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Recent Review on Traditional Use, Phytochemical Studies and Pharmacological Activity of Three Species from *Cucurbita* Genus

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Abstract Pumpkin (*Cucurbita* spp.) is found in many parts of the world and is commonly used in nearby regions as traditional medicine. The aim of this literature review is to compile a comprehensive selection of recent articles related to three pumpkin species: *C. maxima*, *C. pepo*, and *C. moschata*, with a focus on their ethnobotanical applications, chemical composition, and biological activities. Database searches were conducted in Scopus, Science Direct, and PubMed Central, yielding 45 documents, including scientific articles and theses, after filtering. This review highlights that *Cucurbita* spp. have been traditionally employed to address a range of ailments such as cardiovascular disease, atherosclerosis, diabetes, muscle pain, and inflammation, in addition to their use in food (ripe fruit and seeds) and dyes. Their medicinal derivatives, such as hydroethanolic extracts, have demonstrated a wide spectrum of biological activities, including anticancer, antimicrobial, and antiparasitic effects. Key active compounds include polyphenols and carotenoids, which are largely responsible for their effects in both *in vitro* and *in vivo* studies. In conclusion, the findings support the need for ongoing research into these *Cucurbita* species, to validate their traditional uses across different cultures worldwide and to deepen our understanding of their pharmacological mechanisms, especially regarding the interactions between phytochemicals and pharmacological effects.

Keywords: *ethnobotany, pharmacological activity, chemical composition, pumpkin, functional food, Cucurbita*

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1. Introduction

Cucurbita maxima, *Cucurbita pepo* and *Cucurbita moschata* (Cucurbitaceae) are commonly known in various countries as "pumpkin", "auyama", "ayote", "joko", "zapallo" or "zucchini", where they are harvested maturely in the winter season and immaturely in the summer season [1,2]. According to the Food and Agriculture Organization (FAO), the average world production of these vegetables per year is 13.53 t/ha, whereas an average of 13.95 t/ha is found in an American country every five years [2].

Pumpkin is used as a food (pulp, seeds, flowers), in the elaboration of phytocosmetics and dermocosmetics (seeds) [3], and mainly medicinal products [4]. Its fleshy yellow-orange berries and pulp, which is used for gastronomy for its nutritional benefits, are usually dehydrated for preservation, so that they are used in bakery, dairy products, soups, sauces and drinks [2].

Pumpkin seeds are traditionally used for metabolic issues in women, as demonstrated by an Indian study in which five grams of seeds were administered daily for sixty days to a population aged 30-60, yielding beneficial outcomes [5]. Additionally, some communities consume pumpkin fruit as a preventative measure against iron-deficiency anemia and erysipelas [6]. The seeds are also utilized in the treatment of kidney disorders, bacterial infections, diabetes, hyperlipidemia, cancer, high blood pressure, inflammation, parasitic infections, and are primarily valued for their antioxidant properties, encompassing a wide range of ethnomedicinal applications [5,7].

The pharmacological activities of *Cucurbita* species are closely linked to their complex chemical composition, which varies by plant organ [7,8]. Carotenoids are primarily found in the fruit and seeds, while polyphenols and phenolic acids are abundant in the flowers, fruit, and seeds. Additionally, significant quantities of phytosterols and sugars are present in the seeds and fruit, respectively [5,7,8,9]. Sodium hydrosulfide, along with calcium, nitrogen, and nickel chloride, are notably present in the leaves [4].

However, despite the several utilities of these dicotyledonous plants [9], the recent information is extremely dispersed, so that the objective of this review is to collect new information about the traditional uses, phytochemical studies and pharmacological activities of *C. maxima*, *C. pepo* and *C. moschata.*

2. Main Text

The scientific information was collected systematically from the following databases: Scopus, Science Direct, and PubMed Central. The search keys were: “Cucurbita” AND “chemical composition” or “Cucurbita” AND “effects”. The characteristics of the search were carried out from 2018 to 2024. Repeated articles were eliminated, and those that remained were classified by year of access (last 6 years), type of research (research articles) and relevance, obtaining 45 research documents. These articles were included in the section 2, however, other articles that formed the discussion of the results and introduction did not follow the criteria mentioned above, as they are not part of the central theme of the review, but were only considered accessory articles.

2.1. Morphological Characteristics and Tradicional/Ethnomedicinal Uses of *Cucurbita* Species

Table 1 presents the morphological characteristics of three species from *Cucurbita* genus. These plants grow depending on the crop, usually ranging from fifteen centimeters to twenty centimeters and five to six centimeters in diameter, branched root [10], angular stem and creeping branches, oval leaves, simple, precious, male flower [9], staminate, oily fruit and large berries, as well as presents a fruit shape that varies from globular or ovoid [11], besides a flattened, ovoid and oily seeds [12]. Therefore, based on its morphology, *Cucurbita* species are categorized into well-defined morphologies [13,14,15]. The genus *Cucurbita* consists of twenty to twenty-seven species of which five are cultivated: *C. maxima*, *C. moschata*, *C. pepo*, *C. argyrosperma* and *C. ficifolia*. The first three species mentioned, which are the most widely used globally, are characterized as annual herbaceous plants [13] and contain triterpenoids with significant biological properties [16].

Table 2 summarizes the traditional and ethnobotanical uses of *Cucurbita* species, which has served for many years as an empirical medicine due to its therapeutic properties across different regions worldwide [8,17]. The use of each part of the plant depends on ancestral medicinal knowledge, as well as the specific location or community [18]. *Cucurbita* spp. are commonly utilized in diverse areas of Latin America (mainly in Colombia and Brazil), South Africa, and various other countries such as Benin (Africa), China, Pakistan, Saudi Arabia (Asia), and Australia (Oceania) [2,19], being adaptable to different climatic and geographic regions [20]. The most frequently used plant parts are the fruits [21], seeds, and flowers [9], with oral administration being the predominant method [22,23], commonly found in juices, baked goods, dairy products, soups, and sauces [2,9]. Lastly, the *Cucurbita* species demonstrate a wide range of traditional and ethnobotanical uses, including applications for degenerative and cardiovascular diseases, atherosclerosis, pain and inflammation, diabetes, as well as usage as a detoxifying agent, antioxidant, anticancer agent, tonic, dietary supplement, micronutrient source, antimicrobial, dye, food source, and in cosmetics.

2.2. Phytoconstituents and Pharmacological Activities of *Curcuma* Species

The Table 3 presents the phytoconstituents found in the three species of *Cucurbita*, as well as their effect *in vitro*. Different preparations have been evaluated, from dry sample to extracts [7] such as hydroalcoholic extract [24], methanolic extract [25] and hot water/ultrasound-assisted extract from different parts of the plant: seed [12,16], fruit or pulp [25], flowers [9] and leaves [4]. However, it is also important to consider that cooking and other types of processing can alter the main chemical constituents of *Cucurbita*, thereby also altering its functional and pharmacological properties, whether positively or negatively [26,27]. According to the results found, a high antioxidant response is observed in extracts from seed [7] and methanolic/ethanolic extracts from flowers/fruits, respectively [25,9,28]. These findings are probably related to the presence of polyphenols, including flavonoids [29], which are mainly found in the seed and fruit and also involved with antimicrobial activity[28], and carotenoids, most found in the seed, fruit and flowers [24,25,30,18,2]. Also, the variety in antioxidant structures found in pumpkins can be related to the neurologic protection [31], avoiding neurodegenerative diseases, which in turn was described in a ethnomedicinal study [13], besides they are involved with the treatment of aging and menopause disorders, kidney and hepatic protection, and also with immunomodulation response [32,33,34,35].

Table 1. Morphologic characteristics of the three *Cucurbita* species

Size	Root	Stem	Leaf	Flower	Fruit	Seed
Large size	Branched	Creeping or climbing branches	Broadly oval outline.	Solitary male flowers.	Oilseed	Ovoid
Its size usually depends on the crop (15 -20 cm long and 5 cm - 6 cm in diameter)		Angular stem	Simple, alternate, without stipules.	It has 3 stamens with free threads.	Phenotypic variability	Flattened
The fruits weigh 1 to 2 kg			The length of the petiole varies between 9 and 24 cm	Anther supported by a long twisted organ with a very long peduncle.	Big berry	Oilseed
				Staminate flowers	The shape of the fruit varies from globular to ovoid	

References: [13,14,15]

Table 2. Traditional uses of the three *Cucurbita* species

Plant Organ	Ethnobotanic/Traditional Use	Preparation Way	Adminstration Route	Country	References
Seeds	Degenerative diseases	Not reported	Oral	Benin	[13]
	Food and cosmetic manufacturing	Oil extraction	Topic	Australia	[7]
	Heart (cardiac) diseases	Not reported	Oral	Not specified	[12]
	Detoxifying	Fried or raw, oil	Oral	México, USA	[66]
	Atherosclerosis	Not reported	Topic	Brazil	[23]
	Pain and inflammation	Not reported	Oral	Pakistan	[18]
Roots	Dye	Not reported	Not reported	China	[67]
Fruit	Detoxifying	Water Extraction	Oral	China	[8]
	Micronutrient, antimicrobial	Functional food	Oral	Japan	[19]
	Wide range of bioactivities	Freeze-dried	Oral	Italy	[19]
	Nutrient, antioxidant	Flour	Oral	Saudi Arabia	[39]
	Antioxidant, inflammation	Juices	Oral	Germany	[20]
	Dietary supplement, diabetes, toning	Water Extraction and isolation	Oral	China	[8]
	Lipid oxidation (weight loss), anticancer,	Juice	Oral	Germany.	[68]
	Antioxidants	Dehydration	Not reported	Not specified	[24]
		Juice	Oral	China	[38]
		Juice	Oral	USA	[69]
		Bakery, dairy, soups, sauces	Oral	Colombia	[2]
	Vitamins and antioxidants	Dehydration	Not reported	Brazil	[70]
	Lowers blood sugar and lipids	Juice	Oral	China	[22]
Fruit and aerial parts	Wide range of bioactivities	Bakery, dairy, soups, sauces.	Oral	Australia	[25]
Flowers	Lipid metabolism.	Bakery, dairy, soups, sauces.	Oral	Italy	[9]
	Pollinating	Bakery, dairy, soups, sauces.	Oral	Canada	[71]

Table 3. Phytoconstituents and pharmacological effects of the three *Cucurbita* species

Plant Organ	Way of Preparation	Pharmacological Effect	Main Constituents	Species	References
Seeds	Fatty-Free extract	Not specified	Proteins	*C. moschata*	[16]
	Hydroethanolic extract		Polyphenols, coumaric acid, phenolic acids, ascorbic acid.	*C. maxima*	[24]
		Skin care, vermifuge, antihypertensive, antilithiasic, antiprostatic.	Phytosterols, tocopherols, Mg, Cu, Zn.	*C. pepo*	[66]
		Antiparasitic	Does not specify	*C. maxima*	[58]
		Antioxidant, cytotoxic	Propylpiperidine, flavones, oleic acid, and methyl esters of fatty acids	*C. maxima*	[5]
		Analgesic and anti-	Does not specify	*C. maxima*	[18]

Plant Organ	Way of Preparation	Pharmacological Effect	Main Constituents	Species	References
		inflammatory.			
		Hypoglycemic, antimicrobial, hypocholesterolemic, antioxidant, anticancer, antimutagenic, immunomodulatory, anthelmintic, bladder antilithiasis.	Phenolic´acids, p-hydroxybenzoic acid, p-coumaric and p-hydroxybenzaldehyde.	*C. pepo*	[7]
	Hydroethanolic extract obtained by ultrassonication	Antioxidant	K^+, Mg^{2+} and Ca^{2+}.	*C. pepo*	[12]
	Water extract	Treatment of aging and menopause disorders	Palmitic acid, stearic acid, oleic acid, linoleic acid, alpha-linolenic acid, arachidic acid, polyphenols, flavonoids	*C. pepo*	[32]
	In silico assay	Anti-kidney stone effect	Polyphenols and fatty acids	*C. pepo*	[33]
		Hepatoprotective effect	Phytosterols	*C. pepo*	[34]
	Ethanolic, ethyl acetate and water extracts	Immunomodulation activity	Polyphenols, flavonoids	*C. maxima*	[35]
	Peptide fraction	Anti-hipertensive effects	Proteins	*C. moschata*	[48]
		Anticancer and antidiabetic activities	Proteins	*C. moschata*	[49]
	Decoction	Antiparasitic activity on *Trichinella spiralis*	Phytosterols, gallic acid	*C. pepo*	[59]
	Dried and Sieved	Lipid-lowering, Hepatoprotective.	Oleic and linoleic fatty acids, carotenoids, γ-tocopherol, phytosterols, squalene	*C. moschata*	[23]
Fruit	Hot wáter assisted extract	Traditional medicine	Pumpkin polysaccharides (Glucan, galactoglucans, galactomannan, galactan)	*Cucurbita* spp.	[8]
	Dehumidificated	Antioxidant, anticoagulant, antidiabetic.	Glucose, galactose, rhamnose, arabinose, galacturonic acid, glucuronic acid, mannose, xylose, and fucose.	*Cucurbita* spp.	[8]
	Hydroethanolic extract	Not applicable	Polyphenols, including flavonoids	*Cucurbita* spp.	[29]
	Hidroethanolic/Microwave extraction	Antioxidant and antimicrobial	Phenolic compounds	*C. pepo*	[28]
	Sieved and freeze-dried.	Antioxidant, Lipid-Lowering, Hipoglycemic		*C. moschata*	[39]
	Cutting and heat treatment	Not applicable	Carotenoids	*C. maxima*	[2]
	Homogenizated		L –citrulin and nitric oxide	*C. pepo*	[69]
	High pressure treatment		Polyphenols and carotenoids	*C. moschata*	[19]
	Preparation of purees		Pumpkin polysaccharides	*C. maxima*	[68]
	Inoculation	Antimicrobial	Does not specify	*C. pepo*	[21]
	Water-assisted extraction (WAA) or ultrasound, mechanical pulverization, acid hydrolysis	Anti-inflamatory, antioxidant, antimicrobial, antidiabetic, anticancer, antihypertensive, hipocolesterolémic and antirheumatic	Tetracyclic triterpenes, saponins, glucuronic acid, xylose, arabinose, glucose, galactose, oleic acid	*C. moschata*	[11]
	Ultrasonic treatment	Not aplicable	Carotenoids, phenol, carotenoid polysaccharide pectin and mineral salts, ascorbic acid.	*C. moschata*	[22]
	Ultrasonic and enzymatic assisted extraction	Antidiabétic, antioxidant, anticancer, inmunomodulator and antibacterial	Carotene, peptide, phytosterols.	*Cucurbita* spp.	[8]
	Methanolic	Antioxidant activity and anti-	Alkaloids, carbohydrates, flavonoids,	*C. pepo*	[37]

Plant Organ	Way of Preparation	Pharmacological Effect	Main Constituents	Species	References
	extract	inflammatory properties	proteins, aminoacids, tannins, steroids, triterpenoids, saponins, fats and oils, glycosides		
	Alkali-extracted pectic polysaccharides	Probiotic effect	Polysaccharides	*C. moschata*	[50]
	Fiber fraction		Fibers	*C. moschata*	[54]
	Pectic polysaccharides fraction	Anti-inflammatory activity	Pectic polysaccharides	*C. moschata*	[53]
	Polysaccharides fraction	Regulation of sugar blood levels and lipid metabolism	Polysaccharides	*C. moschata*	[51]
		Colitis alleviation		*C. moschata*	[52]
	Ethanolic extract from peels	Acaricidal activity on *Hyalomma dromedarii*	Does not specify	*C. pepo*	[64]
	Sieved powder	Probiotic effect		*C. pepo*	[65]
Flowers	Ethanoiic extract	Antioxidant and hipoglycemic	Catechin, epicatechin, rutin, syringic acid, ac. chlorogenic, B- carotenes.	*C. pepo*	[9]

On the other hand, it has been found that the hydroalcoholic, methanolic, ethanolic extracts, as well as the hot water/ultrasound-assisted extract, have a greater antioxidant effect [9,8,24,25,18], which in turn are important in the treatment of chronic diseases as intestinal inflammations and women metabolic syndrome [5,36,37]. Other studies report the dehumidification, sieving, lyophilization and high pressure treatments of pumpkin fruit, which has *in vitro* antioxidant effects [19,38,39].

Other important phytochemical groups are found in these species of *Cucurbita*, as for example, phytosterols, terpenoids, alkaloids, phenolic acids, and saponins [5]. The variety of metabolites explains the diversity of pharmacological activities of *Cucurbita* extracts, among which can be cited the hypoglycemic activity, due the presence of terpenoids and polyphenols, including flavonoids, which in turn promote glucose uptake by suppressing gluconeogenesis and enhancing insulin sensitivity [40]. The presence of aforementioned antioxidant metabolites, besides tocopherol, ascorbic acid, phenolic acids are also responsible for other significant activities of pumpkins, among them hypolipidemic and nephroprotective effects [41]. The hypolipidemic effect observed in the discussed studies can be also related to the presence of secoisolariciresinol, a phytoestrogen present in pumpkin seeds that increases angiogenesis and decreases apoptosis, as well as saponins, decreasing LDL level and enhancing HDL in blood [42,43]. Furthermore, antioxidants, which includes rutin, coumaric acid and catechin, besides some phytosterols, such as cucurbitacin E and cucurbitin, are aimed to prevent cancer development, so that some studies with *Cucurbita* demonstrated this activity *in vitro* [44,45,46,47]. Similarly, peptides and sugar polysaccharides have demonstrated to possess pharmacological activities. Two peptides extracted from the seed meel showed inhibitory activity on angiotensin-converting enzyme (ACE), besides also performed protective function on EA.hy926 cells by reducing the secretion of endothelin-1, enhancing the release of nitric oxide, and regulating the ACE2 activity [48]. The seed protein fractions of *C. moschata* also demonstrated anticancer and antidiabetic properties, since cytotoxic effects towards HepG2 and MDA-MB-231 cell lines were observed, whereas the water soluble fraction potentiated glucose-stimulated insulin secretion in pancreatic β-cells, in a dose-dependent manner. This fraction also showed uptake of glucose, when compared to the diabetic group, enhancing the expression of GLUT2 and GLUT4 (glucose transporters) in these groups [49]. Recently, it was observed the prebiotic effect and sugar/lipid blood levels regulation activity of *Cucurbita* species, respectively related to alkali-extracted pectic polysaccharide (AkPP) and polysaccharide fraction (PPF) [50,51]. It was also seen that PPF induces the production of 5-hydroxyindolacetic acid by gut microbiota, which in turn alleviates colitis via MAPKs-PPARγ/NF-κB inhibition [52]. Moreover, the pectic polysaccharide isolated from *C. moschata* also presented anti-inflammatory activity [53]. In its turn, the fiber fraction of *C. moschata* also promoted prebiotic effect on gut, incrementing the *Lactobacillus* load [54].

Regarding the anti-inflammatory and analgesic activities mentioned in some studies of this review, the presence of curcubitanes (phytosterols), carotenoids and magnesium seems to be related to them, since curcubitanes possess ciclooxygenase 2 (COX2) inhibition, carotenoids block oxidative stress, whereas magnesium is a antagonist of voltage-gated N-methyl-D-aspartate (NMDA) receptors, interfering the transduction related to acute or chronic pain [37,55,56,57]. On other side, the antiparasitic activities reported by [5,7,58,59] are related to the presence of saponins, cucurbitanes and other phytosterols [60]. Saponins possess a surfactant function that affects helminth parasites by altering membrane permeability. A potential secondary mechanism involves the inhibition of protein synthesis, as observed against certain ruminant parasites [61]. In turn, phytoesterols can act by hormonal interference against different pathogens parasites, since they are able to block sterol 14α-demethylase, an important enzyme for parasites metabolism or up-regulating the intestinal TGF-1β, provoking the “weep and sweep mechanism”, which in turn is also augmented through the administration of gallic acid [62,59]. Moreover, terpenes—including phytosterols—and flavonoids have well-documented antimicrobial activity [63], which may account for the various findings reported in this review [5,8,11,21]. Additionally, noteworthy acaricidal activity of *C. pepo* peel has been observed against *Hyalomma dromedarii*, with the ethanolic extract demonstrating high efficacy, causing over 90% mortality [64].

Furthermore, studies on *Cucurbita* toxicity demonstrated safety of consume. In a study of acute and chronic toxicity test, *C. pepo* fruit powder exhibited low acute toxicity, displaying a median lethal dose (LD_{50}) > 2000 mg/kg., whereas the sub-chronic toxicity test with 200, 400, and 600 mg/kg doses did not cause mortality or significant organ damage in mice. Still, analysis of the gut microbiota after oral administration of *C. pepo* at 400 and 600 mg/kg showed an enhancing of some beneficial gut bacteria [65].

Regarding the phytochemistry of the three *Cucurbita* species, it is noteworthy to highlight the attention given to the protein content of *C. moschata* seeds and the carbohydrate profile of its fruits, while *C. pepo* and *C. maxima* seeds exhibit phenolic and polyphenolic compounds, as well as fatty acids, as metabolites of primary interest. Carotenoid and polyphenolic contents, including flavonoids, are also significant in the fruits and flowers of *Cucurbita* species.

The recently evaluated pharmacological activities of the three *Cucurbita* species not only interact with the descriptions of popular medicinal use, but also include new fields of pharmacological study for these species. The medicinal use of the seed for the treatment of diseases related to the cardiovascular system may be related to studies that demonstrate the hypocholesterolemic and antihypertensive activities observed in *C. pepo* and *C. moschata*, respectively, as well as their high antioxidant potential described in all species. These biological activities are frequently described for polyphenolic substances such as flavonoids, in addition to carotenoids and fatty acids, such as linoleic acid, also including the possible action of peptides in the control of blood pressure [7,12,48]. Also interestingly, the anti-inflammatory use of the seeds may be related to the activity observed in *C. maxima*, described by [18]. Furthermore, *Cucurbita* seeds also present other interesting pharmacological activities such as immunomodulatory, antidiabetic and antiparasitic, among others, which in turn may also explain the medicinal use described in older studies [32,49,58,59]. Concerning the pharmacological activity of the fruits, the antioxidant, antidiabetic and anti-inflammatory activities are highlighted and observed in all species mentioned in the review, which also have a broad relationship with the popular uses previously described for the fruits [8,11,28]. According to the aforementioned studies, the antidiabetic activity, also observed in the flowers, can be explained by the presence of polyphenols, which inhibit carbohydrate-digesting enzymes, as well as triterpenes, which can act on glucose metabolism in the intracellular environment or through the insulin cycle [8,9,11,40]. Other activities related to popular use are also described, such as anticancer, antimicrobial and blood lipid-lowering activities, as well as beneficial effects on the intestine, which probably include anti-inflammatory and probiotic mechanisms of action, in turn related to the phenolic and polyphenolic compounds, carotenoids, as well as carbohydrates and fibers [8,11,50,51,52,65].

Finally, the varied and promising pharmacological activities found in the three *Cucurbita* species must undergo clinical trials to verify their real effectiveness, toxicity and dose definition, in addition to the necessary research into the development of formulations that improve the solubility and efficiency of extracts and active components, such as nanoparticles and nanoemulsions.

3. Conclusions

Pumpkin is one of the most widely used and distributed plants globally. This review presents several recent studies highlighting the use of at least three *Cucurbita* species as versatile natural therapeutic resources, including their antioxidant, antidiabetic, antihypertensive, antihyperlipidemic, anticancer, anthelmintic, and antilithiasic properties. They are also used in treating hypoglycemia, degenerative and cardiovascular diseases, detoxification, and atherosclerosis. Traditional usage occurs mainly in rural areas, and their biological activities have been extensively researched in various countries, where different plant parts serve medicinal purposes. Additionally, the fruits and seeds are widely utilized in food and cosmetics. Key chemical compounds reported in these studies include coumaric acid and other phenolic acids, ascorbic acid, flavonoids and other polyphenols, phytosterols, fatty acids, terpenes, propylpiperidine and other alkaloids, tocopherols, saponins, sugars, and carotenoids.

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