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RESEARCH ARTICLE

A COMPREHENSIVE REVIEW OF THE VERSATILE PUMPKIN SEEDS (*CUCURBITA MAXIMA*) AS A VALUABLE NATURAL MEDICINE

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ABSTRACT

The seeds of *Cucurbita maxima* (pumpkin seeds) have been generally considered as agro-wastes and discarded inspite of having its high nutritional value as well as medicinal benefits. Pumpkin seeds contain high amount of protein, fatty acids, considerable amount of micronutrients like P, K, Mg, Mn and Ca. It is a good source of choline, an essential component for brain development. Pumpkin seed extracts and oils have been found useful in the treatment of Benign Prostatic Hyperplasia (BPH), parasite infestation, acrodermatitis enteropathica, hyperlipidemia, diabetes, depression to name a few. The observed benefits can attributed to the presence of bioactive components like phytosterols (eg, beta-sitosterol, stigmasterol), tocopherols, selenium (antioxidant), cucurbitin, squalene, lignan, and cardioprotective unsaturated fatty acids. Recent research has shone a light on the ever growing list of benefits of pumpkin seeds as a valuable food .

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INTRODUCTION

India has been famous for her many and varied flora since time immemorial, but it is a very common picture in our country that one part of any plant is very familiar to us but we hardly know the usefulness of the other parts of the same plant and as a result these portions are usually discarded without any hesitation. Consequently in India, an immense variety of indigenous seeds have neglected in spite of having great nutritive value, essential medicinal value as well as physiological utility. One such type of seeds is seed of *Cucurbita maxima*. *Cucurbita maxima* has been referred to as pumpkin in various literatures. The species *Cucurbita maxima* originated in South America over 4000 years ago. At the time of discovery of America, the occurrence of *Cucurbita maxima* was confined to Northern Chile, Argentina, Bolivia and Peru. Currently this is widely cultivated all across the world. In India this vegetable is grown in abandon. This plant belongs to the family of "Cucurbitaceae", also well-known as the cucumber family, and typically use their shoots or tendrils to wrap around other objects nearby for support. This plant is monoecious and its fruits are fleshy and usually contain a lot of smooth, oval-shaped seeds.

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The fruits are eaten as a vegetable, mashed or in purees, soups, or pies. The blossoms are also edible, and may be cooked into fritters. Seeds are high in nutrients, and are often eaten raw, roasted, or used to extract oil. The seeds are numerous in number, white or brown to bronze in colour with margin of the same colour and texture as the body. The seeds of *Cucurbita maxima* are exalbuminous, embryo straight, cotyledon large and oily. After the skin is removed, the seeds have a greenish colour on the surface.

Chemical components of the seeds

Pumpkin seeds or seeds of *Cucurbita maxima* still are not very known to us as a common food. Gopalan also has categorized these seeds as less familiar foodstuff in his literature. In the field of research these seeds have not been able to take an appreciable place in comparison to other common seeds like groundnut, mustard seeds, sunflower seeds, almonds etc. It has been observed that some of the active constituents of the seeds of *Cucurbita maxima* have been found to have various physiological actions and medicinal utilities. A few research works have been done worldwide on the seeds of *Cucurbita maxima*. Out of these some topics which may have a bearing on the current study have been taken up for discussion. In India a research conducted by Gopalan and Balasubramaniam in National Institute of Nutrition, Hyderabad in year 1976 has determined the quantities of some nutrients of these seeds seen in Table 1.

Table 1. Nutrient content of seeds of *Cucurbita maxima* per 100 gm of edible portion (Gopalan *et al.*, 2004)

Nutrients	Amounts per 100gm of edible portion
Moisture (gm)	8.3
Protein (gm)	24.3
Fat (gm)	47.2
Carbohydrate (gm)	15.6
Energy (Kcal)	584
Fibre (gm)	0.2
Minerals (gm)	4.7
Calcium (mg)	50
Phosphorous (mg)	830
Iron (mg)	5.5

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

Nutrient	Value per 100 grams	Nutrient	Value per 100 grams
Water (g)	6.92	Iron, Fe(mg)	14.97
Energy(kcal)	541	Magnesium, Mg(mg)	535
Protein (g)	24.54	Phosphorus, P(mg)	1174
Total lipid (fat) (g)	45.85	Potassium, K(mg)	807
Ash(g)	4.88	Sodium, Na(mg)	18
Carbohydrate, by difference(g)	17.81	Zinc, Zn(mg)	7.46
Fiber, total dietary(g)	3.9	Copper, Cu(mg)	1.387
Sugars, total(g)	1.00	Manganese, Mn(mg)	3.021
Calcium, Ca(mg)	43	Selenium, Se(mcg)	5.6
Vitamin C, total ascorbic acid(mg)	1.9	Tryptophan(g)	0.431
Thiamin (mg)	0.210	Threonine(g)	0.903
Riboflavin(mg)	0.320	Isoleucine(g)	1.264
Niacin(mg)	1.745	Leucine(g)	2.079
Pantothenic acid(mg)	0.339	Lysine(g)	1.833
Vitamin B-6(mg)	0.224	Methionine(g)	0.551
Folate, total(mcg)	58	Cystine(g)	0.301
Folate, food(mcg)	58	Phenylalanine(g)	1.222
Folate, DFE(mcg)	58	Tyrosine(g)	1.019
Choline, total (mg)	63.0	Valine(g)	1.972
Vitamin A, IU	380	Arginine(g)	4.033
Vitamin A, RAE	19	Histidine(g)	0.681
Tocopherol, gamma (mg)	19.07	Alanine(g)	1.158
Vitamin K (phylloquinone) (mcg)	51.4	Aspartic acid(g)	2.477
Lipids		Glutamic acid(g)	4.315
Fatty acids, total saturated (g)	8.674	Glycine(g)	1.796
12:0(g)	0.044	Proline(g)	1
14:0(g)	0.052	Serine(g)	1.148
16:0(g)	5.612	Other	
18:0(g)	2.811	Carotene, beta(mcg)	228
Fatty acids, total monounsaturated (g)	14.258		
16:1 undifferentiated (g)	0.099		
18:1 undifferentiated(g)	14.146		
Fatty acids, total polyunsaturated (g)	20.904		
18:2 undifferentiated (g)	20.702		
18:3 undifferentiated (g)	0.181		

Table 3. Active constituents of pumkin seeds

Amino acids	Alanine, Arginine, Cystein, Glycine, Histidine, Isoleucine, Lycine, Tryptophan (Glew *et al.,* 2006) Cucurbitin (Chopra *et al.,*1956)
Essential fatty acids	α-Linolenic acid, Oleic Acid, Palmitic Acid And Stearic Acid, Linoleic Acid (The Wealth of India, 2004)
Minerals	Zinc, Selenium, Manganese (Glew *et al.,* 2006)
Vitamins	Tocopherol (Stevenson *et al.,* 2007)
Carotenoids	Lutein, β–Carotene (Parry *et al.,* 2007)
Phytosterol	β–Sitosterol (Haas *et al*., 2006)
Glycosides	Saponin (Chopra *et al.,*1956)
Phytoestrogens	Lignan (Slavin *et al.,*1999)
Triterpene	Squalene (Ryan *et al.,* 2007)

Seed kernels of pumpkin were rich in oil and protein. It contains considerable amounts of P, K, Mg, Mn, and Ca. Oil extracted from the seeds is high in unsaturated fatty acids with linoleic and oleic acids as the major acids.

Fig. 1. Pumpkin (*Cucurbita maxima*)

Fig. 2. Pumpkin seeds with shell

Fig. 3. Dehusked Pumpkin seeds

Pumpkin seed kernel flour showed high values of chemical score, essential amino acid index, and in vitro protein digestibility. Protein solubility index, water and fat absorption capacities, emulsification properties, and foam stability were excellent in pumpkin seed kernel flours. So the flour samples could be potentially added to food systems such as bakery products (Adawy *et al.,* 2001). Among various amino acids, arginine, glutamic, and aspartic acids showed the highest concentration, while methionine and tryptophan showed the lowest. Pumpkin seed kernel contains 27% saturated fatty acid content and comprises of 16% palmitic acid and 11% stearic acid. The concentration of unsaturated fattyacids is 66% consisting of 13% oleic acid and 53% linoleic acid. The relatively high iodine value indicates a preponderance of unsaturated fatty acids. (Alfawaz *et al.,* 2004). In the USA more analytical work was done on this similar aspect. As per the USDA National Nutrient Database for Standard Reference, Release 20 (2007) the nutrient values and weights for edible portion of pumpkin seed kernel have been listed as follows (USDA Database, 2007).

The seeds of pumpkin contain relatively large amounts of two multiflorane triterpenoids (1a, 2a) esterified with PABA (Appendino *et al*., 1998). β-sitosterol, a phytosterol present in the pumpkin seeds enhance the efficacy of medicines used in the treatment of hypercholesterolemia (Richter *et al.,* 1996). This specific phytosterol primarily lowers cholesterol rich lipoprotein with lower density range than LDL via an accelerated esterification rate of the LCAT (Lecithin: Cholesterol Acyltransferase) enzyme (Zák *et al.,* 1990). As per the USDA National Nutrient Database for Standard Reference, Release 20 (2007), seeds of *Cucurbita maxima* contain approximately 63 mg of Choline per 100gm of edible portion and hence can be considered as a good source of Choline. Choline is a precursor for the formation of acetylcholine which is a neurotransmitter found in cholinergic synapses that provide a stimulatory transmission in the nervous system. Choline has been found to be related with brain development and cognitive improvement (McCann *et al.,* 2006). Choline deficiency also increases the rate of neuronal cell death (Zeisel, 2006).

Therapeutic properties of the seeds

The seeds of *Cucurbita maxima* have been known to have a multitude of health benefits.

Beneficial effect on prostate enlargement

Pumpkin seed oil has been used in combination with saw palmetto in two double blind trials to effectively reduce the symptoms of Benign Prostatic Hyperplasia (Carbin *et al.,* 1989). Scientific studies indicate that β−sitosterol, one of the active constituents of pumpkin seeds consistently improves urinary symptoms related to prostate enlargement (Klippel *et al.,* 1997). The seeds also contain chemical substance called cucurbitin that can prevent the body from converting testosterone into a much more potent form of this hormone called dihydrotestosterone without which it is more difficult for the body to keep producing more prostate cells and enlarge (Gossell-Williams *et al.,* 2006).

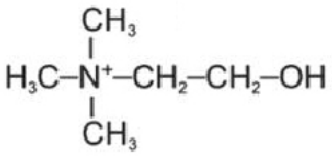

Fig. 6. Chemical structure of choline

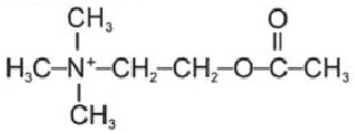

Fig. 7. Chemical structure of acetylcholine

In a recent double blind randomized study on human subjects it was found that the treatment with pumpkin seed results in a substantial improvement in BPH/LUTS. The observed symptom relief was accompanied by a clinically significant improvement in quality of life indicated by related International Prostate Symptom Score (IPSS) (Vahlensieck *et al*., 2014**)**.A study was undertaken to investigate the effects of pumpkin seed oil alone or combined with Phytosterol-F on testosterone/prazosin-induced (T-P) prostate growth in rats. It was found that Pumpkin seed oil alone or combined with Phytosterol-F can block the T-P-induced increases in prostatic weight-to-body weight ratio and protein synthesis (Tsai *et al*., 2006)

Role in healing arthritis

The healing properties of pumpkin seeds have also been recently investigated with respect to arthritis (Fahim *et al.,* 1994). In a research study, it was found that the administration of pumpkin-seed oil to arthritic rats markedly inhibited the chronic phase of inflammation as indicated by the significant reduction of rat paw oedema. Some of the biochemical parameters that were observed during chronic arthritis were found to have been improved by the administration of pumpkin seed oil. A possible reason for this improvement is related to the high enrichment of pumpkin-seed oil with unsaturated fatty acids. The combined antioxidant properties of tocopherols and selenium present in pumpkin-seed oil might also add to this effect. Carotinoids present in pumpkin-seed oil are also recognized as cellular antioxidants. Overall pumpkin seed oil potentially inhibits lipid peroxidation of cell membrane by scavenging free radicals and results in its anti-inflammatory effect during arthritis.

Role in parasite elimination

Native Americans used pumpkin flesh and seeds as food. Their use of the seeds for treatment of intestinal infection eventually led the United States Pharmacopoeia to list these seeds as an official medicine for parasite elimination. The anthelmintic properties of pumpkin seeds was proved in many studies (Díaz Obregón *et al*., 2004). In some preliminary research, pumpkin seed or its constituent curcurbitin has shown some activity against intestinal parasites (Rybaltovski i*et al*., 1966) (Plotnikov *et al*., 1972).The aqueous, ethereal and alcoholic extracts of *C. maxima* seeds demonstrated anthelmintic properties against cestodes, trematodes and nematodes in a study (Srivastava *et al.,* 1967). Phytochemical and pharmacological studies on seeds of *Cucurbita maxima* showed that it contained carbohydrates, flavonoids, tannins, phenolics and saponins (Marles *et al.,* 1995). The anthelmintic activities exhibited by pumpkin seeds were probably due to the presence of tannin. Tannin can bind to free proteins in the G.I. tract of host animal or glycoprotein on the cuticle of the parasite and may cause its death (Sengupta *et al*., 2013). A research work was conducted on the anthelmintic activity of Some Iraqi plants of the cucurbitaceae. The results showed a potent activity against tapeworms.. Some activities against pinworms was also demonstrated by seeds of *Cucurbita maxima* (Elisha *et al*., 1987). The Crude ethanolic extracts (CEEs) from *Cucurbita maxima* seeds showed strong antimalarial activity following oral administration (250 and 500 mg/kg), reducing by 50% the levels of parasitemia in Plasmodium berghei-infected mice (Amorim *et al.*, 1991). *Cucurbita maxima* were found to be among the plants most frequently used as antiparasitics and repellents (Guarrera *et al.*, 1999).The water extracts of areca nut and pumpkin seeds in the treatment of experimental puppies infected with heterophyiasis showed promising results in a research study (Mahmoud *et al.,* 2002).

Hypolipidemic effect

Pumpkin seed oil (PSO) is rich in phytochemicals and animal studies suggest that there may be some benefit to supplementation in hyperlipidemic conditions. The PSO supplementation was found to offset changes in plasma lipids and blood pressure associated with inadequate oestrogen availability in post menopausal women. The most significant finding was an increase in HDL cholesterol, a benefit that is well established to lower the risk of cardiovascular complications. There was an overall improvement in the atherogenic index which is positively correlated to risk of atheroma development (Gossell-Williams *et al.,* 2011).

The elevated level of serum lipids is typically seen in diabetes mellitus and as such presents a risk of coronary heart disease. Lowering of total cholesterol and an increase in HDL-C is very desirable for prevention of coronary heart disease in a diabetic subject. The alcoholic extract of *Cucurbita maxima* had shown significant reduction in TC, LDL, VLDL and TG's and significant rise in HDL-cholesterol in test animals. The observation was considered probably due to presence of flavanoids, phenols or saponins in the extract (Sharma *et al.,* 2013). Pumpkin-seed oil (PSO) is a natural supplement rich with antioxidants and polyunsaturated fatty acids (PUFAs).

It was given in combination with simvastatin, as anti-hypercholesterolemic drug, to high cholesterol-fed rabbits. Concomitant administration of simvastatin and PSO caused marked reduction of the aortic contractile response to norepinephrine and to normalize the most adverse effects observed during hypercholesterolemia. These effects were explained by the potentiating effects of simvastatin with antioxidants and essential fatty acids in PSO (Al-Zuhair *et al.,* 1997).

The Hypoglycemic effect of Pumpkin Seeds

Pumpkin seeds are widely considered to have active hypoglycaemic properties. *Cucurbita maxima* seed extracts produces significant antidiabetic effect in controlling the blood glucose level. The presence of flavanoids, phenols or saponins in the seed extracts of *Cucurbita maxima* could explain its role as potential anti diabetic agents (Sharma *et al.,* 2013). In a research study, it was found that rats, fed aflax and pumpkin seed-enriched diet, were able to partly recover fromalloxan-induced diabetes within a short time compared with rats fed control diet. The observed effect could be related to the partial regeneration or preservation of pancreatic β-cell mass after alloxan treatment. The results obtained showed that flax and pumpkin seed mixture increased hepatic glycogen content. This suggests that the preservation of hepatic glycogen was maintained and the gluconeogenesis rate was depressed (Makni *et al.,* 2011)

Anti-depressant activity

The anti-depressive activity of raw, autoclaved, boiled, germinated and roasted pumpkin seeds powder extract as compared to the standard drug: Imipriamine in normal and depressed control rats has been proved. Significant decrease in duration of immobility time in the treated group of experimental rats compared with depressed control group in Force Swimming Test and Tail Suspension Test (George *et al.,* 2012). Tryptophan is an essential amino acid present in pumpkin seed, and 5-hydroxytryptophan (5-HTP) is the intermediate metabolite of tryptophan in the formation of the neurotransmitter serotonin. Both tryptophan and 5-HTP are promoted as treatment for depression. The purported L-tryptophan content of pumpkin seeds help remedy depression (Eagles *et al.,* 1990)

Role in treatment of Androgenic Alopecia

The pumpkin seed oil supplement has a positive anabolic effect on hair growth and this is due to the possible effects of phytosterols present in pumpkin seeds which are known to inhibit 5α-reductase in patients with mild to moderate male pattern hair loss (Cho *et al.,* 2014).

Antioxidant activity of the seeds

In a research work cold-pressed onion, parsley, cardamom, mullein, roasted pumpkin, and milk thistle seed oils were characterized for their Fatty Acid (FA) composition, tocopherol content, carotenoid profile, Total Phenolic Content (TPC), Oxidative Stability Index (OSI), color, physical properties, and radical-scavenging capacities against peroxyl (oxygen radical-scavenging capacity) and stable DPPH (diphenylpicrylhydrazyl) radicals. Roasted pumpkin seed oil contained the highest level of total carotenoids, zeaxanthin, β-carotene, cryptoxanthin, and lutein. These seed oils may serve as dietary sources of special FA, tocopherols, carotenoids, phenolic compounds, and natural antioxidants (Parry *et al*., 2006). Pumpkin seed extracts have exhibited its lipoxygenase inhibitory activities. The extracts were screened for their antioxidant activity using 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging assay and for their inhibitory activity against lipid peroxidation catalyzed by soybean lipoxygenase. Most extracts tested have demonstrated radical scavenging activity, which depends on their total phenolic content, with fractions rich in phenolics showing the strongest activity (Xanthopoulou *et al*., 2009).

Others

The antifungal activity was isolated from the soluble and cell wall-derived fractions of seeds of pumpkin (*Cucurbita maxima*) using batch-wise chromatography on carboxymethyl-cellulose (CM52) and reverse-phase HPLC. Polypeptide masses were determined by electrospray ionisation mass spectrometry (ESMS). These fraction components were shown to exhibit antifungal activity against a variety of fungi (Vassiliou *et al*., 1997). As pumpkin seeds are high in Zinc it helps to prevent acrodermatitis enteropathica (Neldner *et al*., 1975), an autosomal recessive metabolic disorder affecting the uptake of zinc, characterized by periorificial (around the natural orifices) and acral (in the limbs) dermatitis, alopecia (loss of hair), and diarrhoea (Aggett *et al*., 1983) (Rosalinda *et al.,* 1998).

Some studies have also pointed to another beneficial effect of pumpkin seeds namely prevention of kidney stones (calcium oxalate). It has been observed that these seeds when taken daily acts in a way to reduce substances which lead to stone formation and also promote substances which prevent stone formation (Suphiphat *et al*., 1993). Pumpkin seeds provide high phosphorus levels and can be used as a potential agent in lowering the risk of bladder-stone disease (Suphakarn *et al*., 1987). Pumpkin seeds snack, a high nutritive mixture, has been considered beneficial to improve the nutrients and increased the level of inhibitors of crystal formation or aggregation which subsequently reduced the risk of bladder stone disease (Suphiphat *et al*., 1993). Pumpkin seeds oil preparation remarkably reduce the bladder pressure, increase the bladder compliance and reduce the urethral pressure (Zhang *et al.,* 1994). Cucurbitacin E extracted from pumpkin seed has exhibited its anti-cancer and anti-inflammatory activities. It has not only an apoptotic effect on prostate and lung cancer cells but also an anti-inflammatory activity by inhibiting expression of cyclooxygenase-2, an inflammatory protein, suggesting that cucurbitacin E may be useful as a potential anti-cancerous and anti-inflammatory agent (Jang *et al.,* 2008).

Industrial uses

The seeds of pumpkin (*Cucurbita maxima*) 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 realization that these seeds are rich in protein, fibres, minerals, polyunsaturated fatty acids and phytosterols, they are being considered valuable for the food industry. The new found attention of food technologists has resulted in their introduction into the commercial food sector. Food companies are experimenting with their incorporation into a variety of food products 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 researched. The conversion of these agricultural wastes into value-added ingredients is likely to be a big step towards the alleviation of global food shortage issues; thus, it deserves more investigation. The following review furnishes an account of this emerging nutraceutical.

In 2007 Stevenson *et al*. studied *Cucurbita maxima* for their seed oil content, fatty acid composition, and tocopherol content. Oil content ranged from 10.9 to 30.9%. Total unsaturated fatty acid content ranged from 73.1 to 80.5%. The predominant fatty acids present were linoleic, oleic, palmitic, and stearic. Significant differences were observed among the cultivars for stearic, oleic, linoleic, and gadoleic acid content of oil. The study showed potential for pumpkin seed oil to have high oxidative stability that would be suitable for food and industrial applications, as well as high unsaturation and tocopherol content that could potentially improve the nutrition of human diets (Stevenson *et al*., 2007). The physicochemical properties of the oil showed that the extracted oil could be used as food oil supplement (Mitra *et al*., 2009).

Apart from the studies on the beneficial effects of seeds of *Cucurbita maxima* mentioned so far, there are numerous other examples of these seeds being used as traditional medicines in different parts of the world. Even though there is a sizeable quantum of information available as regards to the beneficial effects of the seeds of *Cucurbita maxima*, still there is an ample scope of research to expose hitherto unknown properties of these seeds and also to determine whether these neglected and underutilized seeds may be treated as a valuable addition to our daily diet. The utilization of such under-utilized agricultural products, as well as by-products to produce food and feed would help maximize available resources.

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