to consumer use, the importance of fruits is reflected in the phytochemical composition of non-edible parts that have low commercial value, but with appropriate technology, it can be used as a renewable source of added-value bioactive compounds. Considering there exist only a few scientific papers dealing with this fruit, the aim of this study is to summarize the current knowledge on the phytochemicals, biological benefits, and potential applications of horned melon edible end non-edible parts (pulp, peel, and seed).

2. Taxonomic Classification and Botanical Features of Horned Melon

Horned melon represents one of the most promising species belonging to the Cucurbitaceae family due to its exceptional characteristics. The taxonomic classification of horned melon is presented in Table 1. This fruit is available for approximately three and a half months in two seasons, namely early spring and autumn. They are characterized by rapid growth, as well as by the fact that they do not tolerate low temperatures. During growth, they need a large amount of water, so if it is a dry season, irrigation is necessary. This plant tolerates a wide range of soil types with a preference for well-drained sandy or loam soils, thus it can grow in the semievergreen forest, woodland, wooded grassland, grassland, and abandoned cultivated areas as well [7,8].

Table 1. Taxonomic classification of horned melon.

Horned Melon	
Domain	Eukaryota
Kingdom	Plantae
Subkingdom	Tracheobionta
Phylum	Spermatophyta
Subphylum	Angiospermae
Class	Magnoliopsida
Order	Violales/Curcubitales
Family	Cucurbitaceae
Genus	*Cucumis*
Species	*Cucumis metuliferus*

The origin of horned melon is common to the cucumber family and refers to Africa, above all Nigeria. Today it is grown in Australia, Kenya, Israel, California, Chile, and New Zealand. The fruit is ellipsoidal-shaped, with an average length of about 12 cm and a diameter of about 8 cm. The color of the horned melon changes during maturing from green to orange with green stripes. The surface of the horned melon fruit contains conical protrusions with thorns, which can be easily removed when the fruit matures. Inside, the pulp is a juicy green slimy mass with numerous smooth white seeds. Seeds are white, about 5 to 9 mm long, edible, ellipsoid, flattened, and there are hundreds per fruit [7,9]. The main parts of the horned melon are presented in Figure 1.

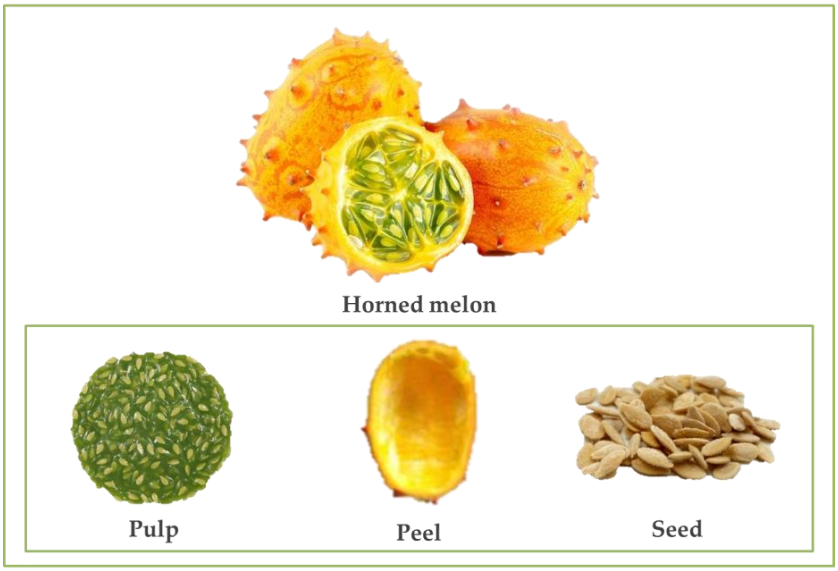

Figure 1. The main structural parts of horned melon fruit.

3. How to Eat and Store a Horned Melon?

Horned melon is often used raw or cooked. The taste of this fruit is represented as a mix of cucumber and (green) banana. In Africa, horned melon is often eaten whole after roasting or boiling together with other vegetables. Although the peel is edible, these are usually eaten without the peel in Europe and America. Eating a juicy green pulp with a jellylike texture, with a relatively soft seed incorporated in the pulp is the most common use of horned melon. Once sliced open, it is easy to extract the pulp, which can be enjoyed as is or when simply added to fruit salads, dairy products, or beverages, or turned into certain food products. In the past decades, some cultivars were improved in view of taste, decreasing the bitterness but increasing the sweetness and overall flavor [10].

Additionally, out of all fruit, horned melon has the best shelf life. The fruits can remain at room temperature for six months, even in tropic areas. Requirements and general characteristics for a storage facility of horned melon are temperatures between 10 and 15 °C, a relative humidity of 90%, and a storage life of 180 days. Horned melon is usually room-cooled. In addition, it has been noticed that they are ethylene-sensitive but not an ethylene producer, odor producer, nor sensitive. Furthermore, these fruits are sensitive to chilling injury [11]. The fruits are best preserved when they do not touch each other because otherwise these can cause damage caused by thorns that are characteristic of the outer surface of the peel [6,7].

4. Nutritional Composition of Horned Melon

Given the fact that some people consume the whole horned melon fruit, it is very important to summarize the nutritional features of each edible and non-edible part, i.e., the pulp, peel, and seed (Table 2). The nutritional composition of horned melon is affected by the fruit maturity degree [6]. In general, horned melon is more nutritious than cucumber, with significantly higher contents for more nutrients.

4.1. Horned Melon Pulp

Figure 2 shows that fresh horned melon pulp has a high-water content (89–96.0 g/100 g) and low levels of calories (22–44 kcal/100 g), carbohydrates (7.56 g/100 g), fiber (4–4.20 g/100 g), lipids (0.03–1.26 g/100 g), and proteins (1.78–1.80 g/100 g) [12]. The pulp also contains a high vitamins content; high concentrations were noted for complex B vitamins and vitamin C, while a lower concentration was determined for vitamin A [12] (Table 2). In contrast, Rowero-Rodriguez [13] and Ferrera et al. [6] detected significantly lower values for vitamin C content. Several researchers suggested that horned melon pulp also stands

out for its mineral content, particularly for potassium, phosphorus, magnesium, calcium, iron, sodium, zinc, and copper [6,12,13].

Vitamins are essential nutrients that cannot be synthesized by the organism and are required in small quantities in the diet of humans to sustain metabolism and life. The complex B vitamins and vitamin C are water-soluble, hence contributing to various metabolic processes. Vitamin A is essential for vision and also serves as an effective antioxidant. The minerals content is also an important nutritional characteristic for horned melon pulp since it plays an important role in growth, bone and teeth health, fluid balance, and several other processes. Potassium, phosphorus, magnesium, and other minerals present in horned melon pulp are significant for nerve transmission, muscle contraction, blood clotting, blood pressure regulation, immune system health, etc. [14].

4.2. Horned Melon Peel

Figure 2 presents the nutritional quality of fresh horned melon peel that has been recently studied by Ezekaibeya et al. [15]; the authors reported high values for carbohydrates (54.80 g/100 g) and fiber (11.30 g/100 g). Other proximate composition values were in the following ranges: moisture (18.4 g/100 g), lipids (8.89 g/100 g), and proteins (2.95 g/100 g). Vitamin C is the principal vitamin, followed by vitamin E, vitamin D, folic acid, vitamin A, riboflavin, vitamin K, and thiamin (Table 2). Vitamin C and E are essential antioxidants that protect cells from oxidative stress-induced cellular damage by scavenging reactive oxygen species [16]. Fat-soluble vitamins, such as vitamin D, E, K, and A, are important in lipid metabolism [17]. Vitamin K concentration, as reported by Ezekaibeya et al. [15], is higher than the recommended daily allowance (RDA) of 70 to 140 µg for an adult. The same observation is also related to thiamine, folic acid, and riboflavin values, which are slightly higher than the RDA for adults. Thiamine and folic acid serve as coenzymes in synthetic and metabolic processes, while riboflavin is an essential vitamin for oxidative phosphorylation [18]. Data on the mineral content of horned melon peel is not available in the literature.

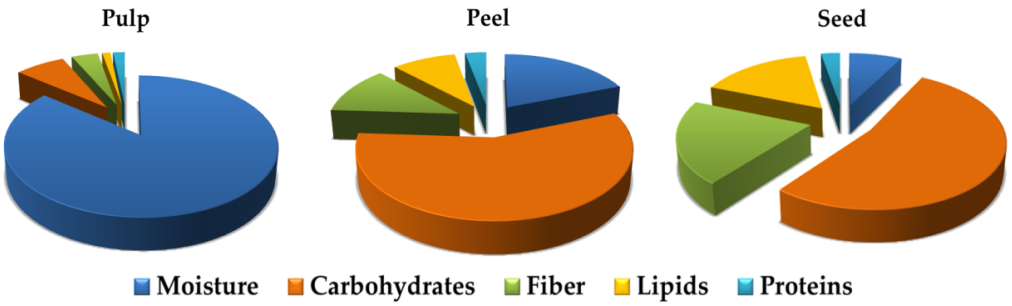

Figure 2. Nutritional composition of raw horned melon fruit [12,13,15,18].

4.3. Horned Melon Seed

Figure 2 shows the nutritional composition of horned melon seed as reported by two authors [18,19]. According to Achikanu et al. [18], the horned melon seed is rich in calories (386 kcal/100 g), carbohydrates (50.2 g/100 g), fiber (19.2 g/100 g), and lipids (15.4 g/100 g), while lower contents are noted for the moisture content (7.31 g/100 g) and proteins (2.63 g/100 g). In contrast, Sadou et al. [19] reported a significantly higher value for lipids and proteins in horned melon seed (23.8 and 23.2 g/100 g, respectively). Table 2 lists the current reported values for the vitamins and minerals present in the horned melon seed. Fat-soluble vitamins (D, E, K, and A) and complex B vitamins (thiamin, folic acid, and riboflavin) are present in higher concentrations than water-soluble vitamin C. These vitamins act as a potent antioxidant for the management of free radical-related diseases, such as cardiovascular diseases, Parkinson's and Alzheimer's diseases, and diabetes [5].

Table 2. Vitamin and mineral contents of horned melon pulp, peel, and seed. fw—fresh weight.

	Horned Melon					
	Pulp [6,12,13]			Peel [15]	Seed [18,19]	
Vitamins (mg/g fw)						
Thiamin (B1)	0.025	-	-	1.69	-	2.20
Riboflavin (B2)	0.015	-	-	1.74	-	1.72
Niacin (B3)	0.565	-	-	-	-	-
Pantothenic acid (B5)	0.183	-	-	-	-	-
Pyridoxine (B6)	0.063	-	-	-	-	-
Folic acid (B9)	0.003	-	-	1.93	-	2.10
Vitamin C	5.30	0.50	0.60	3.44	-	1.72
Vitamin A	0.007	-	-	1.85	-	2.22
Vitamin D	-	-	-	2.28	-	1.86
Vitamin E	-	-	-	2.92	-	2.05
Vitamin K	-	-	-	1.69	-	2.58
Minerals (mg/100 g fw)						
Sodium	2	5.60	2.30	-	247	-
Calcium	13	17	16	-	247	-
Iron	1.13	0.50	0.50	-	10.90	-
Magnesium	40	23	16.2	-	289	-
Phosphorus	37	50	50	-	44.70	-
Potassium	123	266	302	-	1174	-
Zinc	0.48	0.20	0.20	-	1.70	-
Copper	-	0.10	-	-	5.40	-
Manganese	0.039	0.20	0.10	-	-	-

5. Phytochemical Composition of Horned Melon

Phytochemicals are compounds that occur naturally in plants as secondary metabolites. Many epidemiological studies have reported stating that phytochemicals possess significant antioxidant activities, which is also linked with the prevention and therapy of certain chronic diseases [20]. Horned melon has an array of characteristic secondary metabolites, which are presented in Table 3.

5.1. Horned Melon Pulp

The pulp of horned melon fruit is reported to contain 47.2–200 mg GAE/100 g dw of total phenolics depending on the type of extract (water, ethanol, or their mixture) [21–23]. According to the reports of Ferrara [6], the horned melon pulp contains lower levels of flavonol aglycones (myricetin and quercetin) and high amounts of flavonol glycosides (rutin). Busuioc et al. [24] investigated the chemical composition of horned melon fresh juice cultivated in Romania. According to these authors, the horned melon juice contains a large number of triterpenes and significant amounts of both polyphenols and flavonoids. The main metabolites were catechin (928.74 mg/kg), followed by oleanolic (347.67 mg/kg) and ursolic acids (193.92 mg/kg). Catechin is a flavonoid that presents a high antioxidant activity in living systems, while ursolic acid is known for its activity against HIV-1 protease, which is a homodimeric enzyme [24]. Other phytochemicals occurring at noteworthy levels in horned melon juice were rutin (33.78 mg/kg), kampferol-3-glucoside (19.61 mg/kg), epicatechin (17.66 mg/kg), *p*-coumaric acid (6.99 mg/kg), quercetin (5.96 mg/kg), gallic acid (5.76 mg/kg), caffeic acid (5.56 mg/kg), neochlorogenic acid (4.68 mg/kg), kampferol (4.32 mg/kg), and quercetin-3-d-galactoside (2.35 mg/kg) [24]. Carotenoids are less abundant bioactives in horned melon pulp (88 µg β-carotene/100 g dw) [12].

Table 3. Phytochemical composition of horned melon pulp, peel, and seed. dw—dry weight.

	Horned Melon		
Compound	**Pulp [24]**	**Peel [15]**	**Seed [18,19]**
Flavonoids	Rutin, quercetin, quercetin-3-d-galactoside, kampferol-3-glucoside, and kamferol	1.71 mg/g dw	0.97 mg/g dw
Phenolics	Gallic acid, catechin, epicatechin, neochlorogenic acid, caffeic acid, p-coumaric acid, oleanolic acid, and ursolic acid	1.54 mg/g dw	1.20 mg/g dw
Tannins	-	1.38 mg/g dw	2.93 mg/g dw
Alkaloids	-	1.06 mg/g dw	2.54 mg/g dw
Steroids	-	0.93 mg/g dw	2.62 mg/g dw
Carotenoids	β-carotene	-	1.56 mg/g dw; 130 mg/g dw
Glycosides	-	2.19 mg/g dw	-
Saponins	-	0.72 mg/g dw	1.41 mg/g dw
Fatty acids	-	-	C14:0, C16:0, C18:0, C20:0, C16:1n-9, C18:1n-9, C18:1n-7 C8:2n-6, C18:3n-3
Tocopherols	-	-	α-tocopherol, γ-tocopherol

5.2. Horned Melon Peel

Peels of kiwano fruit, in contrast, have more phenolics than pulp, specifically up to 500 mg GAE/100 g dw [22]. Ezekaibeya et al. [15] found that flavonoids (171 mg/100 g) and tannins (138 mg/100 g) are the major bioactive compounds in kiwano peels. Besides polyphenols, kiwano peels are also a source of alkaloids (106 mg/100 g), steroids (93 mg/100 g), and glycosides (219 mg/100 g). Reports for the contents of carotenoids in peels are scarce.

5.3. Horned Melon Seed

Polyphenols are also highly abundant in kiwano seeds (up to 400 mg GAE/100 g dw) [22]. Similar to peels, tannins (293 mg/100 g dw) are also the major class of polyphenols, while alkaloids (254 mg/100 g) and steroids (262 mg/100 g) are even more abundant than in peels [18]. Kiwano seeds are also a better source of carotenoids (156–13000 mg β-carotene/100 g dw) compared to fruit pulp [18,19]. Sadou et al. [19] investigated the fatty acid composition of horned melon seed oil. The principal fatty acids are linoleic acid (56.21%) and oleic acid (18.6%), followed by palmitic acid (16.2%) and stearic acid (7.65%). Dietary supplementation with these fatty acids has provided evidence for their cardiovascular protective effects and ability to lower blood pressure [25]. In addition, Sadou et al. [19] reported the profile in antioxidants of the horned melon seed oil; the high content of α and γ-tocopherols were determined (79.9 and 517 g/100 g, respectively). The consumption of these two tocopherols is correlated with the prevention of cardiovascular diseases, cancer, and inflammatory processes. β-carotene also exercise a beneficial effect against atherosclerosis and vascular diseases. In fact, like tocopherols, βcarotene would increase the low-density lipoproteins' (LDL) resistance against oxidation [19].

6. Biological Benefits of Horned Melon

Biological benefits of horned melon result from the presence of bioactive antioxidants which protect the cells and their structures against oxidative damage. Studies on macromolecules (DNA, nucleotides, and proteins) free radical-related damage showed that diets rich in polyphenols, carotenoids, ascorbic acid, tocopherols, and other antioxidants contribute to the inhibition of oxidation processes. The antioxidant potential is strongly correlated with the reduction in the risk of various human diseases, which is not only due to the effect of individual antioxidants but also may be the result of their synergy [2].

6.1. Antioxidant Potential

Different studies have been proven the antioxidant potential of the edible parts (pulp) as well as non-edible parts (seed and peel) of horned melon. The findings from the study of Bolek [26] have revealed that horned melon seeds contain a rich amount of nutrients and phytochemicals with high radical scavenging potential. The ability of horned melon methanol extract to scavenge DPPH and ABTS radicals was 20.88 and 185.36 µmol Trolox equivalent per g, respectively. Matsusaka and Kawabata [22] analyzed the total phenolics and antioxidant activities of non-edible parts (seed and peel) of eight tropical fruits (including horned melon) and compared them to those of their edible parts. According to the authors, horned melon and papaya peels showed a strong ferrous ion-chelating capacity, although they did not have a high phenolic content. Furthermore, horned melon peel exhibited DPPH and ABTS radical scavenging activities as well. Mester et al. [23] investigated the phenolic profile and antioxidant activity of some species of the Cucurbitaceae family, namely cucumber (*C. sativus*), bitter melon (*M. charantia*), zucchini or courgette (*C. pepo*), and horned melon (*C. metuliferus*). Authors reported that the highest DPPH radical scavenging activities possess the *C. metuliferus* extract (11.16%), while the *C. sativus* plant extract has the lowest antioxidant potential (2.35%). In the study of Arrieta et al. [21], the extraction of antioxidant compounds from horned melon was optimized by evaluating extraction procedures using different solvents, including water, ethanol, and ethanol 50%. As output parameters, two antioxidant assays were used: Ferric Reducing Antioxidant Power (FRAP) and ABTS radical scavenging activity. Aqueous and 50% ethanol extract exhibited higher FRAP values (238.6 and 241. mg TE/100 g fruit, respectively). In terms of ABTS, no significant differences were observed between the three extracts (8–9.6 mg TE/100 g fruit). These results can be related to the fact that the FRAP method is more specific for hydrophilic antioxidants, while ABTS is a good method for evaluating both lipophilic as well as hydrophilic antioxidants [27]. Motlhanka et al. [28] also investigated the antioxidant activity of horned melon pulp and peel extracts (aqueous, methanolic, and chloroformic) using the DPPH assay; the results indicated that the aqueous extract exhibited the strongest antioxidant capacity, while the methanolic extract possessed a moderate antioxidant response and low activity in chloroform.

6.2. Health Benefits of Horned Melon in Specific Disease Conditions

Next, we discuss cardiovascular diseases. According to the World Health Organization database, cardiovascular diseases caused 17.9 million deaths in 2016, accounting for 31% of all global deaths. However, many epidemiological studies and clinical trials confirmed that cardiovascular diseases may be preventable with a healthy diet rich in different kinds of fruits and vegetables. In the literature, scarce information about the association between horned melon consumption and cardiovascular diseases is available. Usman et al. [5] reported that horned melon seeds contain linoleic and oleic acids, with a high potential in reducing blood cholesterol levels (LDL) and preventing both heart attacks and strokes. Striegel et al. [29] investigated the folate content in horned melon fruit and the obtained result amounts to 7.82 mg/100 g of fresh fruit. As folate cannot be synthesized by the human body and must be supplied by food or supplements [8], the author pointed out the importance of horned melon consumption in daily diet for the prevention or reduction of cardiovascular diseases.

Next, we consider diabetes. In 2019, diabetes was the direct cause of 1.5 million deaths [30]. Diabetes mellitus type-2 is characterized by hyperglycemia as a result of insulin resistance and relative insulin deficiency, which may cause many complications, including dysfunction of the eyes, kidneys, nerves, heart, and blood vessels. Up to this date, only two studies have reported a possible association between horned melon phytochemicals and antihyperglycemic activity. Hence, Jimam et al. [31] and Gotep [32] demonstrated that the glycosides extracted from the horned melon pulp possess antihyperglycemic dose-dependent activity in alloxan-induced diabetes mellitus in rats, but the mechanism of action is still unknown.

Next, we consider gastrointestinal diseases. The ulcer is a common gastrointestinal disorder that presents an inflamed break in the skin or mucus membrane lining the alimentary tract. Ulceration occurs when there is a disturbance of the normal equilibrium caused by either enhanced aggression or diminished mucosal resistance affected by factors such as excessive ingestion of non-steroidal anti-inflammatory drugs (NSAIDs), alcohol, infection by *Helicobacter pylori*, and emotional stress. Several authors reported the antiulcer activity of horned melon, emphasizing the class of phytochemicals responsible for this effect. For example, Wannang et al. [33] investigated the effects of horned melon pulp on gastric functions and mucosal integrity using ethanol-induced ulceration in albino rats. A significant dose-dependent decrease in the number and type of gastro mucosal lesions compared to ranitidine (a standard anti-gastric ulcer drug) was reported. The authors reported that flavonoids present in horned melon could be responsible for the antiulcer properties. In addition, Omale et al. [34] investigated the effect of isolated alkaloids from the horned melon pulp in rats with ethanol-induced gastric lesions. The authors' results revealed a significant decrease in hemorrhages and ulcerations of the gastric mucosa for rats treated with 500 and 1000 mg/kg of alkaloids when compared to the control group administered with ranitidine (1 mg/kg). In general, these studies confirmed the potential benefits of horned melon for the treatment of ulcer disease.

Lastly, we consider anti-inflammatory properties. Flavonoid compounds present in a high amount in horned melon are probably responsible for the anti-inflammatory properties of this fruit. In addition, horned melon contains cucurbitacin B, which is a triterpene also well-known for anti-inflammatory activity [8]. Based on this property, it is proposed that horned melon can be employed in the management of asthma by the locals in the Vhembe district of Limpopo, as well as for pregnant women to decrease labor pain [35,36].

6.3. Antimicrobial Activity

Microbial resistance is an emerging problem rising to a dangerously high level and affects all parts of the world. This global problem is threatening our ability to treat even common infectious diseases, thus there is an urgent need to find alternative ways to suppress the growth of bacterial and fungal species which are pathogens for humans, animals, or/and plants. Furthermore, recent research studies have been aimed at finding bio-based fungicides and other alternatives for the reduction of growth of different yeast and fungi on agricultural goods [37]. It is already proven that the secondary metabolites present in the fruit, called phytochemicals, can be used as agents with moderate to high antimicrobial effects on the target bacteria, yeasts, and/or fungi, but, at the same time, with lower negative effects on human health [38]. Therefore, such isolated bioactive components represent a promising alternative approach in fighting microbial infections. The development and application of technologies based on the utilization of large amounts of generated waste has a positive impact on the environment and reduces economic losses, contributing to the development of the circular economy, with the possibility of placing a new product on the market [39]. Secondary raw materials for processing fruits such as horned melons have great potential as a source of the mentioned phytochemicals and the use of them would complete the path of the total utilization of fruits during food processing. Antimicrobial properties of horned melon were extensively studied regarding antibacterial, antifungal, and antiviral activity.

6.3.1. Antibacterial Activity

The increasing use of antibiotics leads to bacterial resistance and there is a need to find alternative ways and means to suppress the growth of, above all, pathogenic bacterial species [37]. Usman et al. [5] reported a minimal inhibitory concentration of 50 mg/mL for *Salmonella* Gallinarium, while the same effect of the methanolic extract of horned melon was not observed for *S*. Typhimurium. Furthermore, it is emphasized that horned melon peel has higher antibacterial activity compared to antifungal activity, which has been proven in the case of *Pseudomonas aeruginosa*, with a much lower MIC value than for fungi. In

research by Aliero et al. [40], the antibacterial activity of acetone, methanol, and aqueous extracts of horned melons did not show a significant effect. The only inhibitory effect was detected against *Staphylococcus aureus* in the concentration of 90 mg/mL of water extract.

6.3.2. Antifungal Activity

Compared to the average antibacterial effect of horned melon, a great antifungal effect was observed for different extracts of horned melon. Namely, Aliero et al. [40] reported a high inhibitory effect against *Aspergillus flavus*, *Fusarium solani*, *Trichophyton mentagrophyte*, and *Microsporum canis*. The minimal inhibitory concentration was between 20 and 80 mg/mL. The results showed that horned melon peel has an antimicrobial effect on all tested fungi, except for *A. niger*. A study by Nwadiaro et al. [41], who analyzed the antifungal properties of crude aqueous and methanol peel extracts, showed a pronounced effect on selected *A. flavus*, *F. oxysporum*, *Mucor* sp., *Penicillium citrinum*, and *Rhizopus stolonifer*.

6.3.3. Antiviral Activity

Most research studies on horned melon are directed to the chemical and antiviral properties of the obtained extracts. For pulp extract has been found to suppress the activity of the Newcastle disease virus on embryonated eggs [42]. Antiviral activity against Avulavirus was obtained using the extracted alkaloid and flavonoid fractions (3.125 and 25 mg/mL) based on a complex test with intramuscularly infected chickens and turkeys [33]. The concentrations of the flavonoid fraction from pulp between 6.25 and 100 mg/mL displayed inhibitory activity against the Bursal disease virus [43]. An antiviral study of horned melon alkaloids extracted from the pulp (concentrations of 6.25 and 200 mg/mL) was successfully conducted for Hepatitis B and Bursal disease virus using fibroblast cells of embryonated chickens and albino rats [44,45]. There are also some indications that horned melon has resistance against many pathogenic viruses because of specific genes encoded in proteinase inhibitors [46].

7. Potential Use as an Antimicrobial Agent

7.1. As Symbiotic Cultivars

In areas with traditional cultivation of melons, horned melon is used for helping its relatives, such as cucumber and melon, due to the fact that it is very resistant to fungal and virus diseases as well as pests. With gene transfer, horned melon can improve characteristics of relatives, transferring, e.g., pest resistance, but to the best of our knowledge, information on the effectual crossing of any relatives with horned melon does not yet exist [47].

7.2. As Biological Fungicides

Although it is applied in the control of the microbiological spoilage of fruits and vegetables through physicochemical methods, fungi are responsible for the loss of about 20% of the yield of fruits and vegetables globally, which is enough food to feed millions of people. It is estimated that in Europe, there is a fungal contamination of at least 125 million tons of fruits and vegetables, with an increasing trend every year, which indicates the importance of this problem. Synthetic fungicides are mainly used to control the spoilage of stored fruits and there is a growing awareness of the toxicity of these substances. Additionally, the development of pathogen resistance to fungicides and their harmful effects on both the environment and human health has led to the need to find an alternative of for synthetic chemical protection [48,49]. The development and application of technologies based on the utilization of large amounts of generated waste has a positive impact on the environment and reduces economic losses, contributing to the development of the circular economy, with the possibility of placing a new product on the market [50]. Secondary raw materials for processing fruits and products have great potential as a source of the mentioned phytochemicals, the use of which would complete the path of the utilization of fruits or other parts of the plant [51]. The secondary metabolites present in a horned melon can be used as agents with a stronger antifungal effect but with weaker negative effects on

human health [52]. Therefore, such isolated bioactive components represent an alternative approach in the fight against the contamination caused by phytopathogenic fungi.

Among alternative methods of protection against fungal contamination and oxidative changes in harvested fruits, the use of natural phyto-based preparations exists. Using waste parts of horned melon for the extraction of dominant bioactive compounds can be directed to the creation of biological treatment based on antifungal activity. Namely, biological fungicides, which are of plan origin, indicate a high degree of safety in the proception against phytopathogens. According to Achikanu et al. [18], horned melon represents a fruit rich in alkaloids, glycosides, saponins, flavonoids, tannins, etc. All the mentioned bioactives have an antimicrobial effect. For example, alkaloids present in plants can inhibit bacterial and fungal contamination, and increase the survival rate of fruits. These structural compounds belong to a group named phytoprotectants [38]. Furthermore, flavonoids and phenols are antioxidants and can act as free radical scavengers [53,54]. The inhibitory effect against fungi can be reflected in the presence of a certain concentration of tannins, which has been repeatedly shown to exhibit antimicrobial activity against species of the genus Candida [55]. The mechanism of action of tannin, as an antifungal agent of phenolic nature, refers to the possibility of binding to the ergosterol present in the structure of the cell membrane [55]. More precisely, the antifungal effect is manifested by binding to ergosterol, an essential lipid of the fungal cell membrane, leading to a violation of cell integrity. In addition to the direct binding to ergosterol, the effect of tannins on ergosterol biosynthesis is significant because they reduce the amount of ergosterol present in the cell by reducing the expression level of the gene encoding the protein involved in the biosynthesis of this lipid [56].

7.3. As a Flavouring Agent

The extracted glycosides, especially cyanogenic, can be used as flavoring agents in pharmaceutical preparations. The high concentration of glycosides present in a horned melon peel can be extracted and used for this purpose [57].

7.4. As a Medicinal Plant with Prospective Benefits

The phytochemical profile of Cucumis metuliferus peel, as waste part, indicates a source rich in phytoconstituents and therefore has medicinal prospective benefits, acting as an anti-cancer and anti-inflammatory agent [15]. For example, steroids, which are present in a horned melon peel, represent well-known phytoconstituents in a plant that can be used as cardiac drugs. The average concentration present in the peel is enough for promoting osteoporosis treatment [58]. Additionally, the presence of terpenoids in horned melon suggests a possibility for use in malaria, ulcer, or cancer treatment [59]. Vitamins are also required for the human body and vitamin C as well as vitamins A, D, E, and K can highlight horned melon as a medical plant.

7.5. As an Ingredient for Functional Foods' Fortification

Functional foods play an important role in the prevention of many diseases and disorders because it contains dietary ingredients that could maintain a healthy lifestyle and potentially cure some diseases. The value-added foods of today with therapeutic effects have attracted international interest and shaped a growing global market [60,61]. There are not many documented studies or published reports on the development of new food products with horned melon. According to Van Wyk [62], different parts of horned melon could be used for food fortification. The edible fruit and flowers of horned melon could be used to obtain novel functional food products (jams, sweets, and chutneys) and healthy beverages (fruit juices, liqueurs, cocktails, beers, fruit wines, and herbal teas). Additionally, it could be used as a healthy component of cakes or ice creams. Bolek [26] published a paper stating that horned melon seeds are rich in fat, vitamins, and carbohydrates, and can be considered as a waste management solution. Thus, food fortification with horned

melon parts could lead to the satisfaction of the daily vitamin requirement and nutrients, and could represent a source of natural antioxidants.

8. Conclusions

The increasing demands for natural nutrients and phytochemicals encourage the search for new sources of these compounds. Fruits and vegetables are known as rich sources of natural antioxidants but only a few of them involve non-edible parts of the products, i.e., seeds and peels. Significant amounts of non-edible parts and waste of fruits and vegetables are discarded during processing. This represents a severe environmental and economic problem with negative impacts on human health. Nowadays, the valorization of phytochemicals present in fruit and vegetable non-edible parts and wastes is a challenge, alongside the development of strategies to reuse these materials.

In the literature, the relevant data on the nutritional value and phytochemical profile of horned melon fruit/pulp is available but scarce information exists regarding the chemical profiles of non-edible parts, i.e., peels and seeds. The antioxidant activity of horned melon has acquired interest in the scientific society due to their potential utilization for health promotion, diseases prevention, and therapy. These compounds provide significant therapy responses against cardiovascular diseases, diabetes, gastrointestinal diseases, and anti-inflammatory diseases, and prevent the growth of different pathogens. Hence, further promotion of horned melon edible but especially non-edible parts as a potentially cheap and, at the same time, rich source of valuable compounds, as well as biological and nutritional studies, are a promising way to create different and innovative value-added products, which would provide many health benefits to consumers' daily diet.

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