# VALUABLE COMPOUNDS DERIVED FROM CUCURBITACEAE SUBPRODUCTS AND POTENTIAL WAYS OF ITS VALORIZATION

# Indira GALIT<sup>1, 2</sup>, Nicoleta RADU<sup>1, 3</sup>, Narcisa BABEANU<sup>1</sup>, Oana COMAN<sup>4</sup>

 <sup>1</sup>University of Agronomic Sciences and Veterinary Medicine of Bucharest, 59 Mărăști Blvd, District 1, Bucharest, Romania
<sup>2</sup>National Agricultural Research and Development Institute Fundulea, 1 Nicolae Titulescu Street, Fundulea, Călărași County, Romania
<sup>3</sup>National Institute of Chemistry and Petrochemistry R&D of Bucharest, 202 Splaiul Independenței Street, District 6, Bucharest, Romania
<sup>4</sup>University of Medicine and Pharmacy "Carol Davila" Bucharest, 37 Dionisie Lupu Street, District 2, Bucharest, Romania

Corresponding author email: nicoleta.radu@biotehnologii.usamv.ro

#### Abstract

The paper shows a short documentary study regarding the main valuable compounds that are present in the subproducts resulting in the fruits from the Cucurbitaceae family, with a main accent on Cucurbita sp. type pumpkins. The compound types (polyphenolic compounds, triterpenoids, carotenoidic compounds), extraction methods and the properties of bioproducts obtained in this way (antimicrobial, antitumor properties, sun protection factor) are presented. The most suitable valorization methods for waste biomass generated by Cucurbitaceae fruits are the following: 1) recovery of the carotenoids and polyphenolics compound from these, with potential applications in obtaining different dermato-cosmetical formulations, and 2) obtaining of nanomaterials with silver and gold, mediated by the phyto-compounds recovered by extraction from Cucurbitaceae peels, with potential applications in medicine.

Key words: antioxidant activity, antimicrobial effect, Cucurbita sp., peel, pumpkin, waste.

# INTRODUCTION

The family Cucurbitaceae belongs to the order Cucurbitales and contains 98 genera and about 975 species of edible and ornamental plants.

This family of plants includes cucumbers, gourds, melons, and squashes. Members can be annual or perennial, and they can grow in temperate or tropical climates on Earth (Encycolpedia Britannica, 2024).

Cucurbitaceae of interest for the food industry and not only, are *Citrullus* sp. (watermelon, citron), *Cucumis* sp. (cantaloupe), *Cucumber* sp. (cucumbers), *Cucurbita* spp. (squash, pumpkins), *Trichosanthes cucumerina*, *Sechium edule*, *Benincasa hispida*, *Coccinia* grandis, Momordica charantia (Botany Illustrated, 2006; Vieira et al., 2019, Perez Gutierrez, 2016). Due to their widespread cultivation and usage in Romania, the byproducts of pumpkins (*Cucurbita* sp.) are the subject of this study.

# CHEMICAL COMPOSITION OF PUMPKIN

The species belonging to this family are rich in carotenoids, terpenoids, saponins, alkaloids, anthocyanins, tannins, and polyphenolic compounds (Rolnik et al., 2020; Harith et al., 2018).

Pumpkins are rich in vitamins,  $\alpha$ ,  $\beta$ ,  $\gamma$ -carotene, lutein, violaxanthin, and neoxanthin, as well as amino acids and proteins that have antifungal activities (Mukherjee et al., 2022; Zaharie et al., 2022).

The fruits peel of *Cucurbita sp.* contains macroelements (Figure 1), microelements (Figure 2) and nutrients such as proteins, carbohydrates, and lipids (Figures 3-4).



Figure 1. Macronutrient content in *C. moschata* peels (adapted after Salehi et al., 2019)



Figure 2. Micronutrient content in *C. moschata* peels (adapted after Salehi et al., 2019)



Figure 3. Nutrients content in *C. moschata* peels (adapted after Salehi et al., 2019)



Figure 4. Nutrients content in C. maxima peels (adapted after Salehi et al., 2019)

*Cucurbita maxima* (pumpkin) is an important source of vitamin A (Ragasa and Lim, 2005; Bawara et al., 2010; Abou-Zaid et al., 2001); B vitamins (thiamine, riboflavin, niacin, folic acid), C, D, F, E vitamins are also found in the fruits of other species of Cucurbitaceae, such as *Lagenaria siceraria, Trichosanthes cucumerina*  (snake squash) (Shah and Seth, 2010: Adebooye, 2008), Coccinia indica (ivy gourd) (Sachin and Trisa, 2018). Other plants belonging to the Cucurbitaceae family, such as Cucurbita maxima (pumpkin). Luffa acutangula (angled loofah, Chinese Okra) contain small amounts of vitamin K and E (Avinash and Rai, 2017). Chemical substances insecticidal possessing and antibacterial properties are prevalent in these species (Rajasree et al., 2016; Yadav et al., 2010; Jamuna et al.. 2015). Studies have demonstrated that the whole extract functions better than the individual compounds, while the exact mechanisms of action remain unclear (Salehi et al., 2019). In a study by Cheong et al. (1997) it was demonstrated that the 8 kDa molecular mass protein derived from *Cucurbita* moschata has antifungal properties in vivo. Experiments conducted in vitro using a protein extracted from this species, known as the PR-5 demonstrated that protein. it strongly suppresses the growth of *Candida albicans* and Fusarium oxysporum (Ramalhete et al., 2011). The methanolic extract of Citrullus lanatus peels (Harith et al., 2018) inhibited the development of some microorganisms such as S. epidermidis and T. mentagrophytes, at concentrations of 20 mg extract/mL. The extracts derived from multiple varieties of pumpkins demonstrated antimicrobial activity against the intestinal flagellate parasite Giardia lamblia and microorganisms of the types of *Staphylococcus* Bacillus aureus, subtilis. Escherichia coli. Proteus vulgaris. Pseudomonas aeruginosa, Salmonella spp. or Klebsiella spp., and Vibrio cholerae (Table 1). According to research of Salehi and colab. (Salehi et al., 2019), the pumpkin peel extracts show antifungal action against the microorganisms such us: Fusarium sp., Trichoderm sp., Aspergillus sp., Verticillium sp., Phytophora sp., Botrytis sp., Candida sp., and Saccharomyces.

Cucurbita spp. Plant part	Solvent	Biological effect	Microorganism/cell line	References
Cucurbita moschata Duchesne, crude proteins obtained from peels	acetone	antimicrobial	Aspergillus fumigatus Aspergillus parasiticus Aspergillus niger; Staphylococcus aureus Bacillus subtilis: Klebsiella	Elhadi et al., 2013
			pneumoniae Pseudomonas aeruginosa; E. coli	
<i>Cucurbita maxima</i> Duchesne, pulp	petroleum ether and methanol	vermifuge	Giardia lamblia	Muruganantham et al., 2016
<i>Cucurbita maxima</i> Duchesne, peels	aqueous	antimicrobial	E.coli;Pseudomonas sp.;Vibrio cholerae	Kabbashi et al., 2014
Cucurbita moschata		antitumoral	Standardized human tumor cell lines: Hela, HCT-8, HepG-2	Feng et al., 2019
		antitumoral	Standardized type tumor cell lines: K562, B16, A549	Hou et al., 2008
		antidiabetic	Asian patients with diabetes mellitus	Salehi et al., 2019
		antifungal antiproliferative, antiulcer	Fusarium oxysporum; Candida albicans	Cheong et al., 1997 Abdel-Rahman, 2006; Gill et al., 2011
Cucurbita ficifolia (pulp)		antidiabetic and antioxidant	Male rats	Xia și Wang, 2007
		treatment for type 2 diabetes	Hyperglycemic rabbits	Roman-Ramos et al., 1992; Acosta-Patino et al., 2001
Cucurbita andreana		antitumoral, anti- inflammatory		Jayaprakasam et al., 2003

Table 1. Biological effects of bioproducts obtained from pumpkin fruits and/or peels

# EXTRACTION METHODS OF BIOACTIVE COMPOUNDS FROM CUCURBITA SP. PEELS

According to Kulczyński et al. (2020), ideal extraction techniques typically involve a mass ratio of dry plant to solvent of 1:10, a maximum temperature of 70°C, and an extraction duration of two hours.

Pumpkin peel extracts that may be utilized straight into cosmetic formulations can be produced by using an ecological extraction process and "green solvents" aqueous solutions (Figure 5), aqueous solution of propylene glycol 20% (Figure 6), or aqueous solution of ethanol 70% (Figure 7).

Investigations performed *in vitro* on normal standardized human cell lines (keratinocytes), have demonstrated that extracts of this kind do not exhibit cytotoxicity at concentrations below  $1000 \ \mu g/mL$ .

Given their high flavonoid content, notable antioxidant activity, and promising sun protection factor, the aqueous extracts were the most promising (Gaweł-Bęben et al., 2022; Indrianingsih et al., 2019).



Figure 5. The sun protection factor for aqueous extracts obtained from peels of different pumpkin varieties (crude extract concentration = 1 mg/mL) (adapted from Gaweł-Bęben et al., 2022)





### PHYTOCOMPOUNDS HIGHLIGHTED IN DIFFERENT PUMPKIN VARIETIES

*Cucurbita* sp. seeds contain 50% oil, primarily linoleic and oleic acid, and are rich in polyunsaturated fatty acids, oleic acid, linoleic acid, stearic acid, and myristic acid. Volatile oils are present in trace amounts in the fruit pulp of *Benincasa hispida*, commonly referred to as wax gourd or winter melon (Al-Snafi, 2013). Sugars, resins, crude fibers, free acids, carotenoids, lutein and zeaxanthin, stereos, and tocopherol are also present (Avinash and Rai, 2017).

**Polyphenolic compounds** are a significant class of phytocompounds. Pumpkin peels can be used to make biopreparations rich in these chemical compounds. Depending on the type of pumpkin used and the extraction solvent (aqueous solutions, ethanolic solutions, aqueous propylene glycol solutions), different extraction yields can be obtained (Figures 8-10) (Gawel-Baben et al., 2022, Radu et al., 2010).



Figure 7. The sun protection factor for aqueous ethanol extracts obtained from peels of different pumpkin varieties (crude extract concentration = 1 mg/mL) (adapted from Gawel-Beben et al., 2022)



Figure 8. The content of total polyphenols in the aqueous extracts obtained from the peels of different pumpkin varieties (adapted from Gawel-Baben, 2022)

If the extraction is carried out by green methods (Sharma et al., 2021), using corn oil as an extraction solvent, and if it is assisted by

ultrasound or microwaves, the content of polyphenols in the extracts obtained in the oil increases significantly. These studies report concentrations between 535-588 mg GAE/g extract, when using vegetable oil as a solvent, under action of microwaves or ultrasound (Sharma et al., 2021).



Figure 9. The content of total polyphenols in the aqueous extracts of propylene glycol obtained from the peels of different pumpkin varieties (adapted from Gawel-Baben, 2022)



Figure 10. Content of total polyphenols in the extracts obtained from the peels of different pumpkin varieties (adapted from Gawel-Baben, 2022)

Nandhini and Sheeba (2020) highlighted the formation of silver nanomaterials using aqueous extracts from the peels of two pumpkin species (Cucurbita sp. and T. cucumerina var. anguila). The aqueous extract was obtained from 20 g of dried pumpkin peels, which were boiled with 100 mL of water for 10 minutes, after which the resulting solution was cooled and filtered. By treating the clear filtrate with AgNO<sub>3</sub> (10 mL of aqueous pumpkin peel extract + 90 mL of 1 mM AgNO<sub>3</sub> solution), silver nanoparticles (AgNPs) are obtained after a 20-minute maturation. After a series of distilled water washes, the newly formed nanomaterials are centrifuged at 1500 rpm, and the pellets are then kept at -4°C. Testing the antibacterial activity of the two types of nanomaterials revealed effects on all tested

bacterial strains; the best results being obtained for *S. aureus* (inhibition diameter = 15.5 mm) in the case of AgNPs phytosynthesized with aqueous extract of *Tricosanthes cucumerina* (Figure 11) and respectively for *Pseudomonas aeruginosa* in the case of AgNPs phytosynthesized with aqueous extract of *Cucurbita sp.* (Figure 12). Soltani and colab. (Soltani et al., 2021) highlighted antitumor effects for AgNps obtained with ethanolic extracts from ground dry peels of *T. cucumerina*.



Figure 11. Antimicrobial activity of AgNPs obtained from *Trichosanthes cucumerina* var *anguina* (adapted from Nandhini & Sheeba, 2020)

The extract was obtained by mixing for 2 hours 10 grams of dried and ground pumpkin peels with 100 mL of 70% ethanol (aqueous solution). After the separation of the two phases, the alcohol is removed from the clear solution under vacuum, in a rotary evaporator, this way obtaining crude extract from pumpkin peels. If the clear alcoholic extract is treated with AgNO<sub>3</sub> (30 cm clear alcoholic extract +70 cmc AgNO<sub>3</sub> 1mM added in drops), a

suspension containing AgNPs is obtained after 24 h of maturation in the dark.



Figure 12. Antimicrobial activity of AgNPs obtained from *Cucurbita* sp. (adapted from Nandhini & Sheeba, 2020)

The obtained results showed that the crude extracts obtained from the peels of T. cucumerina var. anguina in 70% ethanol have cytotoxic effects both on MCF-7 tumor cells and on normal HUVEC type cells (Figure 13 a, b). In contrast, in the case of phytosynthesized nanoparticles with ethanolic extracts from T. cucumerina peels, optimal results are obtained for a concentration of AgNPs of 50 µg/mL, for which the tumor cell viabilities reaches 34.67% and the viability of the normal cells = 70,64%. The use of higher concentrations of AgNps results in the destruction of tumor cells in a proportion of about 82% (cytotoxicity = 82.2%) but also of normal cells, in a proportion of about 70% (cytotoxicity = 69.8%) (Figure 14 a, b).



Figure 13. The antitumor activity of the ethanolic extract obtained from *T. cucumerina*: a) the effect of the crude extract on the standardized cell line MCF-7; b) the effect of the crude extract on the standardized HUVEC cell line (adapted from Soltani et al., 2021)



Figure 14. Antitumor activity of AgNPs obtained from T. cucumerina peels: a) the effect of AgNPs on the standardized cell line MCF-7; b) the effect of AgNPs on the HUVEC cell line (adapted from Soltani et al., 2021)

Studies performed by Kaval and colab (Kaval et al., 2024) indicate that an aqueous extract made from Cucurbita moschata dry peels can be used as a starting point in the production of gold nanoparticles (AuNPs). It is important to highlight that the material was ground and allowed to dry at ambient temperature. At 50°C, the extraction process was conducted using distilled water and a mass ratio of 1: 3 for the plant to solvent. After passing the solution through 45 microm membranes, the filtrate was heated for 15 minutes at  $t = 50^{\circ}C$  and treated with an Au<sup>3+</sup> solution (250 mL Au<sup>3+</sup> 0.01M solution + 750 mL plant extract). After 15 minutes, the heating was stopped, and after about 1 hour the solution changed color from yellow to red. The resulting suspension was centrifuged at 15000 rpm and the resulting pellets were dried at 85°C, cooled, ground, and stored in sealed tubes at 4°C. In this way, nanomaterials with gold were obtained, with a size of about 21.2 nm, containing 30% Au and 56.6% C. Phytosynthesized gold nanomaterials have antimicrobial effects for E. coli (MIC = 0.64  $\mu$ g/mL), *S. aureus* (MIC = 0.25  $\mu$ g/mL) and C. albicans (MIC =  $0128 \mu g/mL$ ) (Figure 15 a-b) (Kaval et al., 2024). Cytotoxicity tests performed with these materials on normal standardized human cell lines type HUVEC and respectively on standardized human tumor cell lines Sk-Ov-3, A549, CaCo-2 showed that they are cytotoxic for the HUVEC line (IC50 = 44.6µg/mL), have average cytotoxicity for the Sk-Ov-3, A549 type tumor cell lines and do not show cvtotoxicity for the CaCo-2 type tumor cell line (Figure 15 d-g) (Kaval et al., 2024; Ciric et al., 2023).





g

Triterpenoids. One important feature of plants in the Cucurbitaceae family is the presence the triterpenoids compounds type cucurbitacins. The cucurbitacins consists of a tetracyclic cucurbitan core with a variety of oxygenated functional groups. Cucurbitacins A-T are among the twelve groups of cucurbitacins non-glycosylated or glycosylated. Different degrees of unsaturation and the presence of several keto, hydroxy, and acetoxy groups are the characteristics of cucurbitacins structural (Chen et al., 2005; Rajasree et al., 2016; Saboo et al., 2013; Montesano et al., 2018; Kaushik et al. 2018). The highest concentrations of curcubitacins are found in mature fruits; the lowest concentrations are found in seeds (Saboo et al., 2013; Kaushik et al., 2015). These compounds are typically harmful, but at the proper dosage, they exhibit beneficial qualities, particularly those related to anti-inflammatory effects, which make them helpful in the treatment of autoimmune disorders. According to Bartalis and Halaweish (2005), the degree of hydrophobicity of cucurbitacins grows linearly and is a primary



Figure 15. Biological activities of AuNps phytosynthesized with pumpkin peel extract: a) antimicrobian effect of AuNP; b) antimicrobial effect of antibiotic reagent; c) antimicrobial effect of Au<sup>3+</sup> raw material; d) antitumor effect on the HUVEC cell line; e) antitumor effect on the Sk-Ov-3 cell line; f) antitumor effect on the A549 cell line; g) antitumor effect on the CaCo-2 cell line (data adapted after Kaval et al., 2024)

regulator of their cytotoxic effects. For cucurbitacins type B and E, therapeutic properties have been highlighted and currently these compounds are used in clinical trials (Rajasree et al. 2016; Saboo et al., 2013; Montesano et al., 2018; Kaushik et al. 2018). Cucurbitacin E and its glycosidic forms are the most abundant chemical constituents in plants of the Cucurbitaceae family (Dhiman et al., 2012). Chanda and colab., (Chanda et al., 2019) used HPLC techniques to study the fruits of the following plants: Lagenaria siceraria (gourd), Benincasa hispida (wax pumpkin), Momordica charantia (bitter cucumber), Coccinia grandis (ivy gourd), and Luffa acutangula (cucumber sponge/loofah with edges) and found in these Cucurbitacin E. Studies conducted in vitro and vivo have demonstrated the in antiinflammatory. anti-angiogenesis, immunomodulatory, cytotoxic, cytostatic, and hepatoprotective properties of cucurbitacins (Attard and Cuschieri, 2004). In the Table 2 are described some cucurbitacins and their biological activity.

Cucurbitacin	Molecular structure	Varieties	<b>Biological properties</b>	References
Cucurbitacin B	Glycosidic form dihydrocucurbitacin Dihydroiso-cucurbitacin isocucurbitacin B	Cucurbitaceae	Antitumor (prostate cancer, small cell lung cancer), Inflammatory, Hepatoprotective, Synergistic effect in the presence of cucurmin (activates the occurrence of apoptosis) for liver tumor	Miro, 1995; Kausar et al., 2013; Wang et al., 2014; Ma J. et al., 2014; Gao et al., 2014; Sun et al., 2015; Mukherjee et all, 2019.
Cucurbitacin D	Glycosidic form dihydrocucurbitacin D deoxycucurbitacin D epi-isocucurbitacin D	Cucurbitaceae	antiproliferative activity, cytotoxic activity, induces cell cycle arrest and apoptosis in breast carcinoma cells	Chen et al., 2005; Abbas et al., 2013; Ku et al., 2015
Cucurbitacin E	Glycosidic form dihydrocucurbitacin E dihydroisocucurbitacin E isocucurbitacin E	Ecballium elaterium, Coccinia grandis	Neuroprotective, anti- inflammatory, antipyretic, anti-tumor (breast cancer), anti-allergic, anthelmintic, purgative activity	Miro, 1995; Yoshikawa et al., 2007; Lan et al., 2013; Abbas et al., 2013; Arel-Dubeau et al., 2014; Abdelkhalek et al., 2017; Lu et al., 2017; Chanda et al., 2020
Cucurbitacin F	dihydrocucrbitacin F, hexanorcucurbitacin F, oxocucurbitacin F și forma glucozidică; 23, Dihydro și 15-oxo cucurbitacin F (3), 15-oxo-23, 24-dihydro cucurbitacin F		used in traditional Chinese medicine, anti-HIV activity	Konoshima et al., 1994; Chen et al., 2005
Cucurbitacin I			cytotoxic activity, antitumor activity, chemotherapy adjuvant agent	Abbas et al., 2013; Johnson et al., 2013
Khekadaengosides D, Deoxycucrbitacin glycoside (Spinosides A)	(Spinosides A)		antitumor activity	Mukherjee și colab., 2022
Cucurbitacin L, or J or K	brydioside A bryoamaride		No therapeutic activity	Mukherjee și colab., 2022

Table 2. Types of cucurbitacins and their biological activities

Carotenoids. Most plants from Cucurbitaceae family are rich in carotenoids. Over 700 carotenoids occur naturally, but only 50 can be absorbed, metabolized, and used by the human body with health benefits. In Cucurbitaceae, they occur as a-carotene, β-carotene, lutein, zeaxanthin (Montesano et al., 2018; Durante et al., 2014). The total carotenoid content of Cucurbita moschata varies from 234.21 to 404.98 mg/g dried fruit. The carotenoid content is often higher in the peel than in the pulp. For example, in Cucurbita moschata the carotenoid content is 10 times higher in the peel than in the pulp (Salehi et al., 2019). In the peels of several varieties of pumpkins derived from C. maxima and C. moschata, grown in Umbria Italy, Pinna and colab. (Pinna et al., 2023) highlighted the existence of compounds such as beta carotene (Figure 16), non-esterified carotenoid compounds (Figure 17) such as  $\alpha$ carotene. β-carotene. lutein. zeaxanthin. violaxanthin and esterified carotenoids

compounds (Figure 18) (Bunea et al., 2014). The studies carried out by Sharma et al. (Sharma et al., 2021) on two varieties of *Cucurbita maxima*, demonstrated that the extraction yield of carotenoid compounds from peels can increase by 100% when using green extraction methods (Figure 19), compared to the variant in which extraction is carried out with organic solvent. The concentration of carotenoids was estimated spectrophotometrically, with the relation (1) (Sharma et al., 2021):

$$C = \frac{A \times 1000000}{2000 \times 100 \times d}$$
(1)

In the green extractions methods studied by Sharma et al. (Sharma et al., 2021) corn oil was used as the extraction agent and the extraction process was assisted by microwaves or ultrasound. In this way, the extraction yield of polyphenolic compounds can increase by 200%, and the color and oxidation stability of biopreparations enriched in carotenoid compounds is greatly improved (Figure 20 a, b). These processes are particularly recommended for specific applications in the food or cosmetic industry.

The studies performed by Gaweł-Bęben and colab. (Gaweł-Bęben et al., 2022) demonstrated that active principles from crude extracts otained from the peels of various varieties of pumpkin (*Cucurbita* spp.) could be used directly in dermato-cosmetic bioproduct formulation.



Figure 16. The content of beta β carotene in peels from different varieties of *Cucurbita* sp. (adapted from Pinna et al., 2023; Bunea et al., 2014)



Figure 17. The content of non-esterified carotenoids in peels from different varieties of *Cucurbita* sp. (adapted from Pinna et al., 2023; Bunea et al., 2014)



Figure 18. The content of non-esterified carotenoids in peels from different varieties of *Cucurbita* sp. (adapted from Pinna et al., 2023; Bunea et al., 2014)



Figure 19. The effect of the extraction process on the content of carotenoid compounds in the final solvent (corn oil) (adapted from Sharma et al., 2021)

(Legend: C.m. var.1\_U= carotenoids obtained from peels of *C. maxima* var. Gold nugget, by extraction in corn oil, assisted by ultrasound; C.m.var.1\_M = carotenoids obtained from peels of *C. maxima* var. Gold nugget, by extraction in corn oil, assisted by microwaves; c.m. var.1\_C=carotenoids obtained from peels of *C. maxima* var. Gold nugget, by extraction with organic solvents; c.m. var.2\_U=carotenoids obtained from peels of *C. maxima* var. Amoro, by extraction in corn oil, assisted by ultrasound; c.m. var.2\_M= carotenoids obtained from peels of *C. maxima* var. Amoro, by extraction in corn oil, assisted by ultrasound; c.m. var.2\_M= carotenoids obtained from peels of *C. maxima* var. Amoro, by extraction with organic solvents)



Figure 20. The effect of the extraction process, on the color difference ( $\Delta E$ ) and stability at oixidation of bioproducts obtained in corn oil (adapted from Sharma et al., 2021)

(Legend: C.m. var.1\_U= carotenoids obtained from peels of *C. maxima* var. Gold nugget, by extraction in corn oil, assisted by ultrasound; C.m.var.1\_M= carotenoids obtained from peels of *C. maxima* var. Gold nugget, by extraction in corn oil, assisted by microwaves; c.m. var.1\_C=carotenoids obtained from peels of *C. maxima* var. Gold nugget, by extraction with organic solvents; c.m. var.2\_U=carotenoids obtained from peels of *C. maxima* var. Gold nugget, by extraction with organic solvents; c.m. var.2\_U=carotenoids obtained from peels of *C. maxima* var. Gold nugget, by extraction with organic solvents; c.m. var.2\_U=carotenoids obtained from peels of *C. maxima* var. Amoro, by extraction in corn oil, assisted by ultrasound; c.m. var.2\_M=carotenoids obtained from peels of *C. maxima* var.Amoro, by extraction in corn oil, assisted by microwaves; c.m. var.2\_C= carotenoids obtained from peels of *C. maxima* var.Amoro, by extraction with organic solvents)

### CONCLUSIONS

The by-products resulting from the processing of Cucurbitaceae fruits (such as the peels) represent a valuable source of raw materials, due to their content in alkaloids, polyphenolic compounds, terpenoids, saponins or carotenoid compounds.

In general, by extraction in aqueous medium or by extraction with organic solvents such as alcohols (ethanol, methanol), acetone, nhexane, water, propylene glycol, from fresh or dry peels, bioproducts with an antibacterial (*S. aureus* and *E. coli*), and antifungal effect (*C. albicans, Fusarium solani, P. chrysogenum, C. gloeosporioides* - anthracnose) can be obtained.

Extracts in ethanol or propylene glycol may contain carotenoid compounds, but the most advantageous methods of extracting them from cucurbit peels are green methods, in which are used as solvents vegetable oils, and the extraction process is intensified by microwaves or ultrasounds. In this case the bioproducts obtained may contain simple carotenoids of type  $\alpha$  or  $\beta$  carotene, lutein, zeaxanthin, violaxanthin, or esterified carotenoids. The bioproducts obtained by green extraction methods have a sun protection factors between (1-7) and can be used directly in the cosmetic formulations.

# REFERENCES

- Abbas, S., Vincourt, J.B., Habib, L., Netter, P., Greige-Gerges, H., Magdalou, J. (2013) The cucurbitacins E, D and I: investigation of their cytotoxicity toward human chondrosarcoma SW 1353 cell line and their biotransformation in man liver. *Toxicol Lett, 216:189-199*
- Abdelkhalek, A.A., Sharaf, A.M., Rabie, M., El-Subbagh, H.I., (2017). Derivatives of cucurbitacineglucose produced by *Curvularia lunata* NRRL 2178: anti-inflammatory, antipyretic, antitumor activities, and effect on biochemical parameters. *Future J. Pharm. SCI. 3, 124–130.*
- Abdel-Rahman, M.K., (2006). Effect of pumpkin seed (Cucurbita pepo L.) diets on Benign Prostatic Hyperplasia (BPH): Chemical and morphometric evaluation in rats. *World J. Chem.*, 1: 33-40.
- Abou-Zaid, M.M., Lombardo, D.A., Kite, G.C., Grayer, R.J., Veitch, N.C., (2001). Acylated flavone Cglycosides from Cucumis sativus. *Phytochemistry* 58, 167–172.
- Acosta-Patino, J. L., Jimenez-Balderas, E., Juarez-Oropeza, M. A., & Diaz-Zagoya, J. C. (2001). Hypoglycemic action of Cucurbita ficifolia on Type 2 diabetic patients with moderately high blood glucose levels. *Journal of Ethnopharmacology*, 77(1), 99-101.
- Adebooye, O.C. (2008). Phyto-constituents and antioxidant activity of the pulp of snake tomato (Trichosanthes Cucumerina L.). Afr. J. Tradit., Complementary Altern. Med. 5, 173–179.
- Arel-Dubeau, A.M., Longpr'e, F., Bournival, J., Tremblay, C., Demers-Lamarche, J., Haskova, P., Attard, E., Germain, M., Martinoli, M.G., (2014). Cucurbitacin E has neuroprotective properties and

autophagic modulating activities on dopaminergic neurons. Oxid. Med. Cell Longev. 425496, 1–15.

- Attard, E., Cuschieri, A., (2004). Cytotoxicity of cucurbitacin E extracted from Ecballium elaterium in-vitro. J. Nat. Remedies 4, 137–144
- Avinash, T.S., Rai, V.R., (2017). An ethanobotanical investigation of Cucurbitaceae from South India: a review. J. Med. Plants. Stud. 5, 250–254.
- Bartalis, J., Halaweish, F.T., (2005). Relationship between cucurbitacins reversed phase highperformance liquid chromatography hydrophobicity index and basal cytotoxicity on HepG2 cells. J. Chromatogr. B 818, 159–166.
- Bawara, B., Dixit, M., Chauhan, N.S., Dixit, V.K., Saraf, D.K., (2010). Phyto pharmacology of Momordica dioica roxb. Ex. Willd: a review. *Int. J. Phytomed. 2*, 1–9.
- Botany Illustrated. Gourd Family (Cucurbitaceae). 10.1007/0-387-28875-9(Chapter 94), 94–94. doi:10.1007/0-387-28875-9 94 2006, Springer, Boston, MA
- Britannica, The Editors of Encyclopaedia. "Cucurbitaceae". *Encyclopedia Britannica*, accesed 9 Feb. 2024, https://www.britannica.com/plant/Cucurbitaceae.

Accessed 28 February 2024

- Bunea, A., Socaciu, C., & Pintea, A. (2014). Xanthophyll esters in fruits and vegetables. *Notulae botanicae horti agrobotanici Cluj-Napoca*, 42(2), 310-324.
- Chanda, J.(a), Mukherjee, P.K., Kar, A., Maitra, P.K., Singha, S., Haldar, P.K., Gajbhiye, R., Vishnuvardh, R., (2020a). LC–QTOF–MS-based metabolite profiling and evaluation of α-glucosidase inhibitory kinetics of *Coccinia grandis* fruit. *Biomed. Chromatogr.* 34 (e4950), 1–9.
- Chanda, J., Biswas, S., Kar, A., Mukherjee, P.K., (2019). Determination of cucurbitacin E in some selected herbs of ayurvedic importance through RP-HPLC. J. Ayurveda Integr. Med. 11, 287–293.
- Chen, J.C., Chiu, M.H., Nie, R.L., Cordell, G.A., Qiu, S.X., (2005). Cucurbitacins and cucurbitane glycosides: structures and biological activities. *Nat. Prod. Rep. 22, 386–399.*
- Cheong, N. E., Choi, Y. O., Kim, W. Y., Bae, I. S., Cho, M. J., Hwang, I., & Lee, S. Y. (1997). Purification and characterization of an antifungal PR-5 protein from pumpkin leaves.*Molecules and cells*, 7(2), 214-219.
- Ciric, A., Radu, N, Zaharie, M.G.O., Neagu, G., Pirvu, L.C., Begea, M., Stefaniu, A. (2023) Potential Antitumor Effect of Functional Yogurts Formulated with Prebiotics from Cereals and a Consortium of Probiotic Bacteria. *Foods.* 12(6):1250.
- Dhiman, K., Gupta, A., Sharma, D.K., Gill, N.S., Goyal, A., (2012). A review on the medicinally important plants of the family Cucurbitaceae. *Asia Pac. J. Clin. Nutr. 4, 16–26.*
- Durante, M., Lenucci, M. S., & Mita, G. (2014). Supercritical carbon dioxide extraction of carotenoids from pumpkin (Cucurbita spp.): A review. *International Journal of Molecular Sciences*, 15(4), 6725-6740.

- Elhadi, I. M., Koko, W. S., Dahab, M. M., El Imam, Y. M., & El Mageed, M. A. (2013). Antigiardial activity of some Cucurbita species and Lagenaria siceraria. *Lab. Anim*,3(8).
- Feng, W., Zhou, Y., Zhou, L. Y., Kang, L. Y., Wang, X., Li, B. L., ... & Niu, L. Y. (2019). Novel cucurbitane triterpenes from the tubers of Hemsleya amabilis with their cytotoxic acitivity. *Molecules*, 24(2), 331.
- Gao, Y., Islam, M. S., Tian, J., Lui, V. W. Y., & Xiao, D. (2014). Inactivation of ATP citrate lyase by Cucurbitacin B: A bioactive compound from cucumber, inhibits prostate cancer growth. *Cancer letters*, 349(1), 15-25.
- Gaweł-Bęben, K, Czech K, Strzępek-Gomółka M, (2022). Assessment of *Cucurbita spp*. Peel Extracts as Potential Sources of Active Substances for Skin Care and Dermatology. *Molecules*, 27(21):7618. Published 2022 Nov 6. doi:10.3390/molecules27217618
- Gill, N. S., Supreet Kaur, S. K., Arora, R., & Bali, M. (2011). Screening of antioxidant and antiulcer potential of *Citrullus colocynthis* methanolic seed extract. *CABI Digital Library*
- Harith, S. S., Mazlun, M. H., Mydin, M. M., Nawi, L., & Saat, R. (2018). Studies on phytochemical constituents and antimicrobial properties of *Citrullus lanatus* peels. *Malaysian Journal of Analytical Sciences*, 22(1), 151-156.
- Hemmige, N.N., Abbey, L., Asiedu, S.K., (2017). An overview of nutritional and anti-nutritional factors in green leafy vegetables. *Horticult. Int. J. 1, 58–65.*
- Hou, X., Meehan, E. J., Xie, J., Huang, M., Chen, M., & Chen, L. (2008). Atomic resolution structure of cucurmosin, a novel type 1 ribosome-inactivating protein from the sarcocarp of Cucurbita moschata. *Journal of Structural Biology*, 164(1), 81-87.
- Indrianingsih, A. W., Rosyida, V. T., Apriyana, W., Hayati, S. N., Nisa, K., Darsih, C. & Indirayati, N. (2019). Comparisons of antioxidant activities of two varieties of pumpkin (Cucurbita moschata and Cucurbita maxima) extracts. In *IOP Conference Series: Earth and Environmental Science* (Vol. 251, No. 1, p. 012021). IOP Publishing.
- Jamuna, S., Karthika, K., & Paulsamy, S. (2015). Phytochemical and pharmacological properties of certain medicinally important species of Cucurbitaceae family–a review. J. Res. Biol, 5(6), 1835-1849.
- Jayaprakasam, B., N.P. Seeram and M.G. Nair, (2003). Anticancer and antiinflammatory activities of cucurbitacins from Cucurbita andreana. *Cancer Lett.*, 10: 11-16.
- Johnson, M. D., O'Connell, M. J., & Walter, K. (2013). Cucurbitacin I blocks cerebrospinal fluid and platelet derived growth factor-BB stimulation of leptomeningeal and meningioma DNA synthesis. *BMC Complementary and Alternative Medicine*, 13, 1-8.
- Kabbashi, A. S., Koko, W. S., Mohammed, S. E. A., Musa, N., Osman, E. E., Dahab, M. M., ... & Mohammed, A. K. (2014). In vitro amoebicidal, antimicrobial and antioxidant activities of the plants

Adansonia digitata and Cucurbit maxima. Adv. Med. Plant Res, 2(3), 50-57.

- Kausar, H., Munagala, R., Bansal, S. S., Aqil, F., Vadhanam, M. V., & Gupta, R. C. (2013). Cucurbitacin B potently suppresses non-small-cell lung cancer growth: identification of intracellular thiols as critical targets. *Cancer Letters*, 332(1), 35-45.
- Kaushik, S., Kaushik, S., Sharma, V., & Yadav, J. (2018). Antiviral and therapeutic uses of medicinal plants and their derivatives against dengue viruses. *Pharmacognosy Reviews*, 12(24).
- Kaval, U., & Hoşgören, H. (2024). Biosynthesis, Characterization, and Biomedical Applications of Gold Nanoparticles with Cucurbita moschata Duchesne Ex Poiret Peel Aqueous Extracts. *Molecules*, 29(5), 923.
- Konoshima, T., Kashiwada, Y., Takasaki, M., Kozuka, M., Yasuda, I., Cosentino, L.M., Lee, K.H., (1994). Cucurbitacin F derivatives, anti-HIV principles from Cowania mexicana. *Bioorg. Med. Chem.* 4, 1323– 1326.
- Ku, J. M., Kim, S. R., Hong, S. H., Choi, H. S., Seo, H. S., Shin, Y. C., & Ko, S. G. (2015). Cucurbitacin D induces cell cycle arrest and apoptosis by inhibiting STAT3 and NF-κB signaling in doxorubicin-resistant human breast carcinoma (MCF7/ADR) cells. *Molecular and Cellular Biochemistry*, 409, 33-43.
- Kulczyński, B., Gramza-Michałowska, A., & Królczyk, J. B. (2020). Optimization of extraction conditions for the antioxidant potential of different pumpkin varieties (Cucurbita maxima). *Sustainability*, 12(4), 1305.
- Lan, T., Wang, L., Xu, Q., Liu, W., Jin, H., Mao, W., ... & Wang, X. (2013). Growth inhibitory effect of Cucurbitacin E on breast cancer cells. *International journal of clinical and experimental pathology*, 6(9), 1799.
- Lu, J., Zhang, Y., Sun, M., Liu, M., & Wang, X. (2017). Comprehensive assessment of Cucurbitacin E-related hepatotoxicity and drug-drug interactions involving CYP3A and P-glycoprotein. *Phytomedicine*, 26, 1-10.
- Ma, J., Jiang, Y. Z., Shi, H., Mi, C., Li, J., Nan, J. X., ... & Jin, X. (2014). Cucurbitacin B inhibits the translational expression of hypoxia-inducible factorla. *European Journal of Pharmacology*, 723, 46-54.
- Miro, M., (1995). Cucurbitacins and their pharmacological effects. *Phytother Res.* 9, 159–168.
- Montesano, D., Rocchetti, G., Putnik, P., & Lucini, L. (2018). Bioactive profile of pumpkin: An overview on terpenoids and their health-promoting properties. *Current Opinion in Food Science*, 22, 81-87.
- Mukherjee, P. K., Singha, S., Kar, A., Chanda, J., Banerjee, S., Dasgupta, B., & Sharma, N. (2022). Therapeutic importance of Cucurbitaceae: A medicinally important family. *Journal of Ethnopharmacology*, 282, 114599.
- Mukherjee, P.K., (2019). Ethnopharmacology and ethnomedicine-inspired drug development. In: Mukherjee, P.K. (Ed.), Quality Control and Evaluation of Herbal Drugs. *Elsevier*, 29–51. https://doi.org/10.1016/B978-0-12-813374-3.00002-8.

- Muruganantham, N., Solomon, S., & Senthamilselvi, M. M. (2016). Anti-oxidant and anti-inflammatory activity of Cucumis sativas (cucumber) flowers. *Int J Pharm Sci Res*, 7(4), 17-40.
- Nandhini, S., & Sheeba, D. (2020). Vegetable peel extract mediated synthesis of silver nanoparticles and its antimicrobial activities. *Res. J. Chem. Environ*, 24, 39-44.
- Perez Gutierrez, R. M. (2016) Review of Cucurbita pepo (Pumpkin) its Phytochemistry and Pharmacology. *Med chem 6*: 012-021. doi:10.4172/2161-0444.1000316
- Pinna, N., Ianni, F., Selvaggini, R., Urbani, S., Codini, M., Grispoldi, L.,& Blasi, F. (2023). Valorization of Pumpkin Byproducts: Antioxidant Activity and Carotenoid Characterization of Extracts from Peel and Filaments. *Foods*, 12(21), 4035.
- Radu, N., Ghita, I., Coman, O., & Rau, I. (2010). Therapeutic Effect of Flavonoids Derived from *Plantago Species Molecular Crystals and Liquid Crystals*, 523(1), 273-281.Ragasa, C.Y., Lim, K., (2005). Sterols from Cucurbita maxima. *Philippine J. Sci.* 134, 83–87.
- Rajasree, R.S., Sibi, P.I., Femi, F., Helen, W., (2016). Phytochemicals of Cucurbitaceae family – a review. Int. J. Pharmcog. Phytochem. Res. 8, 113–123.
- Ramalhete, C., Lopes, D., Molnár, J., Mulhovo, S., Rosário, V. E., & Ferreira, M. J. U. (2011). Karavilagenin C derivatives as antimalarials. *Bioorganic & medicinal chemistry*, 19(1), 330-338.
- Rolnik, A., & Olas, B. (2020). Vegetables from the Cucurbitaceae family and their products: Positive effect on human health. *Nutrition (Burbank, Los Angeles County, Calif.)*, 78, 110788. https://doi.org/10.1016/j.nut.2020.110788
- Roman-Ramos, R., A. Lara-Lemus, F.J. Alarcon-Aguilar and J.L. Flores-Saenz (1992). Hypoglycemic activity of some antidiabetic plants. *Arch. Med. Res.*, 23,105-109.
- Saboo, S.S., Thorat, P.K., Tapadiya, G.G., Khadabadi, S.S., (2013). Ancient and recent medicinal uses of Cucurbitaceae family. *Int J. Therap. Appl.* 9, 11–19.
- Sachin, B., & Trisa, P. (2018). Comparative Analysis of Vitamin C Content of Coccinia Indica W. & A And Trichosanthes Dioica Roxb. In The Nine Agro Climatic Zones of Maharashtra. *Indian J. Appl. Res.*, 8, 23-24.
- Salehi, B., Capanoglu, E., Adrar, N., Catalkaya, G., Shaheen, S., Jaffer, M., & Capasso, R. (2019). Cucurbits plants: A key emphasis to its pharmacological potential. *Molecules*, 24(10), 1854.
- Shah, B.N., Seth, A.K., (2010). Pharmacognostic studies of the Lagenaria siceraria (molina) standley. Int. J. Pharm.
- Sharma, M., & Bhat, R. (2021). Extraction of carotenoids from pumpkin peel and pulp: Comparison between innovative green extraction technologies (ultrasonic and microwave-assisted extractions using corn oil). *Foods*, 10(4), 787.
- Snafi, A.E. (2013). The pharmacological importance of Benincasa hispida. A review. *Int. J. Pharma Sci. Res.* 4, 165–170.

- Soltani, L., & Darbemamieh, M. (2021). Biosynthesis of silver nanoparticles using hydroethanolic extract of Cucurbita pepo L. fruit and their anti-proliferative and apoptotic activity against breast cancer cell line (MCF-7). *Multidisciplinary Cancer Investigation*, 5(3), 1-10.
- Sun, Y., Zhang, J., Zhou, J., Huang, Z., Hu, H., Qiao, M., & Chen, D. (2015). Synergistic effect of cucurbitacin B in combination with curcumin via enhancing apoptosis induction and reversing multidrug resistance in human hepatoma cells. *European journal of pharmacology*, 768, 28-40.
- Vieira, E. F., Pinho, O., Ferreira, I. M., & Delerue-Matos, C. (2019). Chayote (Sechium edule): A review of nutritional composition, bioactivities and potential applications. *Food chemistry*, 275, 557-568.
- Wang, Y., Zhao, G. X., Xu, L. H., Liu, K. P., Pan, H., He, J., & He, X. H. (2014). Cucurbitacin IIb exhibits antiinflammatory activity through modulating multiple cellular behaviors of mouse lymphocytes. *PloS one*, 9(2), e89751.

- Xia, T., & Wang, Q. (2007). Hypoglycaemic role of *Cucurbita ficifolia* (Cucurbitaceae) fruit extract in streptozotocin-induced diabetic rats. *Journal of the Science of Food and Agriculture*, 87(9), 1753-1757.
- Yadav, S., Tomar, A.K., Yadav, R.N., Yadav, S. (2013). Screening of antifungal proteins from plants of Cucurbitaceae family against Fusarium oxysporum: potential as biofungicides. *Int. Res. J. Environ. Sci.* 2, 91–96.
- Yoshikawa, M., Morikawa, T., Kobayashi, H., Nakamura, A., Matsuhira, K., Nakamura, S., Matsuda, H. (2007). Bioactive saponins and glycosides, XXVII. Structures of new cucurbitanetype triterpene glycosides and antiallergic constituents from Citrullus colocynthis. *Chem. Pharm. Bull.* 55, 428–434
- Zaharie, M.G.O., Radu, N., Pirvu, L., Bostan, M.;, Voicescu, M., Begea, M., Constantin, M., Voaides, C., Babeanu, N., Roman, V. (2022). Studies Regarding the Pharmaceutical Potential of Derivative Products from *Plantain. Plants 11(4)*, 1827.