



Research Article

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Potential Pharmacological Activities of Pumpkin Seeds as a Functional Food: A Comprehensive Review

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ABSTRACT

Pumpkin, belongs to the family *Cucurbitaceae* and genus *Cucurbita*, is gaining appeal across the world for a number of reasons. Pumpkin seeds have always been discarded as waste even with containing essential pharmaceutical micro and macro constituents such as proteins, antioxidative phenolic compounds, tocopherols, triterpenes, saponins, phytosterols, lignans, and carotenoids as well as these compounds D-chiro-inositol, trigonelline, and nicotinic acid. Pumpkin seeds are also rich in fibre, polyunsaturated fatty acids, vitamins, and minerals including zinc, iron, magnesium, calcium, manganese, and copper that may be used in the food industry. Pumpkin seeds are now generally used in traditional medicine in treatment of many diseases, including hypertension, rheumatoid arthritis, hyperglycemia, inflammation, dyslipidemia, bacteria, fungal infections, and tumours. As a result, pumpkin seeds are now often utilised as a herbal treatment or health-improving agent for both people and animals, and food scientists are providing the pumpkin-infused products to the food and health industries. Hence, food manufacturers have worked to broaden the range of appetiser, baking, and snack uses for pumpkin seeds. This review article provides insights into the pharmacological activities of pumpkin seeds and the possible processes which, might reduce the chance of a wide range of problems.

Keywords: Functional food, Pharmacological activities, Antioxidative phenolic compound, Pharmaceutical.

INTRODUCTION

Natural products have been used as functional and nutraceutical foods for centuries [1]. Scientists have been intending to understand the molecular impacts of various nutrients on a number of chronic and severe diseases for the past few years [2]. Bioactive substances are naturally found in plants, which are frequently used as functional food ingredients. Foods that fall into the category of foods with a diet-health relationship are known as functional foods since there are several studies that link bioactive and natural food components to health promotion and disease prevention [3]. Due to the significant nutraceutical and therapeutic potential of their bioactive components, seeds and nuts have garnered growing popularity over the past few years. Because of their medicinal and nutritional benefits, seeds including flax, chia, hemp, sesame, sunflower, and pumpkin are frequently referred to as healthy edible super seeds [4].

Pumpkin belongs to the genus *Cucurbita*, which is in the *cucurbitaceae* family. *Cucurbita pepo*, *Cucurbita mixta*, *Cucurbita maxima*, and *Cucurbita moschata* are a few varieties of pumpkin plant species that have flourished as a vegetable in different regions across the globe [5]. Seeds and nuts are receiving more attention in recent years due to the significant medicinal and nutraceutical benefits of their bioactive compounds [6]. Although there are many different types of pumpkin seeds around the world, *Cucurbita pepo* L. is the species that is most important for commercialization [7]. The native species of North America is *Cucurbita pepo* L. that has been harvested there for many centuries. In accordance with the quality of the extracted oil, pumpkin seeds have been characterised as more resilient and less apt to perish [8]. Researchers have focused their attention on this crop for the treatment of disease because of the presence of numerous edible and medicinal components [9]. Although pumpkin seeds are broadly perceived as agricultural waste and discarded while having a wealth of medicinal benefits and essential nutrients [10]. Today, salted and roasted pumpkin seeds are offered as a concentrated source of protein and are widely consumed as baked, roasted, and sprouted snacks.

Pumpkin seeds are nutrient-dense foods that come in a variety of morphological forms, including hulled, semi-hulled and thin-layer seeds [11]. Since the flavonoid cucurbitacin is known for its anticancer activity, the presence of flavonoids and triterpenoids may be a contributing element in the anticancer action. Protein, vitamin E, carotenoids, saponin, phytosterol, provitamins, unsaturated fatty acids, flavonoids, phenolic substances, and their derivatives all are pervasive in pumpkin seeds [12]. Even so, the polyunsaturated fatty acids, tocopherol, potassium, phosphorus, zinc, manganese, copper, calcium, iron,

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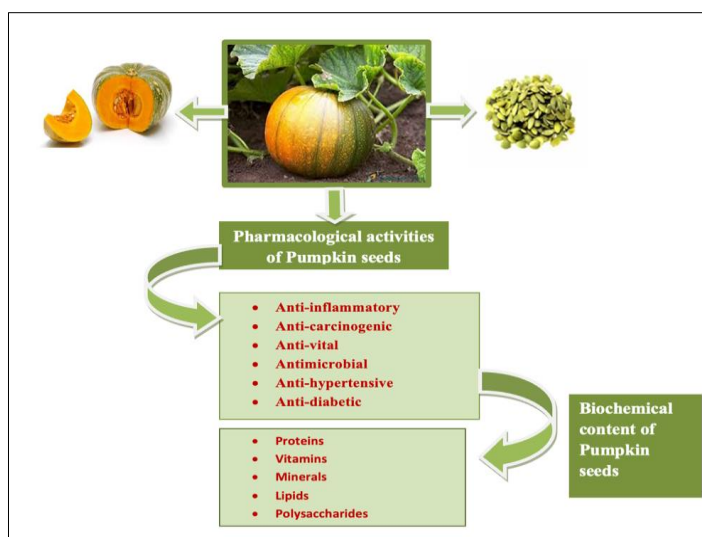


Figure 1: Pharmacological activities and biochemical content of Pumpkin seeds

sodium, and magnesium present in pumpkin seeds make them a valuable source of nutrients [8]. Minerals and bioactive substances simultaneously perform a variety of potential roles, such as reducing oxidative stress, non-communicable illnesses, hyperglycemia, diabetes, prostatic problems, urine bladder, and other conditions that affect the urinary system and overall health. Extracts of pumpkin seeds possess antibacterial, wound-healing, and hair-growth-promoting effects [13]. According to a new market estimate by Accuray Research LLP, the global market for pumpkin seeds would be worth around 1.88 USD by 2025, highlighting the seeds' economic potential as well as their technical and biological functions [14].

1. PUMPKIN SEEDS AS FUNCTIONAL FOOD INGREDIENT

Pumpkin is well regarded as a nutrient powerhouse and disease-preventive food with its abundance of rich nutrients, primarily phosphorus, zinc, magnesium, potassium, manganese, and selenium [15]. Currently, public health and medical professionals are very interested in functional foods as a means of illness prevention [16]. Usually, pumpkin seeds are discarded as waste, but nowadays, they serve a vital purpose in food products. Many anti-disease qualities exist in pumpkin seeds, some of which treat arthritis, prostate cancer, and inflammation [17]. Pumpkin seeds have a good amount of protein (35%). The synthesis of protein key components and as an intermediate in metabolism, amino acids perform numerous significant physiological functions. Similar to soybean (84.4%) and sunflower (88.6%), pumpkin seeds contain 95% of fatty acids that constitute 75% of unsaturated fatty acids [18]. According to research, the unsaturated fatty acids in pumpkin seeds are beneficial for the growth and development of the neurological system, as well as for preventing cardiovascular disease, hypertension, and arthritis. Likewise with other essential amino acids, alpha-linolenic and linoleic are not synthesised by the body and can only be acquired through diet [19].

It has been observed that pumpkin seed oil contains high amounts of phenolic chemicals (tocopherols and tocotrienols), which are associated with a lower risk of breast, lung, stomach, and colorectal cancer [20]. According to the study, phenolic compounds found in pumpkin seeds include ferulic, vanillic, p-hydroxybenzoic, and tyrosol, as well as trace levels of syringic, luteolin, and trans-p-coumaric acids. Furthermore, phytosterols in pumpkin seed are important for treating prostate issues and lowering blood cholesterol levels [21]. The pumpkin seed can be encapsulated in a micro- or nano scale to prevent functional loss, which could remediate the problem. It is thought that encapsulation of these bioactive proteins protects them from degradation, metabolic influences, and other harmful reactions within the digestive system [22]. Pumpkin seeds have enormous amounts of trace elements as zinc and iron in addition to minerals like potassium, calcium, manganese, phosphorus, magnesium, and sodium [23]. Zinc is essential for male reproduction, structural protection, and cellular defence. Likewise, pumpkin seeds' high potassium and low sodium content that protect against cardiovascular disease [24], tocopherol and tocotrienol isomers of vitamin E are plentiful in pumpkin seeds. Similarly, pumpkin seeds are a vital source of phytosterols. Furthermore to being widely investigated for their decreased risk of blood low-density lipoprotein cholesterols, which relates to a decreased level of cardiovascular threats [25]. It has also been revealed in various studies that phytosterols can lower the risk of many types of cancers. Due to the presence of phytosterols, pumpkin seeds are a suitable alternative nutraceutical for treating a variety of non-communicable diseases in individuals [8].

2. HEALTH BENEFITS OF PUMPKIN SEEDS

Pumpkin seeds are usually discarded as waste products during the processing despite of having high amounts of protein, minerals, dietary fibre, monounsaturated fatty acids, vitamin E, zinc and phytonutrients. Pumpkin seeds are renowned and relished over the world in direct and baking products for their unique greenish sweet and nutty flavour [26]. The presence of health-protective qualities, high levels of pharmacological substances, and a good quantity of unsaturated fatty acids in pumpkin seeds oil is receiving more and more attention. Pumpkin seeds are suitable for use as a food supplement since they are a good source of the macronutrients calcium, magnesium, and phosphorus, as well as a moderate amount of the micronutrients calcium, manganese, and copper. Moreover, pumpkin is a cheap and nutritious source, and pumpkin seed flour is fortified in supplementary food mixtures to create cheap and widely favoured food products [27]. Stevenson [24] stated that pumpkin seeds were a tasty, wholesome snack meal and food ingredient. Similarly, Rani *et al.*, [28] conclude that pumpkin seeds are rich in phosphorus, magnesium, zinc, and selenium, which improve their ability to prevent diseases including prostate cancer, arthritis, inflammation, and cardiovascular disease.

Table 1: Functional role and component of pumpkin seeds (Hussain et al., 2022) ^[33]

Functional role	Components	References
Improve cardiovascular health	Magnesium	Elinge et al., 2012 ^[23, 24]
Abolish intestine worm	Cucurbitin	Colagar and Souraki, 2012 ^[14]
Improve nerves or muscle health	Phosphorous	Maheswari et al., 2015 ^[43]
Decrease LDL levels and improve heart health	Omega-3 Fatty acid	Nakic et al., 2006 ^[52]
Decrease the risk of hypertrophy	Unsaturated fatty acids	Colagar and Souraki, 2012 ^[14]
Enhance sleeping patterns and balanced moods	Serotonin, L-tryptophan	Peter et al., 2013 ^[55]
Eliminate kidney stones	Potassium	Elinge et al., 2012 ^[23, 24]
Act as anti-emetic	Seeds oil	Marie- Magdeleine et al., 2011 ^[45]
Protect cellular damage	Selenium	Maheshwari et al., 2015 ^[43]

3. SUPPLEMENTATION OF PUMPKIN SEEDS IN NUMEROUS FOOD PRODUCTS

As a good source of nutrients, pumpkin seeds can be used in supplementary food products. The physical-chemical quality, digestibility, and reduction of phytic acid components in pumpkin seed flour are all significantly improved by roasting pumpkin seeds [34]. In vitro tests on protein digestibility are improved by adding pumpkin seeds to food items. A study was conducted to assess the nutritional composition of developed value-added cookies incorporating germinated pumpkin seed powder and discovered that the value addition of pumpkin seed powder enhanced the nutritional value of cookies in terms of ash, fat, protein, and fibre as well as total and available minerals like calcium, magnesium, zinc, and iron [35]. Hussain *et al.*, [36] developed biscuits by addition of pumpkin seeds flour, rich in Fe and Zn, could be used as a functional food as immunity boosters of children in the present COVID 19 epidemic issues. Kumari and Rani [37] developed value-added whole wheat flour biscuits by combining whole wheat flour with germinated pumpkin seed flour and in nutritional analysis were found out that the addition of pumpkin seed flour enhanced the cookies' nutritional value in terms of ash, fat, protein, fibre, and total minerals. The mineral profile of the products improved as a result of value addition respectively, calcium, magnesium, zinc, and iron.

4. PHARMACOLOGICAL ACTIVITIES OF PUMPKIN SEEDS

I. ANTICARCINOGENIC EFFECT

It is a significant issue for researchers, investigators, and medical professionals to select health-preventative and therapeutic techniques to prevent and treat cancer disorders since cancer is a problem that is gradually becoming more widespread in the world. Many veggies and fruits contain phytochemicals and nutraceuticals that can reduce the risk of developing cancer. The carotenoid pigments found in pumpkin seeds have been linked to a lower risk of developing cancer [38].

Furthermore, Aghaie *et al.*, [39] reported that Cyclophosphamide is a cancer treatment drug that is unsafe for reproduction systems. Rathinavelu *et al.*, [40] study on the in vitro cytotoxic effects of pumpkin seed ethanolic and aqueous extracts on prostate cancer showed that these effects were mediated through oxidative stress, mitochondrial depolarization, and apoptotic pathways. In addition, Cucurbita pepo extract has the potential to be created as a novel chemotherapeutic treatment to stop or slow the growth of tumours and cancer [41].

II. ANTIDIABETIC EFFECT

Among all diseases affecting older individuals, diabetes mellitus is the most common. Diabetes mellitus is a condition of the metabolic system in which the body either does not create enough insulin or responds improperly to the insulin that is produced. By conducting an oral glucose tolerance test on rats, Teugwa *et al.*, [42] reported that the most popular storage protein is globulin (295.11 mg/g) dry matter and is capable of significantly lowering blood sugar (88-137.80%). And conclude that several species of *Cucurbitaceae*, including *Cucurbita moschata*, showed hypoglycaemic activity. Combination of pumpkin seeds and flax seeds has hypoglycemic and antioxidant effects in diabetic rats, chloramphenicol acetyltransferase, growth stimulating hormone, superoxide dismutase, reduced malondialdehyde and antioxidant enzyme are the features of histopathological abnormalities, Increases in plasma levels of glucose, total lipid, triglycerides, and cholesterol were largely resistant [43].

III. ANTI-ARTHRITIS EFFECT

In-vivo study by compared to indomethacin (a synthetic anti-inflammatory drug), giving arthritis-prone rats, *C. pepo* L. seed oil significantly reduced their chronic inflammation, which was determined by a clear healing of the paw oedema. The high level of unsaturated fatty acids and the combined antioxidant properties of selenium, carotenoids, and tocopherols in pumpkin seed oil may be the reason for this recovery by [44]. Specifically, pumpkin seed oil may play an anti-inflammatory effect during arthritis by scavenging free radicals,

which in turn may prevent lipid peroxidation of the cell membrane [45].

IV. ANTIMICROBIAL EFFECT

Bacteria, parasites, viruses, and fungi are thought to be the primary causes of many diseases and the path that ultimately results in death, instead of clean, germ-free environments and foods. In the oil of pumpkin seeds, there are antibacterial chemicals that have been recognized by [46]. According to Hammer *et al.*, [47], 2% pumpkin seed oil concentration inhibits the growth of *Staphylococcus aureus*, *Salmonella enterica*, *Enterococcus faecalis*, *Escherichia coli*, *Aeromonas veronii*, *Candida albicans*, and *enterococcus faecalis*. The basic proteins of pumpkin seeds MAP2, MAP11 and MAP4 had been investigated to inhibit the development of the yeast cell. The MAP11 protein displayed the highest levels of inhibitory effects compared to other basic proteins [48]. The MAP2 and MAP4 did not prevent the gram-negative (G-ve) bacteria from growing as *Escherichia coli*. According to Aziz *et al.*, [6] phloem from pumpkin seeds releases antifungal qualities and inhibits pathogenic fungi. The potent nutritional and health-protective qualities of pumpkin seeds as well as their pharmacological benefits, including their anti-diabetic, anti-fungal, anti-bacterial, anti-inflammation, and antioxidant actions, have received a lot of attention recently [49].

V. ANTIDEPRESSANT EFFECT

Depression is a common disorder which leads to phases of inhibited psychosocial functioning, reduces quality of life, and is apparent as symptoms such as disturbed sleep and appetite, decreased attention, excessive guilt, and even suicidal thoughts [50]. LaChance and Ramsey [51] found 47% anti-depressant food in pumpkin seeds. This leads to pumpkin seeds having the potential to be an anti-depressant. Another study investigated the effectiveness of imipramine standard drugs and pumpkin seed extracts in rats using forced-swimming and tail-suspension tests and its premise that pumpkin seeds had a significant amount of antidepressant potential. Although the exact mechanism of action of pumpkin seed extract is still unidentified. Eby and Eby [52] connected the antidepressant effect to the amino acids tryptophan and 5-hydroxytryptophan, both of which are advertised as treatments for depression. Tryptophan is an essential amino acid and 5-hydroxytryptophan is an intermediate metabolite of tryptophan that is used for synthesis of the neurotransmitter serotonin.

VI. ROLE IN BREAST CANCER

Phytoestrogens have differing impacts on hormone-dependent tumours. The treatment with pumpkin seed extract can increase the synthesis of estradiol and the ER-/ER-/PR state on MCF7, BeWo, and Jeg3 breast cancer cells, according to prior studies conducted on a rat model of breast cancer [53]. Richter *et al.*, [54] identified the dose-dependent increase in estradiol synthesis in MCF7, BeWo, and Jeg3 cells. These findings reveal the possible relevance of pumpkin seeds in the therapy and prevention of breast cancer, particularly in MCF7 cells where a significant down regulation in ER- and an elevation in PR were seen [55].

VII. ANTIOXIDANT ACTIVITY

Oxidative stress has been recognised as a common factor in a number of chronic diseases and associated sequelae, including diabetes,

obesity, cardiovascular disease, and cancer. A potentially harmful imbalance between pro-oxidants and antioxidants favouring the former is present [56]. According to Szasz *et al.*, [57] certain pumpkin extracts may have significant antioxidant activity that may be beneficial for those with vascular damage, pre-diabetics, and diabetes. Both the trace elements selenium and zinc, which are found in pumpkin seeds, are thought to be potent antioxidants. Zinc has the capacity to inhibit the consequences of free radical release or form a direct connection to the copper or iron-binding sites of proteins, lipids, and DNA molecules antioxidant vitamin E, which is rich in pumpkin seeds [44]. Pumpkin extract supplementation significantly raised the serous and hepatic activities of glutathione peroxidase and superoxide dismutase in mice, and decreased the quantity of malonaldehyde as observed [58]. According to Xia and Wang [59] streptozotocin-induced diabetic rats showed cytoprotective effects from pumpkin seed extract's hypoglycaemic action as an antioxidant. Pumpkin polysaccharide has also been discovered to be able to boost glutathione peroxidase and superoxide dismutase activity while decreasing the malonaldehyde concentration in tumor-containing mouse serum [60].

VIII. ROLE IN IRON-DEFICIENCY

According to Miller, [61] iron deficiency anaemia is a commonly seen dietary issue worldwide. Ramapersuad *et al.*, [62] stated that supplementing with another naturally occurring source of iron, such as dehusked pumpkin seeds, may significantly improve blood iron levels. Fortified supplements help maintain an optimal nutritional status and lower the likelihood of iron scarcity, and fortified prepared cereals are also thought to be a widely used technique. Hematocrit, haemoglobin, reticulocyte count, serum ferritin, total iron-binding capacity, and transferrin saturation percentage were all the biochemical parameters assessed on the 20th day of menstrual cycles before and after pumpkin seeds treatment. Throughout a consuming period, significant positive results for iron status were seen [63]. Dehusked pumpkin seeds and iron-fortified prepared cereals are two sources of dietary supplements with iron. An in-vivo experimental study has been conducted to compare the effectiveness of these two sources and discuss their effects on iron nutrition status and the changes in haematological parameters in women of reproductive age. For one month, 30 g of iron-fortified prepared cereals and 30 g of pumpkin seeds were given to eight healthy, non-pregnant women between the ages of 20 and 37 and it has been found out that addition of pumpkin seeds in their diet improved the iron status [64].

5. OTHER NUTRACEUTICAL ROLES OF PUMPKIN SEEDS

In addition to the therapeutic nutraceutical effects mentioned above, pumpkin seeds have been shown to have an ameliorative effect on lipotoxicity and hepatic inflammation in animal models during clinical trials [65]. Additionally, compared to the placebo group they studied, pumpkin seeds exhibited a strong anti-androgenic impact, and self-rated improvement score was also much greater than that of the control group recorded [66]. Experimental researches have provided conclusive statements that pumpkin seeds have been shown to improve bladder and prostate health [67], manage hypertension [68], reduce inflammation [69], have wound healing qualities, and reduce sleep disorders [70].

6. INDUSTRIAL APPLICATIONS OF PUMPKIN SEEDS

Along with the various pharmaceutical uses, pumpkin seeds are additionally utilised extensively in the confectionery industry to flavor dishes and add flavor to cookies, cheese, crisps, candies, sandwiches, and snack bars [71]. Additionally, pumpkin seeds are an essential source of protein for all types of agricultural animals and are used as an ingredient in baked goods, salad dressing, margarine, and cake dinners [72]. In the industrial market Seed oil is used in the production of soap, paint, coatings, medicines, detergents, and cosmetics [73].

CONCLUSION AND FUTURE DIRECTIONS

The above research concluded that the pumpkin seeds have pharmacological properties as well as being considered delicious food in many regions of the globe. Pumpkin seeds offer medicinal purposes that have been used to cure and control diabetes, cancer management, inhibit microbial growth, treat anaemia, and reduce stress. With increased awareness in environmental friendly agriculture, clean and efficient energy sources, waste management technologies, pumpkin seeds have the opportunity to gain a new and growing market share in the snack food sector also have the chance to introduce new ideas for creating innovative nutraceuticals, pharmaceuticals, and cosmeceuticals products from pumpkin seeds for the large range application.

Conflicts of Interest

The author reports no conflicts of interest in this work.

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