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REVIW ARTICLE

The Critical Nutraceutical Role of Pumpkin Seeds in Human and Animal Health: An Updated Review

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Abstract

Publicity of pumpkins in traditional medicine for relieving diverse disturbances such as hypertension, arthritis, hyperglycemia, inflammation, dyslipidemia, fungal or bacterial infections, tumors, and intestinal parasites made a highlight for more research on pumpkin fruits as well as seeds. Multiple studies have been fulfilled on animal models, clinical trials or cell cultures to assess these medicinal activities. Pumpkin is admitted for its ingested seeds, fruits, and greens. Pumpkin seeds are enhanced by micro- and macro-constituent compositions include proteins, antioxidative phenolic compounds, tocopherols, triterpenes, saponins, phytosterols, lignans, and carotenoids; among these compounds: D-chiro-inositol, trigonelline, and nicotinic acid, those are reflected as insulin action mediators. Pumpkin seeds are also fortified with polyunsaturated fatty acids (PUFA), fibers, vitamins, and minerals including zinc, iron, magnesium, calcium, manganese, and copper, thus pumpkin seeds have become commonly used as health booster or herbal therapy for human as well as animals, and the food technologists have conquered the commercial food and alternative medicine sectors with pumpkin products. Furthermore, Food companies intend to exploit pumpkin seeds in the starters and snacks industry. This review article provides an update on the therapeutic impacts of pumpkin seeds and mechanisms by which they may limit the risk of diseases.

Keywords: Pumpkin seed oil, phytosterols, antioxidant, anthelmintic, pumpkin waste, livestock feed.

Introduction

Pumpkins or gourds are related to "*Cucurbitaceae*" family of plant kingdom [1]. Utmost of the family species used in foodstuff and organized in five genera: *Citrullus* (wild colocynths, and water melons), *Cucumis* (cucumbers, gherkins and melons), *Sechium* (chayotte), *Lagenaria* (gourds) and *Cucurbita*. The genus *Cucurbita* encompasses five distinctive species, which are: *Cucurbita moschata*, *C. pepo*, *C. ficifolia*, *C. maxima* and *C. turbaniformis* [2].

Cucurbita pepo L. is a mutual species with a floppy spread, mostly in North America, as pumpkins were implanted there for the previous thousands of years [3]. It is assumed that *C. pepo* is more enduring and less susceptible to spoil, which is inverted in the extracted oil quality [4]. In the United States, pumpkins are immensely consumed in Halloween engravings and Thanksgiving feasts, they are packaged into tinned pumpkins or pie mix, however, the copious oval, flat seeds were discarded previously as agricultural residues [5].

Pumpkins are annual creeps or trailing plants that can be planted from the sea level to the high peaks, with expanded cultivation from northern Mexico to Chile and Argentina and broaden to Europe and Asia, China and India in particular, and Western America [6].

Lately, great attention has been intensified on the exploitation of by-products and wastes in feed-processing, also the untapped agricultural products. Indeed, previously a small ration of plant parts is directly exploited for human

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consumption; however the other remaining portions of plant material or parts may be transformed into fertilizers or feedstuff, therefore a significant involvement in industrial products or food resources can be prepared. After the exploitation of the flesh and pulp of pumpkin squashes, still remaining high quantities of husked seeds as waste products [7].

Pumpkin seeds

Pumpkin seeds are distinctive in flavor and nutty-tasted, which can be picked as snacks in salted-roast or unroasted form, whereas the kernels are used in baking, cooking and in gravies and soups as flavor improvers. These days, pumpkin seeds are sold as sprouted, fermented, or pumpkin protein isolate [8], as the pumpkin seeds are immensely nutritional and fortified with nutraceuticals such as carotenoids, phytosterols, phytoestrogens, triterpenes, tocopherols, lignans, and saponins; these compounds termed as phenolic compounds or secondary metabolites with significant antioxidative capacity [9].

Pumpkin seeds involve vitamins and significant amounts of minerals particularly phosphorus, magnesium, potassium, and iron [10], as shown in Table (1). Thus pumpkin seeds consumption is highly profitable to hypertensive patients treating with diuretics and loss excess of potassium levels [11]. Pumpkin seeds are fortified with a substantial concentration of proteins [12], thus eating pumpkin seeds can help in reaching the approximated value of recommended daily protein demand in adults ≈0.9 gram of protein/kg/day, and this according to the US/Canadian Dietary Reference Intakes [13]. Evaluation of amino acid concentrations in pumpkin seeds revealed that arginine, glutamic and aspartic acids are the most considerable residues, but tryptophan and methionine are the least [14], as shown in Table (2). On account of the whole constituents, pumpkin seeds were found to possess antihyperglycemic, hypolipidemic, antioxidative, anticancer, anti-inflammatory and anti-prostatic hypertrophy efficiencies [15].

Table 1: Nutrient values per 100 grams of pumpkin seed kernel according to Patel [6]

Nutrient	Value per 100 g
Protein	30.23 g
Energy	559 kcal
Total lipid	49.05 g
Fiber	6 g
Carbohydrates	10.7 g
Micronutrients (Vitamins)	
Vitamin C	1.9 µg
Niacin	4.98mg
Thiamine	0.27 mg
Riboflavin	0.15 mg
Pantothenic acid	0.75 mg
Vitamin A	16 IU
Vitamin E	35.1 mg
Folate	58 µg
Mineral Deposits	
Iron	8.82 mg
Phosphorous	1233 mg
Magnesium	592 mg
Potassium	809 mg
Zinc	7.81 mg
Manganese	4.54 mg
Copper	1.3 mg
Selenium	9.4µg
Sodium	7 mg
Phytochemicals	
β-Carotene	9 µg
β-Cryptoxanthin	1 µg
Leutin-Zeaxanthin	74µg

Table 2: Amino acid values per 100gm of edible portion of pumpkin seed kernel as per USDA National Nutrient Database for Standard Reference, Release 20 (2007).

Amino acid	Value per 100 g
Glutamic acid	4.315 g
Arginine	4.033 g
Aspartic acid	2.477 g
Leucine	2.079 g
Lysine	1.833 g
Isoleucine	1.264 g
Threonine	0.903 g
Tryptophan	0.431 g
Methionine	0.551 g
Cysteine	0.301 g
Phenylalanine	1.222 g
Tyrosine	1.019 g
Valine	1.972 g
Histidine	0.681 g
Alanine	1.158 g
Glycine	1.796 g
Proline	1 g
Serine	1.148 g

Pumpkin seed oil

There is an overstate concern of the distinctive formulation of vegetable oils; the oil of pumpkin seeds is a promising ambition in this regard. Oil can be extracted by either cold press or steam distillation yielding a dark greenish-colored pumpkin seed oil that can be used in cooking and salad dressing [16]. Moreover, oil can be consumed in cereal bars, chocolates, cakes, bread, muffins, soups, pasta, pesto and a garnish of stew [17], furthermore, the butter of pumpkin seeds are employed as an adorable alternative to peanut butter [18].

Pumpkin seed oil possesses a comparatively modest composition of fatty acids, predominantly the essential fatty acids: linoleic, stearic, oleic and palmitic acids [12], those four fatty acids estimate almost (98 ± 0.13%) of the total amount of fatty acids [19], as presented in Table (3). Besides, phytoestrogens and phytosterols such as β-sitosterol, secoisol ariciresinol, genistein, daidzein are included [13]. Pumpkin seed oil also includes elevated amounts of numerous non-triacylglycerol constituents such as tocopherols that play a vital role in suppression of free radical formation in biological systems [9]. Tocopherols are highly affected by the processing methods utilized in oil extraction from the pumpkin seeds [20]. Moreover, pumpkin seed oil contains specific amounts of polyphenols; Andjelkovic *et al.* [21] evaluated the total concentration of polyphenols in pumpkin seed oil with ≈25-51 mg/kg as gallic acid equivalents. The HPLC analysis of individual phenolic ingredients valued the polyphenolics of pumpkin seed oil including vanillic acid, tyrosol, o-coumaric acid, caffeic acid [22] and trans-cinnamic acid [23]. Conventionally, the pumpkin seed oil is attained by pressing either roasted pumpkin seeds or the unroasted pumpkin seeds to gain the cold-pressed pumpkin seed oil, where the difference in the two oils is in the sensory appearances such as taste, color and odor [24]. Researches on vegetable oils got from roasted seeds disclose that pumpkin roasted seed oil are enriched with mono- and poly-unsaturated fatty acids, minerals, vitamins, pigments, phytosterols, phenolic compounds, and pyrazine derivatives [25]. For all that, the pumpkin seed oil is considered as desirable edible oil as well as it attracts interest as potential nutraceutical oil.

It was found that pumpkin seed oil attains numerous critical medicinal impacts, including suppressing growth and decrease size of the prostate, delay of the hypertension progression, alleviation severity of arthritis and hypercholesterolemia and diabetes, suppression of urethral and bladder pressure, and depressing the levels of breast, gastric, colorectal and lung cancer cells [20].

Table 3: Means of duplicate determinations of fatty acid composition of pumpkin seed oil (*Cucurbita pepo*) according to Ardabili *et al*. [12].

Fatty acid	Content (%)
Palmitic acid	10.68 ± 0.42
Stearic acid	8.67 ± 0.27
Oleic acid	38.42 ± 0.37
Linoleic acid	39.84 ± 0.08
Palmitoleic acid	0.58 ± 0.14
Linolenic acid	0.68 ± 0.14
Gadoleic acid	1.14 ± 0.00
Total unsaturated fatty acids	80.65 ± 0.16
Total saturated fatty acids	19.35 ± 0.16

Estrogenic-like effects

Phytoestrogen is a poly-phenolic constituent that has the binding ability with the estrogen receptor so it holds estrogenic-like properties. The pumpkin seed oil has been confirmed to comprise a great amount of sterols and phytoestrogens like lariciresinol and secoisolariciresinol [26]. Supplying of pumpkin seeds oil led to substantial hepato-protective and anti-atherogenic impacts in hyper-cholesterolemic rats [27]. Another research stated that pumpkin seeds retain estrogenic-like effects comprising the bone remodeling, lipid metabolism regulation, and uterus and mammary gland epithelial cells amelioration, since phytoestrogen compounds have a vital role to suppress the cardiovascular problems and control blood lipid levels [13].

Role in breast cancer

Phytoestrogens have an argumentative impact on hormone-dependent tumors [28]. Former research applied on breast cancer rat model has revealed that treatment with pumpkin seed extract can enhance estradiol production and estrogen receptor (ER)-α/ER-β/progesterone receptor (PR) state on *MCF7, BeWo* and*Jeg3* breast cancer cells. In this search, Richter *et al*. [28] determined the elevation in estradiol production in *MCF7, BeWo,* and *Jeg3* cells in a dose-dependent mode. Particularly in *MCF7* cells, a considerable downregulation in ER-α and upregulation in PR were monitored, these results can detect the potential role of pumpkin seeds in breast cancer treatment and/or prevention.

Anti-diabetic effect

Pumpkin seeds have considerable amounts of phenolic antioxidant compounds, among these: trigonelline, D-chiro-inositol, and nicotinic acid, those are considered to be insulin action mediators or insulin sensitizers. Their potential mechanisms affect pancreatic β-cell qualification, insulin release and activities of enzymes associated with glucose metabolism [29]. D-chiro-inositol included in the seeds assumed to be an intracellular insulin action mediator via stimulating the glycogen synthase dephosphorylation, pyruvate dehydrogenase and the rate-limiting enzymes of both the oxidative and non-oxidative glucose uptake pathways [30]. Trigonelline, a plant alkaloid included in pumpkin seeds, can ameliorate hyperglycemia and hyperlipidemia. The previous study [31] informed that trigonelline and nicotinic acid in pumpkin seeds can boost the capacity of enzymes related to the metabolism pathway of glucose; glucokinase and glucose-6-phosphatase. The further study [9] proposed that the rich content of protein constituents with wide molecular weight range (3-60 kDa) in pumpkin seeds may consolidate blood insulin level and blood glucose tolerance.

Antimicrobial Effects

It has been found that the 28-kDa antifungal PR-5 protein (pathogenesis related protein 5) extracted from pumpkin leaves, significantly suppressed the growth of *Fusarium oxysporum* in the agar plate at a concentration greater than 2 μM. It also exhibited a potentiated effect with nikkomycin (a chitin synthase inhibitor), in inhibition of *Candida albicans* growth [32]. Furthermore, Park et al. [33] have isolated antifungal protein, M_r = ca. 40 kDa, from the pumpkin rind, which named as pr-1 protein. Pr-1 could inhibit the growth of *Fusarium oxysporum*, *Botrytis cinerea*, *Rhizoctonia solani and Fusarium solani*, as well as *Candida albicans* at the concentration 10-20 μM. However, it could not suppress the growth of *Staphylococcus aureus* or *Escherichia coli* even at the concentration 200 μM. Sener *et al.* [34] confirmed that the seed oil of *C. pepo L.*, growing in Turkey, holds a worthy antibacterial efficiency against *Klebsiella pneumoniae* and *Acinobacter baumannii* at a concentration of 16 μg/mL, potent antifungal efficiency against *Candida albicans* at 8 μg/mL, also a moderate antiviral efficiency towards *Parainfluenza* virus type-3 at 16-8 μg/mL.

Anthelmintic activity

According to botanical data and numerous scientific searches, pumpkin seeds have been consumed in traditional medicine for prostate, urinary tract diseases, and parasitic infestations. Díaz *et al*. [35] have determined the minimum effective quantity of the seeds of *C. maxima* was 23 grams (almost 73 pumpkin seeds) in mice, they monitored that the pumpkin seeds had a proteolytic impact and demolitions on tegument comprising the base membrane, also led to a decrease in quantity of eggs of parasite rings.

Another study has assayed the anthelmintic actions of distilled-water and ethanolic extracts of *C. maxima* seeds on *Aspiculuris tetraptera* in the intestines of rats, which were significantly high (81% and 85% respectively), explaining that ethanolic extract is more efficient than aqueous extract [36]. Moreover, Mahmoud *et al.* [37] stated that the oral administration of pumpkin seed extract added to boiled water for14 days led to damage of the parasite eggs of *Heterophyesheterophyes* in the infected puppies.

Furthermore, Elhadi *et al.* [38] investigated the antigiardial efficiency of both methanolic and petroleum ether extracts of *C. maxima* and *C. pepo* seeds at doses of 250, 500 and 1000 ppm. They showed that petroleum ether extract of *C. maxima* at 500 and 1000 ppm has 48 h, while 250 ppm dose has 100% efficacy against giardia in 72 h. However, *C. pepo* has 83.7% activity against giardia in 96 h at a dose of 500 ppm; inferring that *C. maxima* can be considered as an effective anti-giardial agent. They reflected the antigiardial activity of *C. maxima* to the presence of triterpenes such as Cucurbitacin E and Cucurbitacin L 2-0-β glucosides.

In addition, an *in-vitro* experimental study has been performed by Marie-Magdeleine *et al.* [39] who used three extracting agents (water, dichloromethane and methanol) of *C. moschata* seeds against *Haemon cuscontortus*. The trial revealed that only the aqueous extract could inhibit the larval developments of *H. contortus*. Magi et al have investigated that when the *Oesophagostomum* spp.larvae-infected pigs were treated with pumpkin seeds three times weekly with a dose of 5 g/kg, pumpkin seeds revealed therapeutic efficiency, almost reach the ivermectin (an anthelmintic drug)efficiency treatment, The anthelmintic potential of pumpkin seeds was about (96.1%), while the ivermectin was (97.5%)[40].

Role in healing of arthritis

An *in-vivo* study has reported that supplying arthritic rats with *C. pepo L.* seed oil led to a significant suppression in their inflammation at chronic phase which determined by a clear healing of the paw oedema, comparing with indomethacin (a synthetic anti-inflammatory medication).The potential justification for this recovery is associated with the great content of unsaturated fatty acids and synergistic antioxidant capacities of selenium, carotenoids and tocopherols in pumpkinseed oil [41]. Entirely, pumpkin seed oil potentially reduces lipid peroxidation of the cell membrane through scavenging free radicals resulting in its anti-inflammatory role during arthritis [42].

Antioxidant activity

In pumpkin seeds, both of trace minerals selenium, and zinc are considered as powerful antioxidants; zinc possesses the ability to counteract the effect of free radical release or directly occupy the copper or iron-binding sites of proteins, lipids and DNA molecules [43].

Experimental research has revealed that the roasted pumpkin seed oil enclosed total carotenoids, cryptoxanthin, zeaxanthin, and lutein, with greater levels than parsley, cardamom and mullein seed oils [44]. Also pumpkin seed extracts have demonstrated a lipoxygenase inhibitory activity, and their antioxidant abilities can be checked by using DPPH (2, 2-diphenyl-1-picrylhydrazyl) free radical scavenge analysis, also checking for their inhibitory effect against lipid peroxidation, which is catalysed by soybean lipoxygenase [45].

Furthermore, Saavedra *et al.* [46] have evaluated the potential of pumpkin seeds with shells as a source of antioxidative nutrients and bioactive materials, investigating the influence of various solvents for extraction and two drying methods. The seeds (fresh and cooked) were oven-dried and freeze-dried, then extracted by using five solvents which are: 70 % methanol, 70 % ethanol, 70 % acetone, 100 % dichloromethane, and pure water; at which the ethanolic and methanolic extracts exhibited the most significant antioxidative capacities, also the oven-dried seeds exhibited higher levels of antioxidants and phenolic contents than freeze-dried ones.

Antihypertensive effect

Plant proteins are vital functional constituents, exploited in various processed food products. Specifically, globular proteins from several plant sources have a significant role in different food products [47]. Experimental research has located and extracted the cucurbitin protein from pumpkin seeds through precipitation of ammonium sulfate and purification via anion-exchange chromatography on a DEAE-Sephadex column with 20×30cm, where cucurbitin protein related to the 11S globulin family. This study has revealed that cucurbitin protein isolated from pumpkin seeds consisted of the basic (20−25 kDa), and acidic (35−42 kDa) polypeptides. The α-amylase-inhibitory effect of cucurbitin protein was (86%), which was significantly greater than 11S globulin of sesame (82.6%) and amandin protein of almond seeds (76%) in the same study, given that the antihypertensive efficiency of the three proteins was assessed by the chrioallantoin membrane assay in the chick embryos, which exhibited that cucurbitin protein possesses a greater vasodilatation action than the other two proteins [48].

In another research, hypertension was induced in a rat model by the nitric oxide synthase inhibitor 1-NAME (N^{ω}-nitro-l-arginine methyl ester hydrochloride). Hypertensive rats were treated with pumpkin seed oil and compared the effects with amlodipine (a calcium channel-blocker, antihypertensive drug). Pumpkin seed oil was administered with doses (40 and 100 mg/kg) and amlodipine (0.9 mg/kg), orally once daily for 6 weeks. The l-NAME administration led to a substantial increase in blood pressure (BP) appearing at the second week. However, the pumpkin seed oil treatment revealed a significant decline in the elevated BP and normalized the l-NAME-stimulated ECG (Electrocardiography) disturbances. Moreover, pumpkin seed oil reduced the high levels of MDA (Malondialdehyde) and inverted the low concentrations of nitric oxide (NO) metabolites nearly to the normal levels compared with the untreated control group. Pumpkin seed oil saved also from pathological modulations in aorta and heart caused by l-NAME. Therefore, pumpkin seed oil was reported to have an antihypertensive and cardioprotective impacts via a mechanism that may involve production of nitric oxide [49].

Hypolipidemic effect

The isocaloric shift from a diet enriched with saturated fats to a diet enriched with unsaturated fats can alleviate severity of non-alcoholic fatty liver disease (NAFLD) and atherosclerosis development. Given that the virgin (unrefined) pumpkin seed oil enhanced with phytoconstituents holds further anti-inflammatory effects leading to better pronounced health results, researchers reported the positive long-term health effects of virgin pumpkin seed oil on amelioration of NAFLD, related atherosclerosis and hepatic steatosis [50].

Pumpkin seed oil administration has been shown to ameliorate blood pressure and blood lipids disorders related with estrogen deficiency in postmenopausal women, where the most significant impact is the elevating high density lipoprotein cholesterol (HDL-C), which helps in alleviating the risk of cardiovascular complications [51].

Ethanolic extract of pumpkin seeds exhibited a considerable decrease in total cholesterol (TC), triacylglycerol (TAG), low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL-C), and increase in HDL-C in experimental mice, these positive outcomes attributed to the existence of carotenoids, phenolics, flavanoids, and saponins in the extract [52]. Another research revealed that administration of pumpkin seed oil in combination with simvastatin (anti-hypercholesterolemic synthetic drug) led to a remarkable reduction of the aortic contractile response to the norepinephrine and alleviation severity of hypercholesterolemia in high fat diet-provided rabbits, these synergistic effects ascribed to the therapeutic action of simvastatin and the antioxidative ingredients and essential fatty acids in pumpkin seed oil [53].

Role in iron-deficiency

The iron deficiency anemia is considered a prevalent nutritional trouble all over the world lately [54]. An in-vivo experimental study has been performed to compare the efficiency of dehusked pumpkin seeds with the iron fortified-prepared cereals, where both are two sources of dietary supplement with iron, discussing their effects on iron nutrition state and the alterations of hematological parameters of women at reproductive ages. Eight non-pregnant healthy women, aged from 20 to 37 years, administered 30 g of iron fortified-prepared cereals (that provides 7.1 mg iron/day) and30 g of pumpkin seeds (that provides 4.0 mg iron/day) for a month. Biochemical parameters were assayed on the 20thday of menstrual cycles before and after pumpkin seeds treatment; including hematocrit (Ht), hemoglobin (Hb), reticulocyte count, serum ferritin, total iron-binding capacity (TIBC), and transferrin saturation percent. Significant preferable outcomes were monitored for iron state after the consumption period. The statistical analysis displayed a worthy difference between the pre- and post-treating phase for elevating serum iron (60 ± 22 versus 85 ± 23 µg/dl), elevating transferrin saturation percent (16.8 ± 8.1versus 25.6 ± 9.1%), and decrease in TIBC (367 ± 31 versus 339 ± 31 µg/dl).Therefore, these findings presented that adding another natural source of iron like dehusked pumpkin seeds can significantly recover blood iron levels [55]. Enhanced supplements participate in preserve the optimal nutritional state and reducing the probability of iron scarcity, also keeping administration of fortified-prepared cereals is considered a wide spread strategy [56]. Additional researches using these two supplementary products are recommended to investigate the impact of iron enhancement on iron nutritional cases among different target population, particularly in adolescents, young children, pregnant women and females of reproductive ages [57].

Role in prostate hyperplasia

Gossell-Williams *et al.* [58] have illustrated the impact of pumpkin seed oil on testosterone-induced hyperplasia of prostate in rats; the oral intake of pumpkin seed oil with the dose (2 mg/100 g BW) for 20 days, significantly suppressed the induced enlarged prostate, these results have been determined after slaughtering the rats and weighing their prostates, moreover the protective effects were considerably increased at the higher dose.

Clinical trials have been performed to discuss the efficiency of pumpkin seed oil on diverse pathological cases in men. These trials have focused the light on administrating the pumpkin seed oil as an alternative medicine in benign prostatic hyperplasia (BPH), urinary bladder hyper-activity, and androgenic alopecia. It was informed that the oil therapeutic effects are assigned to phytoestrogens and the involved unsaturated fatty acids, in particular. The suggested mechanisms associated with these impacts are imputed to suppression of 5-α-reductase [59];

the enzyme involved in metabolic processings of a diversity of endogenous steroids, thus pumpkin seed oil can help in preventing the transformation of testosterone to the more efficient androgen "dihydrotestosterone" (DHT) [60]. Furthermore, pumpkin seed oil possesses relaxation properties on the bladder sphincter, which may relief the patients with urination difficulties [61]. Thus, the need is increasing for further pharmacological studies and clinical trials on these biological impacts of pumpkin seed oil.

ProstaCaidTM®, a polyherbal medication, includes pumpkin seed extract as a constituent and contributes to suppress the cell proliferation of greatly invading human hormone-independent prostate cancer (PC-3) cells in a time- and dose-dependent method [62].

Experimental studies stated that β-sitosterol, a phytosterol included in pumpkin seeds, may consistently recover the urinary symptoms linked with prostate enlargement [63].

Pumpkin seed oil improves male fertility

It has been mentioned previously that pumpkin seed oil is fortified with various antioxidative components including essential fatty acids, phytosterols, amino acids, β-carotenes, tocopherols, selenium and lutein. An experimental research has revealed that, the oral treatment of sodium valproate-induced testicular damaged male rats with pumpkin seed oil and its combination with vitamin E, significantly enhanced the testes weight, regulated the serum levels of testosterone, FSH (Follicle stimulating hormone) and LH (Luteinizing hormone), enhanced the semen quantity and quality, and alleviated the testicular degenerative damage. Moreover, a considerable reduction in lipid peroxidation and improvement in antioxidant enzymes actions in the testicular tissue were monitored [55]. The existence of selenium in pumpkin seed oil stimulates the glutathione antioxidant system, as selenium is integrated into proteins to form selenoproteins; which considered vital antioxidant enzymes [56].

Industrial applications

Besides the therapeutic uses, pumpkin seeds are the convenient head of oil required for cooking, salad, margarine, cake meals, as ingredient in baked products [18], and as valued protein supplement for all kinds of farm animals. Also pumpkin seeds are warden in confectionery industries such as cookies, cheese, crisps, sweets, sandwiches, and in flavoring foods. Additionally, pumpkin seed flour may be added into infant diets such as tuber- and root-based diets; that are less in protein to boost their protein content and enhance flavor [64].

In the industrial field, seed oil is incorporated into paint, coating, pharmaceuticals, detergents, soap fabrication and cosmetic industry [65]. Physical or analytical parameters, displayed in table (4), such as iodine value, saponification value, ester value, peroxide value and acid value have been discerned to be important in assay of many consumptions in which pumpkin seed oil can be effective [66].

Table 4: Physicochemical characteristics of the pumpkin seed oil (*Cucurbita pepo*) according to Ardabili *et al.* [12]

Parameter	[a] Value
Acid value (mg KOH/g oil)	0.78 ± 0.02
Free fatty acid content (% as oleic acid)	0.39 ± 0.01
Peroxide value (meq O_2/kg oil)	10.85 ± 0.62
Iodine value (g of I_2/100 g oil)	104.36 ± 0.04
Saponification number (mg KOH/g oil)	190.69 ± 1.4
Unsaponifiable matters content (% of oil)	5.73 ± 0.82
Total sterol content (% of oil)	1.86 ± 0.1
Total phenolics content (mg gallic acid/kg oil)	66.27 ± 3.69
Total tocopherols content (mg α-tocopherol/kg oil)	882.65 ± 18.32
Oxidative stability index (OSI)	6.57 ± 0.09
State at room temperature	Liquid
Color	Greenish brown

[a]Means ± standard deviation of three determinations.

Pumpkin waste as livestock feed

Livestock needs various resources of nutrition such as fodder and grains. Millions of tons of plant wastes all over the world are generated without further processing, causing pollution. Proper management of the plant wastes can provide an ideal feed for livestock, and alleviating feeding costs. In this regard, pumpkin waste (*Cucurbita* sp.) is a good alternate for several domestic animals feed such as equines and ruminants. Pumpkin waste has been used for the animal nutrition; as it has great nutritional value for the protein and fat contents in the case of seeds, and fibers, carbohydrates, vitamins and minerals in the case of fruits and leaves [67].

Dorantes *et al.* [68] stated that the dry residue of peel and pulp of *C. argyrosperma* retains less protein content (<9%), however retains about 50% of neutral detergent fibers, and 40% of the acid detergent fibers, that makes it convenient for the diet formulations for dairy cattle and rabbits. Furthermore, Crosby *et al.* [69] determined that the ruminal digestibility of dry matter rises about 21% when 30% of corn stubble is replaced with the dry residue of *C. argyrosperma,* but the digestibility of neutral detergent fiber lowers 7%, attributing to the dissolution of non-fibrous carbohydrates like sugars that are rapidly fermented. Probably, the conjunction of pumpkin with the livestock feed highly improves its palatability due to the pumpkin's sugar content.

Respecting the pumpkin seeds, Klir *et al.* [70] did not determine alterations in milk production or composition via adding pumpkin seed flour (16%) to the feed of dairy goats, completely replacing soybean meal. Also, Antunovic *et al*. [71] investigated that exchanging the soybean meal for 15% of pumpkin seed meal of the sheep feed did not change the meat colour or the carcass yield.

Most of the studies have been performed on pumpkin seeds consumption for animal diets were related to broiler chickens at which the elevation in weight and carcass yield was detected, Martínez *et al.* [72] reported weight gain, greater breast, and less abdominal fat when 6% of seed flour of *C. moschata* added to the diet. In addition, Zinabu *et al.* [73] have added only 1% of seed flour of *C. maxima* to the chicken feed to improve weight gain. However, Hajati *et al.* [74] showed that 5 g/kg of pumpkin seed oil, when added to the ration, did not promote the productive performance in broiler chickens. Pumpkin fruit feed to laying hens could preserve the polyunsaturated fatty acids of egg yolk due to the richness of antioxidants in their diet, resulting in prolong of egg shelf life and avoid rancid or stale odors [75].

Pumpkin waste for livestock treatment

Alongside the feed consumption, the biovital components includedin seeds, fruits and leaves of *cucurbita sp.*retain animaltherapeutic properties such as antioxidant, antiparasitic, antibacterial, and anti-inflammatory [76]. Thus, the health status and subsequently productivity and wealth of livestock can be enhanced with pumpkin added to their feed. *In-vitro* experimental studies on birds investigated that the ethanolic extract of *C. pepo* is efficient against *Tetratrichomonas gallinarum, Histomonas meleagridis,* and *Blastocystis* sp. infections; those are considered as the protozoans of economic value in poultry farming, although it reported a limited effect *in-vivo* [77]. Moreover, pumpkin seed lectins showed antibiotic efficiency against *Salmonella* Gallinarum, *Pseudomonas, Salmonella Typhymurium*, and *Escherichia coli* infections, thus their use canreduce the dose of antibiotics [78]. In pigs, the fermented pumpkin fruit of *C. pepo* could reduce the occurrence of diarrhea, morbidity and mortality piglets without affecting their productivity [79]. Bahramsoltani *et al.* [80] revealed that 20% of peel extract of *C. moschata* can be applied in treating burns due to the high mucilage content that lowers the oxidative stress of burned tissue.

Conclusion

The generic conclusion of this updated review is that pumpkin seeds, fruits and the seed oil possess critical bioactive components that can boost human and animal health. These findings push us to advanced ideas in innovating and progressing nutraceutical and pharmaceutical formulations with included pumpkin products or extracts for a large scale of applications.

Conflict of Interest

The authors declare no conflicts of interest, financial or otherwise.

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الملخص العربي

الدور الهام للمغذيات في بذور القرع لصحة الإنسان والحيوان: دراسة مرجعية محدثة

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اشتهر القرع العسلي في الطب التقليدي بالحد من كثير من الاضطرابات مثل ارتفاع ضغط الدم ، التهاب المفاصل، ارتفاع السكر في الدم ، الالتهابات ، ارتفاع دهون الدم ، العدوى الفطرية أو البكتيرية ، الأورام والطفيليات المعوية مما أدي إلي تسليط الضوء علي ثمارو بذور القرع في مجال البحث العلمي. وقد أجريت دراسات متعددة على النماذج الحيوانية ، والتجارب السريرية و زراعة الخلايا من أجل تقييم هذه التأثيرات العلاجية. يشتهر القرع بالبذور والثمار والأوراق التي يتم تناولها. تعد بذور القرع غنية بالمركبات الجزئية والكلية فتتضمن البروتينات، مركبات الفينول المضادة للأكسدة ، توكوفيرول ، ترايتيربين ، سابونين ، فيتوستيرول ، قشور ، كاروتينويدات. ومن بين هذة المركبات: إينوزيتول، تريغونيللين، حمض النيكوتينيك، وتلك المركبات تعد محسّنات للأنسولين أو وسطاء لعمل الأنسولين. كما أن بذور القرع مدعمة بالأحماض الدهنية المتعددة الغير مشبعة والألياف والفيتامينات والمعادن بما في ذلك الزنك والحديد والمغنيسيوم والكالسيوم والمنجنيز والنحاس ، لذلك أصبحت بذور القرع شائعة الاستخدام كمعزز للصحة و العلاج العشبي للإنسان وكذلك الحيوان وقد غزا تقنيو الأغذية قطاعات الأغذية والطب البديل بمنتجات القرع. علاوة على ذلك، تستغل شركات الأغذية بذور القرع في صناعة المقبلات والوجبات الخفيفة. ستركز هذه المقالة على الآثار العلاجية لبذور القرع و الآليات التي من خلالها يمكن أن تحد من مخاطرتلك الأمراض.