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REVIEW

Pumpkin (*Cucurbita* sp.) seeds as nutraceutic: a review on status quo and scopes

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Abstract The seeds of pumpkin (*Cucurbita* sp.) are generally considered to be agro-industrial wastes and discarded. In some parts of the world, the seeds are consumed raw, roasted or cooked, but only at the domestic scale. With the discovery of their richness in protein, fibres, minerals, polyunsaturated fatty acids and phytosterols, they are being regarded valuable for the food industry. The attention of food technologists has resulted in their foray into the commercial food sector. Food companies are experimenting with their incorporation into a slew of savouries and consumers are showing interest in them. Also, their beneficial effects on blood glucose level, immunity, cholesterol, liver, prostate gland, bladder, depression, learning disabilities and parasite inhibition are being validated. The conversion of these agro-wastes into value-added ingredients is likely to be a big step towards the global sustainability efforts; thus, it deserves more investigation. This review furnishes an updated account of this emerging nutraceutical.

Keywords Pumpkin seed · Functional food · Polyunsaturated fatty acid · Phytosterol · Prostate health

Introduction

Pumpkins (*Cucurbit sp.*) belonging to the Cucurbitaceae family are grown widely around the world as a vegetable (Fig. 1a). In the USA, they are vastly used for Halloween carvings and thanksgiving feasts. Most of the crops are processed into canned pumpkins or pie mix. However, the plentiful flat, oval seeds are generally discarded as agricultural residues (Fig. 1b). The seeds are uniquely flavoured with nutty taste and are consumed as roasted, salted snack in some parts of Canada, Mexico, USA, Europe and China. Now, grocery stores are also selling these seeds as baked, sprouted, fermented, pumpkin protein concentrate and pumpkin protein isolate, as their richness in protein, iron, zinc, manganese, magnesium, phosphorous, copper, potassium, polyunsaturated fatty acids, carotenoids and γ-tocopherol is beginning to surface.

There is a growing interest in vegetable oils of special composition, and pumpkin seed oil is a promising candidate in this regard. Cold press or steam distillation is used for oil extraction. The dark greenish-red oil is used for cooking, as marinade or salad dressing and it has already been touted as a contender to olive oil. It is being used in many epicurean delights, viz. chocolate, cereal bar, bread, cake, muffin, soup, pesto, stew and pasta garnish. Pumpkin seed butter is considered as a great alternative to peanut butter. Major US food stores such as Costco, Trader Joes and Walmart sell myriad varieties of pumpkin seed-based food products, viz. granola chunks, tortilla chips, vegetable salad, sourdough bread, cookies and quinoa salad.

Pumpkin seeds and derived oil comprise a multi-million dollar industry in Europe. Most of the oil is manufactured in Austria, Slovenia, Serbia and Hungary. Its popularity is at the nascent phase in other regions of the globe, which slowly but surely is gathering momentum. This review strives to provide an updated account of the established and putative benefits, bottlenecks and scopes for broader uses.

Nutrients

The phytochemical composition renders the seeds valuable for nutritional purposes. Stevenson et al. [1] studied several

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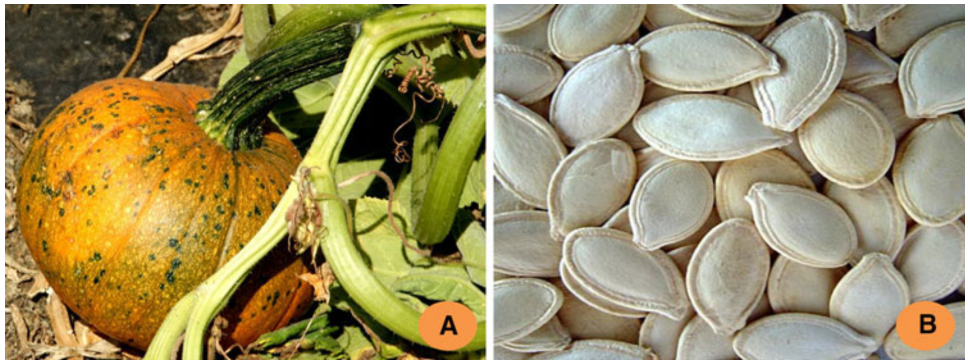

Fig. 1 **a** A ripe pumpkin in vine. **b** The seeds

pumpkin cultivars (*Cucurbita maxima* D.), for their seed oil content, fatty acid composition and tocopherol content. The oil content ranged from 11 to 31 %. Total unsaturated fatty acid content ranged from 73 to 81 %. The predominance of linoleic, oleic, palmitic and stearic acids was observed. The α-tocopherol content of the oils ranged from 27 to 75 mg/g, while γ-tocopherol ranged from 75 to 493 mg/g. Ryan et al. [2] determined the levels of phytosterols, squalene and tocopherols in pumpkin seeds. The method comprised acid hydrolysis and lipid extraction followed by alkaline saponification, prior to analysis by HPLC. Beta-sitosterol was the most prevalent phytosterol, ranging in concentration from 24.9 mg/100 g seed. Squalene was particularly abundant (89 mg/100 g) and the total oil content amounted to 42.3 % (w/w) in pumpkin seeds. Veronezi and Jorge [3] reported variation in total phenolic compounds in the lipid fractions of different cultivars of pumpkins (Mini Paulista and Nova Caravela showed highest). Kim et al. [4] reported that the major fatty acids in the pumpkin seeds were palmitic, stearic, oleic and linoleic acids. *C. pepo* and *C. moschata* seeds had significantly more γ-tocopherol than *C. maxima*, whose seeds had the highest β-carotene content. *C. pepo* seeds had significantly more β-sitosterol than the others. Among 11 types of nuts and seeds profiled for their nutritional abundance, pumpkin seeds scored highest for iron content (95.85 $\pm$ 33.01 ppm) [5]. The nutrient distribution in pumpkin seed is presented in Table 1.

Antioxidant activity

Andjelkovic et al. [6] measured the total phenolics content in the pumpkin seed oil, which ranged from 25 to 51/mg GAE/kg of oil. The individual phenolics were tyrosol, vanillic acid, vanillin, luteolin and sinapic acid. The maximum antioxidant capacity measured by the reduction of the DPPH radical was 62 %. Ardabili et al. [7] reported that the addition of pumpkin seed oil improved the frying

Table 1 Bioactive components and their percentages in pumpkin seed (nutrient value per 100 g)

Components	Nutrient value	Percentage of RDA
Energy	559 kcal	28
Carbohydrates	10.71 g	8
Protein	30.23 g	54
Total fat	49.05 g	164
Cholesterol	0 mg	0
Dietary fibre	6 g	16
Vitamins		
Folate	58 µg	15
Niacin	4.987 mg	31
Pantothenic acid	0.750 mg	15
Pyridoxine	0.143 mg	11
Riboflavin	0.153 mg	12
Thiamine	0.27 mg	23
Vitamin A	16 IU	0.5
Vitamin C	1.9 µg	3
Vitamin E	35.10 mg	237
Electrolytes		
Sodium	7 mg	0.5
Potassium	809 mg	17
Minerals		
Calcium	46 mg	4.5
Copper	1.343 mg	159
Iron	8.82 mg	110
Magnesium	592 mg	148
Manganese	4.543 mg	198
Phosphorus	1,233 mg	176
Selenium	9.4 µg	17
Zinc	7.81 mg	71
Phytonutrients		
Carotene-β	9 µg	–
Cryptoxanthin-β	1 µg	–
Lutein–zeaxanthin	74 µg	–

Courtesy: USDA National Nutrient Database stability of canola oil. The better antioxidative effect of the former was attributed to its phenolic composition.

Nkosi et al. [8] investigated the antioxidative effects of pumpkin seed protein isolate on rats kept on a low-protein diet for 5 days. The rats were subjected to acetaminophen intoxication and then given pumpkin protein isolate. The rats were killed at 24, 48 and 72 h after their respective treatments. The isolate exhibited about 80 % radical scavenging activity, chelating activity of approximately 64 % on Fe^{2+} ions and an inhibition of approximately 10 % of xanthine oxidase. CCl_4-induced liver injury was alleviated by pumpkin protein isolate as evidenced from the improved antioxidant level and lowered levels of lipid peroxidation. El-Boghdady [9] reported that pumpkin seed oil protected the small intestine of rats from methotrexate-induced damage through antioxidant and anti-inflammatory effects. Oral gavage of the oil alone or with ellagic acid for 5 days prior to methotrexate treatment decreased the intestinal damage, serum prostaglandin E2, tissue malondialdehyde, nitric oxide, myeloperoxidase, xanthine oxidase and adenosine deaminase activities and increased GSH level.

Functional food and technical developments and hurdles

Naghii and Mofid [10] studied the effect of consumption of iron-fortified ready-to-eat cereal (30 g providing 7.1 mg iron/day) and pumpkin seed kernels (30 g providing 4.0 mg iron/day) for 4 weeks. Indices of iron status such as reticulocyte count, haemoglobin, haematocrit, serum ferritin, iron, total iron-binding capacity and transferrin percent were determined. Better response for iron status as indicated by higher serum iron was observed after the consumption period. Young children, adolescents, women of reproductive ages and pregnant women who are often prone to iron deficiency-caused anaemia may be benefitted. Norfezah et al. [11] investigated the effect of incorporation of flour from the three different fractions (peel, flesh and seed) of Crown pumpkin (*C. maxima*). The flour was incorporated into an extruded snack formulation at various levels and processed in a twin-screw extruder to make ten expanded snack products. Inclusion of the peels and seeds at 10 % yielded extruded products with similar expansion and density characteristics to the control sample; however, an inclusion of greater than 10 % led to hardness of the product. Radocaj et al. [12] developed a stable spread rich in ω-3 and ω-6 fatty acids using a hull-less pumpkin seed oil press cake. Response surface methodology (RSM) was employed to optimize the spreads. The spread resembled commercial peanut butter, in appearance, texture as well as spreadability. The product contained ω-3 fatty acids and showed no visual oil separation even after 1 month of storage. An optimum spread was produced using 1.25 % (w/w) of stabilizer and 80 % of hemp oil (w/w of the total added oil) which had 0.97 g of ω-3 fatty acids per serving size and oil separation of 9.2 % after 3 months of storage.

Ward and Ainsworth [13] developed an inexpensive weaning food with adequate dietary energy, protein and fat for malnourished infants in Kenya. The porridge was cooked, dried and blended with ground pumpkin seeds followed by heat treatment and storage at ambient temperature for 8 weeks. The in vitro protein digestibility was 82.5 %, confirming a high-quality protein food. HPLC analysis detected no free-floating water-soluble amino acids, indicating food stability. A low peroxide value was found, confirming the absence of rancidity, and viscometer analysis approved the consistency for infant feeding, though flavour got a less favourable score. El-Soukkary [14] determined the effect of incorporation of pumpkin seed into wheat flour and dough properties. The results indicated that pumpkin seed products could be added to wheat flour up to a 17 % protein level for raw, roasted and autoclaved pumpkin meal, 19 % level for germinated, fermented and pumpkin protein concentrate and 21 % level for pumpkin protein isolate without a detrimental effect on dough or loaf quality. On the other hand, the addition of pumpkin seed proteins resulted in increasing protein, lysine and mineral contents compared to the control. In vitro protein digestibility improved when the pumpkin seed proteins were added. Procida et al. [15] investigated the carotenoid (lutein and zeaxanthin), vitamin E (α- and γ-tocopherol) and fatty acid contents of 12 samples of pumpkin seed oils along with the volatile fraction resulting from the roasting process. The roasting temperature played a crucial role in the concentrations of volatile substances originating from Strecker degradation, lipid peroxidation and Maillard reaction. The findings suggest that high-temperature roasting leads to the production of an oil with intense aromatic characteristics, while mild conditions lead to a product with a minor characteristic pumpkin seed oil aroma. The nutraceutical properties of the product are confirmed by the high content of α- and γ-tocopherol and carotenoids.

Adulteration is a major risk in deriving the optimal therapeutic benefits of pumpkin seeds and oil. Butinar et al. [16] employed a set of HPLC triacylglycerol determinations for the evaluation of the novelty of pumpkin seed oil from Slovenia. Vujasinovic et al. [17] optimized the roasting condition for hull-less pumpkin seeds using RSM, for maximum yield of the bioactives and antioxidants from the virgin pumpkin oils. The optimum conditions for roasting the seeds were 120 °C for 49 min, which resulted in oil with phospholipids 0.29 %, total phenols 23.06 mg/kg, α-tocopherol 5.74 mg/100 g, γ-tocopherol 24.41 mg/100 g and antioxidant activity of 27.18 mg oil/mg DPPH. Bowman and Barringer [18] determined the dominant volatiles in raw and roasted pumpkin seeds. Also, the effect of seed coat, moisture content, fatty acid ratio, total lipids, reducing sugars and harvest year on volatile formation was assessed. Hull-less seeds contained higher volatile lipid aldehydes and Strecker aldehydes. Seeds dehydrated to a moisture content of 6.5 % before roasting had higher initial and final volatile concentrations than seeds starting at 50 % moisture. Sensory analyses showed that hull-less seeds were preferred significantly than hulled seeds.

Pumpkin seeds and health

Substantial amount of research findings have accumulated in recent times that endorse the health benefits of pumpkin seeds and vouch for their use in dietary intervention.

Hypolipidaemic effect

Makni et al. [19] evaluated the effect of flax and pumpkin seed mixture intake in rats fed with a 1 % cholesterol diet. In the seed-fed group, significant increase in poly- and monounsaturated fatty acids was observed. Plummeted malondialdehyde level and bolstered antioxidant defence system indicated the anti-atherogenic potential of the seed mixture. Gossell-Williams et al. [20] examined the effect of pumpkin seed oil supplementation on the total cholesterol, and low-density and high-density lipoprotein cholesterol, and systolic and diastolic blood pressure in rats. Both non-ovariectomized and ovariectomized rats were supplemented with corn oil or pumpkin seed oil for 5 days/week for 12 weeks (40 mg/kg given orally). Blood analysis showed healthy lipid level in the pumpkin seed oil-supplemented group. Barakat and Mahmoud [21] examined the efficacy of pumpkin seed used along with flax or purslane seed on hyperlipidaemia in high cholesterol diet-fed rats. A 2 % cholesterol administration caused a significant increase in total cholesterol, total lipids and triacylglycerol in both serum and liver. The consumption of flax/pumpkin or purslane/pumpkin seed mixtures resulted in a significant decrease in lipid parameters suggesting the anti-atherogenic potential of the seed mixture.

Antihypertensive and cardioprotective effect

Pumpkin seeds play an important role in relaxing vessels and lowering blood pressure. El-Mosallamy et al. [22] determined the effects of pumpkin seed oil treatment on chemical-induced hypertension in rats. The oil (40–100 mg/kg), was given once daily for 6 weeks. Intake of the oil significantly reduced the abnormal increase in blood pressure caused by the chemical and normalized the electrocardiogram changes. Also, it decreased the elevated levels of MDA and reversed the decreased levels of NO metabolites to normalcy. The results showed the protective effect of pumpkin seed oil against pathological alterations in the heart and aorta, the mechanism of which was attributed to the generation of NO. NO production is attributed to amino acid L-arginine. Also, the high magnesium content is credited to reducing the risks of heart attack. The seed supplements have shown comparable efficiency to the calcium channel blocker prescription drug amlodipine.

Anti-diabetic effect

While diabetes patients are barred from consuming pumpkin for its obvious carbohydrate richness, the seeds pose no threats. Makni et al. [23] investigated the hypoglycaemic and antioxidant effects of flax and pumpkin seed mixture on the kidney of alloxan-induced diabetic rats. The characteristic histopathological changes were less pronounced as the supplement ameliorated the antioxidant enzymes CAT, SOD and GSH and decreased MDA levels. The increases in glucose, total lipid, total cholesterol and triglycerides in plasma were significantly subdued. Further, Makni et al. [24] observed that a pumpkin seed oil diet attenuated the increased levels of the plasma enzymes aspartate aminotransferase and alanine aminotransferase that pose a risk of diabetes. Its use in regular food may be effective in the prevention of diabetes and its complications. Teugwa et al. evaluated the hypoglycaemic activity of proteins derived from several species of Cucurbitaceae, including *C. moschata*. The result of the oral glucose tolerance test performed on rats revealed that globulin was the most abundant storage protein which measured 295.11 mg/g dry matter and capable of causing significant drop in blood sugar (88–137.80 %) [25]. However, supplemental work must be undertaken to lend further credence to the above findings.

Cancer management

Pumpkin seed consumption has shown considerable benefits in benign prostatic hypertrophy (enlarged prostate gland). Gossell-Williams et al. [26] examined the effect of pumpkin seed oil on testosterone-induced hyperplasia of the prostate in rats. During the course of hyperplasia induction, oral administration of either pumpkin seed oil or corn oil (vehicle) was given for 20 days. On day 21, rats were killed and the prostate was weighed. The induced increase in prostate size was inhibited in rats fed with pumpkin seed oil (2 mg/100 g). The protective effect of pumpkin seed oil was significant at the higher dose. The result builds hope for management of benign prostatic hyperplasia. Hong et al. [27] conducted a randomized, double-blind, placebo-controlled trial on benign prostatic hyperplasia patients. Continuation for 3 months resulted in reduction in cancer symptoms and improved overall quality of life. After 12 months, the hyperplasia-caused urination and bladder problems subsided and conspicuous progress in urinary flow was observed. Jiang et al. [28] showed that ProstaCaid^{TM} treatment (a polyherbal preparation with pumpkin seed as an ingredient) resulted in the inhibition of cell proliferation of the highly invasive human hormone-independent prostate cancer PC-3 cells in a dose- and time-dependent manner. DNA-microarray analysis demonstrated that it inhibited the proliferation of cancerous cells through the modulation in expression of CCND1, CDK4, CDKN1A, E2F1, MAPK6 and PCNA genes. The formulation suppressed the metastatic behaviour of cancer cells by the inhibition of cell adhesion, cell migration and cell invasion, which was associated with the down-regulation of expression of CAV1, IGF2, NR2F1 and PLAU genes. Also, it controlled the secretion of the urokinase plasminogen activator from PC-3 cells. Zaineddin et al. [29] administered a food-frequency questionnaire to a vulnerable group of women. It was found that the consumption of sunflower and pumpkin seeds was associated with significantly reduced postmenopausal breast cancer risk.

Gynaecological effect

Phytoestrogens are plant metabolites with structural and functional similarity to 17β-estradiol, recognized to lower the risk of osteoporosis, heart disease, breast cancer and menopausal symptoms [29]. Pumpkin seed oil has been discovered to be as rich in phytoestrogens as other plant sources as soy foods, flaxseed, sunflower seed, sesame, etc. Gossell-Williams et al. [30] evaluated the probable beneficial effects of pumpkin seed oil on postmenopausal women. The randomized, double-blinded and placebo-controlled study involved 35 women who had undergone menopause naturally or due to surgery. The subjects receiving pumpkin seed oil showed a significant increase in high-density lipoprotein and decrease in diastolic blood pressure. A decrease in the severity of hot flushes, less frequent headaches and less joint pains were reported in the pumpkin seed oil-administered group. The placebo group dispensed with wheat germ oil complained of more depression and emotional insecurity. The positive response warrants further probing into the menopause remedial effects of pumpkin seeds.

Anthelmintic effect

In many cultures throughout the world, pumpkin seeds are used as a natural treatment for parasites. Several Native American tribes used it to get rid of internal worms. Taeniasis refers to the infection with adult tapeworms of *Taenia* spp. in the upper small intestine of humans. Exposure to eggs of *Taenia* spp. leads to tissue infection, cysticercosis. The conventional chemical drugs often cause induction of epileptic seizures or convulsions in carriers with asymptomatic concurrent neurocysticercosis. Li et al. [31] assessed the curative effect of pumpkin seed/areca nut extract treatment on 115 suspected taeniasis cases. The mean time period for complete elimination of tapeworms in the studied cases was 2 h. Though both plant extracts showed tapeworm elimination, a synergistic effect was observed accounting for 89 % efficacy. The seeds were found to be beneficial in cases of acute schistosomiasis, a type of parasite contracted from freshwater snails that causes fever, chills, headache, fatigue and intense gastrointestinal discomfort. Cucurbitine, an amino acid and carboxypyrrolidine (structural similarity with proline) found in the seed was found to be the active anti-worming agent. When cucurbitane extracted from *C. moschata* seeds was given at a daily dose of 350–400 mg/kg for 28 days to mice, *Schistosoma japonicum* development was retarded. Shrinkage of size, atrophy of uterus and reductions in the number of ova led to fall in the worm population to about 44–69 %.

Safety issues

Despite the litany of health benefits, consumption of pumpkin seeds are not entirely free from risks. Ingestion of whole pumpkin seeds results in minor stomachache in some consumers. Rectal seed bezoars commonly occur due to seeds, especially in children living in countries south of the Mediterranean and in the Middle-East. Inadequate chewing or hasty eating of dried pumpkin seeds without removing the hull may lead to their impaction as bezoars, which may require manual removal under general anaesthesia [32]. Manne et al. [33] reported a case of a 62-year-old man with a rectal bezoar composed of pumpkin seeds which necessitated manual disimpaction and colonoscopy. Rodriguez-jimenez et al. [34] reported a case of allergy to pumpkin seed in which an IgE-mediated hypersensitivity mechanism was demonstrated both in vivo and in vitro. A protein of approximately 12 kDa seemed responsible for the allergy. Roasted seeds contain trans-fat that may deposit plaque in the arteries. Saucedo-Hernandez et al. [35] reported that the quality control of pumpkin seed oils is important because the cultivar types are the determinants of their pharmaceutical properties. Willis et al. [36] conducted a study on contamination of several edible seeds in the UK, out of which *Escherichia coli* was detected in 9 % of samples. Also, mycotoxins have been found to be a threat. These findings highlight the importance of impurity-free pumpkin seeds, good hygiene practices and rigorous decontamination procedures.

Conclusion and future perspective

The findings above confirm that pumpkin seed not only serves as delicious food, but also possesses therapeutic values. There are several cultivars of pumpkins, but so far only *C. pepo, C. maxima* and *C. moschata* have been studied. Nutritional assessment of other seed varieties and breeding of the high-yield varieties can open up new food formulation opportunities. With sufficient investigative focus, it may emerge as a substitute to sunflower seed or a complement to flaxseed. Pumpkin seed oil could be an alternative to the expensive olive oil. The optimal use of this nutrition-dense seeds must be given due attention, for it could address the food security issue to a significant degree. The popularization of innovative nutraceuticals for mass nourishment is being given a fast-track status, and in this regard this review discusses a highly relevant candidate.

Apart from the validated medicinal properties, pumpkin seeds hold other health-restorative prospects. They are anticipated to avoid kidney stones, treat incontinence, drive away depression, prevent osteoporosis, promote ocular health, nourish skin etc.; however, there are insufficient studies in these directions. Microbial fermentation for subduing the anti-nutritional components and value addition could be explored. Its blending with other beneficial botanicals could result in desirable supplements. Genetic as well as environmental factors may influence the seed nutrient contents, so this aspect could be delved into [37]. More clinical trials are required to appreciate and utilize the optimal nutritional potential of pumpkin seeds.

Conflict of interest There is no conflict of interest in submitting this work to this journal.

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