



Pumpkin seeds and oil as sources of bioactive compounds and their therapeutic uses: A review

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ABSTRACT

For the cure of diseases, herbal remedies are used on an individual basis or together with standard medicines in numerous medical studies. Due to many medicinal properties and the presence of natural edible substances. Pumpkin is considered as an edible plant and has various medicinal properties. It has several phyto-constituents such as alkaloids, flavanoids, palmitic, oleic and linoleic acids. Several studies describes the medicinal properties such as anti-diabetic, cardioprotective, anti- depressive, antioxidant, anti-carcinogenic, anti-inflammatory of Pumpkin seeds and seed oil. Here, this article is presented with the purpose to discuss about the pumpkin seeds properties that can impart further research developments with this plant for human health benefits.

Keywords: Pumpkin, Herbal medicine, Male Reproductive Health, Anti-carcinogens, Nephroprotective

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INTRODUCTION

The Pumpkin seeds (*Cucurbita* sp.) are discarded and are considered as agro-industrial wastes. At domestic scale, the seeds are consumed raw, roasted or cooked in some parts of the world. The pumpkin seeds are rich in protein, fibres, minerals, polyunsaturated fatty acids and phytosterols, hence these are valuable for food industry. Patel 2013 reported the beneficial effects of seeds on blood glucose level, immunity, cholesterol, liver, prostate gland, bladder, depression, learning disabilities and parasite inhibition [1]. For global sustainability, the conversion of these agro-wastes seeds into value-added ingredients is very important thus, there is a need to explore its properties and uses.

Due to macro- and micro-constituent composition of Pumpkin seed and seed oil, they are contributed to many health benefits. Proteins, phytosterols [2,3] antioxidant vitamins, such as carotenoids and tocopherol [4], polyunsaturated fatty acids [5], and trace elements, such as zinc [6] are found abundantly in the seeds and seed oil.

The pumpkin, *Cucurbita maxima* belongs to family cucurbitaceae. The plant is a trailing annual herb having simple leaves with hairy or prickly stem and axillary tendrils. The seeds are compressed, ovoid or oblong in shape. The flowers are large, yellow in colour, unisexual and solitary. The fruit is fleshy having oval or round shape. Patel 2013 noticed that in some parts of Canada, Mexico, USA, Europe and China, the seeds are also sold in market as baked, sprouted, fermented and consumed by people [1]. Due to antidiabetic, antitumor, antihypertensive, anti-inflammatory, immuno-modulatory and antibacterial properties the plant has been traditionally used in many countries [7] and due to lower cholesterol and antidepressant qualities the seeds have many health benefits [8].

Now a days, pumpkin seed oil due to its special composition, is considered as a promising candidate with regards to vegetable oil. For cooking purpose, like marinade or salad dressing, the dark greenish-red oil is already in the race to compete with olive oil and also being used in various items, such as chocolate, cereal bar, bread, cake, muffin, soup, pesto, stew and pasta garnish [1].

NUTRIENTS

The nutritional purpose of seeds depends on its phytochemical composition. The seed oil content of pumpkin cultivars (*Cucurbita maxima* D) ranged from 11 to 31%, total unsaturated fatty acid composition ranged from 73 to 81% [4]. Phytosterols, squalene and tocopherols levels in pumpkin seeds were determined by [3]. The seed oil have α -tocopherol content varied from 27 to 75 mg/g, while γ -tocopherol content varies from 75 to 493 mg/g. The most common phytosterol was Beta-sitosterol whose concentration ranges from 24.9 mg/100 g seed. Pumpkin seeds have 42.3% (w/w) total oil content and

Squalene was present in higher quantity (89 mg/100 g). Kim et al. 2012 reported that palmitic, stearic, oleic and linoleic acids were the major fatty acids present in pumpkin seeds. γ -tocopherol content in *Cucurbita maxima* seeds was significantly less as compared to *Cucurbita pepo* and *Cucurbita moschata* seeds. β -carotene content was highest in *Cucurbita maxima* seeds while β -sitosterol content was significantly more in *Cucurbita pepo* seeds. Pumpkin seeds have highest iron content (95.85 ± 33.01 ppm) in comparison with 11 types of seeds and nuts known for its nutritional value [9].

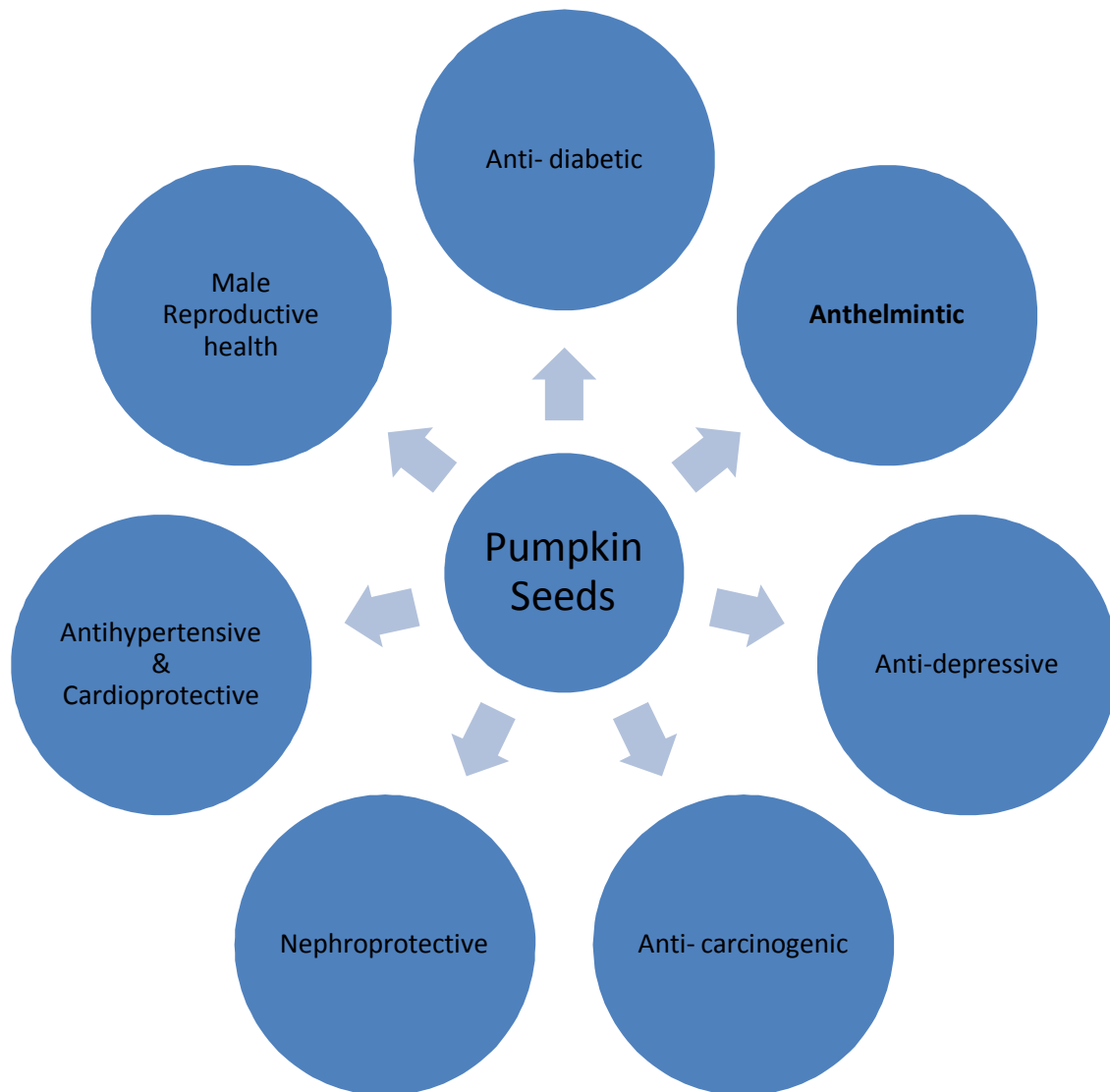


Fig.1 Biological activities of Pumpkin Seeds

EFFECT ON MALE REPRODUCTIVE HEALTH-

In cultures of human fibroblasts, the conversion of testosterone into dihydrotestosterone is inhibited by pumpkin seed. Pumpkin seeds are rich source of zinc and are found in men's health products. Bach 2000 and Liu et al. 2007 reported that pumpkin seeds helps in improvement in bone mineral density and prostate health [10, 11]. Banks *et al.* [12]; Bjorbaek and Kahn [13] also reported that Serum leptin reduction, serum quality and libido improvement is due to serum testosterone level which is raised by Squalene present in pumpkin [12,13].

Jayaprakasam *et al.* [14] reported that pumpkin seed oil helps in the protection of older men's urinary tracts from the aging effects of testosterone. Zinc ion is required by all the steroid hormone receptors to maintain their secondary structure and function and to normalise the concentration of testosterone, LH

and FSH. Treatment with pumpkin extract, oil and zinc is helpful and reactivation of normal functioning of receptors might be due to high zinc availability [15]. High concentration of zinc in the human prostate gland helps in normal functioning. Bataineh *et al.* 2002 and Vartsky *et al.* 2003 mentioned the important role of zinc in proteins structure, cell membranes and protection against damage, as it helps in growth and development of the immune response, functioning of nervous system and reproduction and the enzymes involved in testosterone synthesis rely on it [15,16]. Osaretin and Gabriel 2008; Takeda *et al.* 2005 commented that the Zinc supplements stimulates the number of sperms which depends on enzymes involved in testosterone synthesis and production. Daily intake of pumpkin seeds and zinc rich diet could help in improving the sexual health status [17, 18]. Hyper glycemia-induced pathogenesis and complication in cellular oxidation stress can be reduced by using pumpkin extract which has high phenolic content and antioxidant activity which helps in coupling of moderate to high alpha-glucosidase and anti giotensin converting enzyme inhibitory activities (Kwon *et al.* 2007) [19]. Tsai *et al.* 2006 reported the action mechanism of pumpkin seed oil in the conversion of testosterone into dihydrotestosterone by 5- α -reductase inhibition [20].

Gossell-Williams *et al.* 2006 and Tsai *et al.* 2006 stated that pumpkin oil have high content of β - sitosterol which is beneficial for the treatment of benign prostate hyperplasia [21, 20]. Fruhwirth and Hermetter 2007 reported that benign prostate hyperplasia can be treated by administering pumpkin seed extract rich in phytosterol and Styrian oil which act as phytotherapeutical agents and are used in the treatment of symptomatic micturition disorders [22].

ANTIDIABETIC EFFECT

Acosta *et al.* 2001 and Kwon *et al.* 2007 reported that for the treatment of non-insulin-dependent diabetes mellitus or type 2 diabetes, intake of crude extract of pumpkin fruit is beneficial [23,19]. Acosta *et al.* 2001; Andrade *et al.* 2005; Alarcon *et al.* 2002 also reported that in alloxan-induced rabbits, in temporarily hyperglycaemic rabbits and in type 2 diabetic patients, pumpkin helps in lowering blood sugar level as it shows acute hypoglycaemic activity [23,24,25].

Makni *et al.* 2010 investigated that in alloxan-induced diabetic rats, mixture of flax and pumpkin seeds showed hypoglycaemic and antioxidant effects [26]. Makni *et al.* 2011 stated that risk of diabetes was due to the increased levels of the plasma enzymes aspartate, alanine aminotransferase and aminotransferase which might be reduced by rich diet of pumpkin seed oil. Prevention of diabetes and its complications could be reduced by intake of pumpkin seed oil regularly [27].

Teugwa *et al.* 2013 reported that the most abundant storage protein is globulin (295.11 mg/g) dry matter and is capable of causing significant drop in blood sugar (88–137.80 %) by performing oral glucose tolerance test on rats, thus concluded that several species of Cucurbitaceae, including *Cucurbita moschata* showed the hypoglycaemic activity. The pharmacological and phytochemical studies indicates that *Cucurbita maxima* extracts prepared from alcohol, petroleum ether, ethyl acetate contain phenolics, saponins, tannins, carbohydrates and flavanoids [28]. Marles *et al.* 1995 stated that Saponins were involved in insulin secretions which was due to stimulation of pancreatic β -cells [29].

Sharma *et al.* 2013 investigated that *Cucurbita maxima* seed extract contain phenols, flavanoids and saponins which act as a source of antidiabetic and antihyperlipidemic agents. In streptozotocin induced diabetic rats, oral administration of *Cucurbita maxima* seed extracts showed antihyperlipidemic effect by lowering total cholesterol and triglycerides and increasing HDL-cholesterol and also showed antidiabetic effect by controlling blood glucose level [30].

ANTI- CARCIOGENIC EFFECT

Huang *et al.* 2004 reported that rich diet of pumpkin seeds helps in lowering the risk of lung, breast, gastric and colorectal cancers [31]. Binns *et al.* (2004) and Jian *et al.* (2005) stated that pumpkin fruit contain carotenoids which helps in the prevention of prostate cancer [32,33]. Hong 2005 reported that in Sarcoma-180-bearing mice, pumpkin fruit extracts markedly reduced tumour weight [34].

Cheong *et al.* 1997 reported the leukemia K-562 cells growth inhibition through some proteins named MAP2 (Mw 2249 Da) and MAP4 (Mw 4650 Da), isolated from pumpkin seeds [35]. Xia *et al.* 2003 reported the inhibition of melanoma cells M₂₁ growth by moschatin, a novel ribosome-inactivating protein (RIP) isolated from mature *C. moschata* seeds and a novel immunotoxin moschatin-Ng76 [36]. Hou *et al.* 2008 investigated that cucurmosin, novel type 1 RIP was isolated from the sarcocarp of *C. moschata* that exhibits strong cytotoxicity to three cancer cell lines of both human and murine origin, besides rRNA N-glycosidase activity. Induction of apoptosis, gene modification, activation and inhibition of pro- or antiapoptotic proteins and transcriptional activities might be due to Cucurbitacins present in the pumpkin seed [37]. Chari *et al.* 2018 reported that intake of pumpkin seeds normalize the levels of antioxidant enzymes, increases the colon length and weight ratio, inhibits hyperplastic cells and decreases aberrant crypt foci (ACF) count thus helps in the treatment of colon cancer [38].

ANTIHYPERTENSIVE AND CARDIOPROTECTIVE EFFECT

For lowering the blood pressure and blood vessels relaxation, pumpkin seeds plays a vital role. El-Mosallamy *et al.* (2012) observed that when chemical induced hypertension rats were given 40-100mg/kg dose of pumpkin seed oil for 6 weeks, there was reduction in abnormal increase in blood pressure, decrease in elevated levels of MDA and normalization in decreased level of NO metabolites. Pumpkin seed oil showed protective effect against pathological alterations in the heart and aorta through generation of NO. It also showed reduction in risk of heart attacks as oil have high magnesium content. Studies showed that supplements of pumpkin seeds have more efficiency of blocking calcium channel as compared to amlodipine drug [39].

Gossell-Williams *et al.* 2006 investigated that in ovariectomized rats, pumpkin seed oil supplements prevents the elevation of systolic and diastolic blood pressure and observed the negative influence on the plasma lipid profile associated with low estrogen concentration [21]. Al-Zuhair *et al.* [40] reported that in hypertensive rats, pre-treatment with pumpkin seed oil for 4 weeks and then intravenous administration of felodipine or captopril significantly elevated their hypotensive action. Pumpkin seed oil administration resulted in 50–55% reduction of felodipine induced reflex tachycardia, which may be due to its antioxidant action or by blocking the entry of calcium to the myocardial muscle.

Bonaa 1989 stated that pumpkin seed oil helps in reduction of blood pressure as it contains linoleic and linolenic fatty acids [41]. Tobian *et al.* [42] stated that salt induced hypertension, Kawahara *et al.* [43] also stated that deoxycorticosterone acetate-salt hypertension in rats was inhibited by linoleic acid. γ -Linolenic acid, a metabolite of linoleic acid, attenuated stress-induced hypertension in rats. Mills and Ward, 1984 investigated that stress- induced hypertension in rats was reduced by a metabolite of linoleic acid named γ -Linolenic acid [44]. Fruhwirth and Hermetter 2007 reported that pumpkin seed oil contain oleic acid which helps in lowering the blood pressure by enhancing the vasodilator pathway as oleic acid helps in blocking of Ca²⁺ + -mediated cell signalling by inhibiting the production of inositol 1,4,5-triphosphate and diacylglycerol [22].

Fruhwirth and Hermetter [22] also reported that Secoisolariciresinol is the main phytoestrogen present in pumpkin seed oil.

EFFECT AGAINST LUNG INJURY

Farrell *et al.* (2015) and Tang *et al.* (2014) reported that pumpkin seed oil shows anti-inflammatory effects by various mechanisms as oil contains polyphenols and many bioactive phtochemicals [45, 46]. Lai *et al.* (2014) stated that pumpkin seed oil have antioxidant property which helps in reduction of acid aspiration pneumonia thus protects the lung tissue from acid injury [47]. Due to presence of vitamin A and E in pumpkin seed oil, it showed antioxidant activity which helps in prevention of lipid peroxidation by binding to free radicals [48]. Halliwell 2007 also reported that pumpkin seed oil contains selenium which showed antioxidant activity as it enters in the structure of enzyme glutathione peroxidase (GSH-Px) and this enzyme helps in converting hydrogen peroxides into harmless compounds [49]. Letelier *et al.* [3] investigated that pumpkin seed oil contain phenol content which can bind with free radicals and metals like iron and copper which are involved in free radical-generating reactions [50]. Ryan *et al.* (2007) reported that pumpkin seed oil showed antioxidant activity as it contains squalene which protects membrane lipid peroxidation [3].

Omar and Sarhan (2017) studied that in male albino rats, pumpkin seed oil administration reduced the iNOS expression and scavenge the ROS, thus showed antioxidant activity and helps in protection of acid aspiration lung injury [51].

ANTI DEPRESSIVE EFFECT

Eagles 1990 reported that pumpkin seeds have purported L-tryptophan content which helps in the treatment of depression. Pumpkin seed contain tryptophan, an essential amino acid and 5-hydroxytryptophan (5-HTP) which helps in the treatment of depression and for formation of the serotonin neurotransmitter, 5-hydroxytryptophan (5-HTP) act as the intermediate metabolite of tryptophan [52]. Eby (2006) and Hibbeln (2008) stated that patients who suffered from mental disorders have nutritional deficiencies of vitamin B, omega-3 fatty acids, minerals, and amino acids which are precursors of neurotransmitters [53,54].

NEPHROPROTECTIVE EFFECT

Caili *et al.* (2006) reported that intake of pumpkin seed snacks in diet helps in inhibition of formation and aggregation of crystal and reduces risk of stone in bladder [55]. Suphakarn *et al.* 1987 also reported that incidence of bladder stones could be reduced by long period supplementations of pumpkin seeds or 60mg/kg (body weight) orthophosphate supplementations. Some studies reported that pumpkin seed oil helps in reduction in urethral pressure, reduction in bladder pressure and increase in bladder compliance [56].

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ANTI-HELMINTHIC EFFECT

Patel 2013, reported that for natural treatment for parasites, pumpkin seeds are used throughout the world. To get rid of internal worms, Native American tribes also use pumpkin seeds [1]. Lans et al. 2007; Srivastava and Singh 1967 also reported that Pumpkin seeds (*Cucurbita pepo*) and pomegranate peels (*Punica granatum* L.) have anthelmintic properties and are used as traditional medicinal plants. Another widely use of seeds of *C. maxima* (winter squash) is in the treatment of gastrointestinal parasites as an anthelmintic [57, 58]. Cappelletti 1985 also described the use of pumpkin seed kernel in the treatment of Taeniasis [59]. Cucurbitine found in pumpkin seeds has been noted to have antihelmintic effect and is effective on turbellaria by paralyzing them [60,61].

Li *et al.* (2012) described the therapeutic effect of pumpkin seeds on 115 taeniasis cases: with the use of plant extract, the efficacy of tapeworm elimination was increased upto 89%. In case of acute schistosomiasis which lead to fever, headache, intense gastrointestinal discomfort and fatigue, the beneficial effect of seeds were recorded [62].

Active anti-worming agent noticed in pumpkin seeds were Cucurbitine (an amino acid) and carboxypyrrolidine. Mice feeded with cucurbitane extracted from *C. moschata* seeds at a daily dose of 350–400 mg/kg for 28 days leads to retardation of *Schistosoma japonicum*.

Feitosa *et al.* 2013 also mentioned anthelmintic efficacy of pumpkin seeds on gastrointestinal nematodes in ostrich [63]. Grzybek *et al.* (2016) also reported the antihelmintic effect of pumpkin seeds in *Heligmosoides bakeri* *in vitro* and *in vivo* studies in mice [64]. Grzybek *et al.* (2016) stated that Cucurbitine, fatty acids, berberine, amino acids and palmatine content in *Cucurbita maxima* seeds was related to the anthelmintic effect [64].

Aziz *et al.* (2018) reported the anthelmintic efficiency on *A. galli* adult worm *in vitro* by comparing ethanolic extract of pumpkin seeds and aqueous extract of pomegarante peel with fenbendazole and concluded that pumpkin seed ethanolic extract was more effective [65]. Mahmoud *et al.* (2002) reported that puppies infected with *Heterophyes heterophyes* for 2 weeks showed parasite eggs destruction when administered orally with boiled water pumpkin seed extract [66].

Amorim *et al.* [68] investigated that when ethanolic extract of *C. maxima* seeds at a dose of 250/500 mg/kg were given to the rats infected with *Plasmodium berghei*, there was 50% reduction in blood parasite thus shows antimalarial effect [67]. Rats infected with *A. tetraptera* showed high anthelmintic efficacy around 81 and 85% when treated with aqueous extract and ethalonic extract of pumpkin seeds respectively.

OTHER MEDICINAL EFFECTS

Sotelo and Perez 2003 reported that the consumption of pumpkin, vegetable oils, rice and chicken in diet by children suffering from diarrhoea were benefited [69]. Pumpkin can be used epidermally in the form of massage oil, lotion, body and face masque and lotion [70]. Gossell-Williams *et al.* 2006 reported that pumpkin seed oil has abundant phytoestrogens which might be beneficial on postmenopausal women [22]. Yadav *et al.* 2010 reported that pumpkin-supplemented foods helps in curing many diseases like arthritis as it is a good source of anti-inflammatory substances [7]. Many health benefits such as sharper vision, skin protection, immune system improvement and aid weight loss due to intake of pumpkin were reported.

CONCLUSION

Intake of pumpkin in our daily diet can help in improving our overall health as it has high nutritive value. Pumpkin seeds has many medicinal properties such as antioxidant, anti-diabetic, anti-depressive, anti-carcinogenic, anti-helmintic potential, improving male reproductive health, anti-inflammatory and blood-coagulatory, improving lung injury, inhibition of kidney stone formation, hypotensive, anti-inflammatory and blood-coagulatory which are beneficial to human health.

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CONFLICT OF INTEREST

No conflict of interest.

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