

Pumpkin (*Cucurbita* sp.)

Subjects: **Integrative & Complementary Medicine**

Contributor: Samy Selim , , Modassar Ranjha , Ume Roobab Qazalbash , Muhammad Faisal Manzoor , Umar Farooq , Hafiz Rehan Nadeem , Muhammad Nadeem , Rabia Kanwal , Hamada Abdelgawad , SOAD ALJAOUNI , Salam Ibrahim

Pumpkin is a well-known multifunctional ingredient in the diet, full of nutrients, and has opened new vistas for scientists during the past years. The fruit of pumpkin including the flesh, seed, and peel are a rich source of primary and secondary metabolites, including proteins, carbohydrates, monounsaturated fatty acids, polyunsaturated fatty acids, carotenoids, tocopherols, tryptophan, delta-7-sterols, and many other phytochemicals.

pumpkin

phytochemicals

bioactive compounds

therapeutic potential

1. Introduction

Products from natural sources have been used for centuries as functional and nutraceutical foods ^{[1][2][3][4][5][6]}. During the past years, scientists have been working on understanding the molecular-level effects of various nutrients on several chronic and deadly diseases ^{[7][8][9]}. People can adjust to different climate and habitat changes due to a wide range of nutrients that alter multiple genes' natural mode at the molecular level ^[10]. In other words, molecular changes are due to nutrients. Keeping this in mind, researchers are engaged in preventing and treating diseases with the use of pertinent food(s) rather than medicines. Moreover, studies have demonstrated that healthy eating is a reasonable and economical method to treat diseases ^[11].

Pumpkin has attracted increasing attention from scientists due to its nutritional profile. It is a nutritious and economical product and belongs to the Cucurbitaceae family. *Cucurbita pepo* L., *Cucurbita maxima* Duchesne, and *Cucurbita moschata* Duchesne are harvested worldwide due to their economical and environmentally friendly properties ^[12]. In many countries, pumpkin is used as a medicine for its anti-inflammatory, antioxidant, antiviral, and antidiabetic properties, particularly in Austria, Hungary, Mexico, Slovenia, China, Spain, and various European, Asian, and African countries ^[13]. Worldwide, pumpkin is harvested for its peel, flesh, and seeds. The seeds are usually large in size with a high content of polyunsaturated and monounsaturated fatty acids. Linoleic acid, oleic acid, palmitic acid, ECN-44, ECN-46, tocopherols, β -sitosterol, and delta-7-sterols constitute a large quantity of pumpkin seed oil ^[14].

For decades, several research studies have been conducted on the active ingredients of pumpkin peel, flesh, and seeds to provide a thumbnail sketch of their health-related impacts, which have demonstrated its anti-inflammatory ^[15], antibacterial ^[16], anticarcinogenic ^[17], antidiabetic ^[18], and antihypertensive properties, associated with this climber for diabetes ^[19].

Figure 1 illustrates the health-friendly properties of pumpkins.

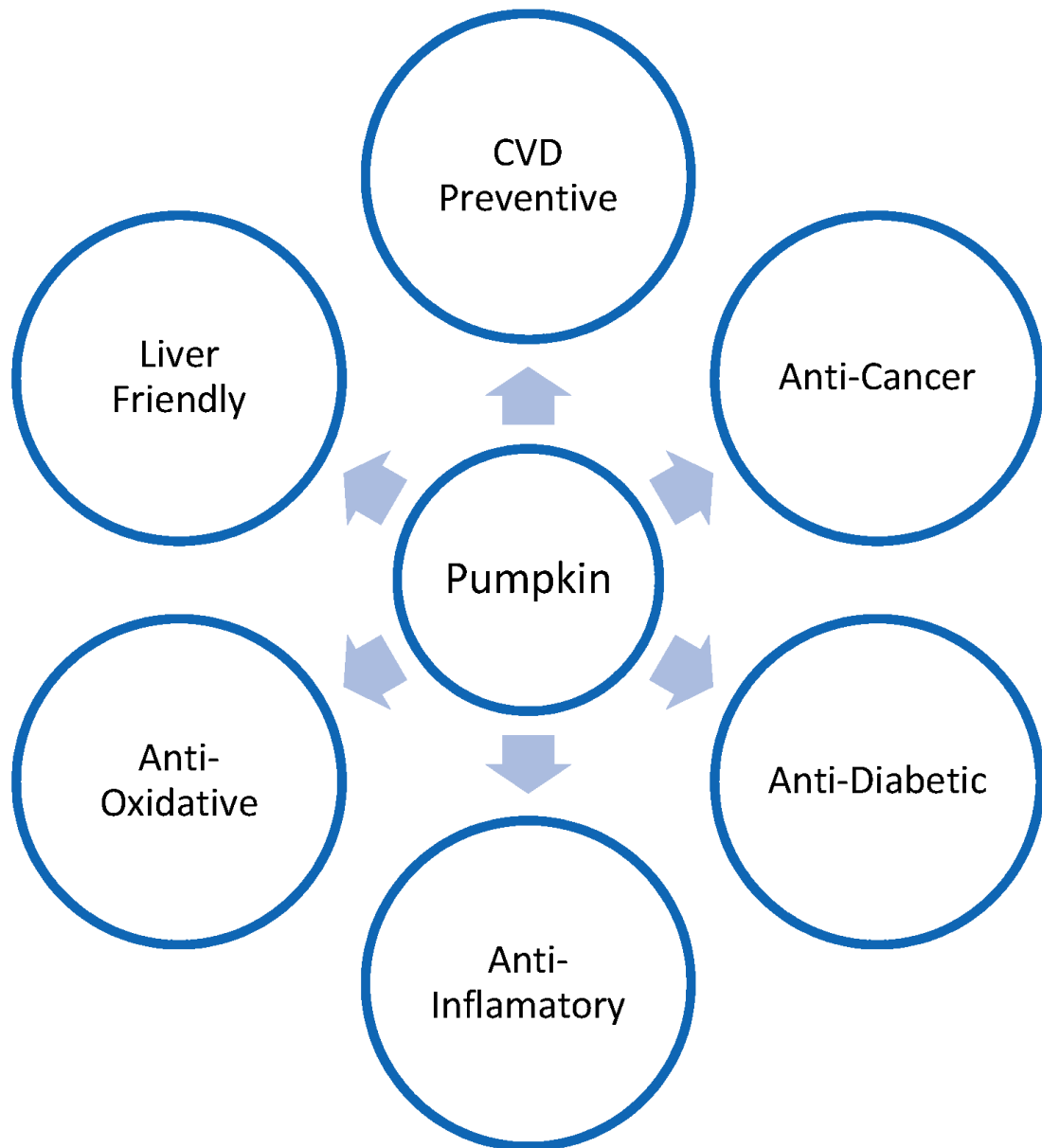


Figure 1. Health-friendly properties of pumpkin.

2. Health-Promoting Properties of Cucurbita

2.1. Hypoglycemic Properties

Hyperglycemia, which may result from the absence of insulin (DM-type 1) or due to a low response to insulin (DM-type 2), is one of the world's emerging problems. Chronic hyperglycemia leads to severe complications, such as damage to the eyes (retinopathy), brain (neuropathy), and kidneys (nephropathy) ^[20]. Diabetes is remarkably spreading worldwide, suggesting a considerable rise to about 82 million sufferers by 2030 ^[21]. People in third world and middle-class countries suffer from DM as more than 80% of diabetes-associated deaths occur in these regions

[22]. Several drugs, such as glucagon-like peptide-1 (GLP-1) analogs, α -glucosidase, metformin, etc. are used to cure DM-2. Nevertheless, these drugs have an effect on longevity, resulting in many adverse side effects. Due to the side effects of anti-hyperglycemic medicines, healthcare providers worldwide focus on the use of herbs and dietary ingredients to cure DM-2 [23].

In Mexico and China, herbal extracts are used to treat hyperglycemia as they usually contain pumpkin [24][25]. In recent years, extensive research has been conducted to study the antidiabetic effects of pumpkin flesh, seeds, and peel [26]. Pumpkin fruit powder was reported to contain antidiabetic properties [27]. In light of this study, it is reported that pumpkin powder tends to enhance the level of insulin in the body, leading to a lower level of glucose. Therefore, it also lowers the risk of kidney damage [28].

The breakdown of complex carbohydrates usually occurs in the small intestine by α -glycosidase, which is present in epithelial mucosa. α -glycosidase is responsible for the breakdown of glycosidic bonds present within complex carbs, and thus increases the blood glucose level [29]. It is often highlighted that the use of pumpkin can lower the activity of α -glycosidase. Moreover, in the same research, it has been reported that pumpkin scavenges ROS and can act as an ACE inhibitor [30]. However, further research is required to understand the effect of pumpkin on α -amylase.

Diabetic rats are one of the most commonly used tools to study the antidiabetic effect of any therapeutic agent. Alloxan is a toxin that affects the B-cells of pancreas, and thus leads to diabetes in rats [31]. A case-control study on rats demonstrates the anti-hyperglycemic properties of pumpkin. It further strengthens the research that pumpkin has the tendency to enhance insulin production and lowers the glucose level in the blood. The use of pumpkin in the earlier stages of diabetes may reduce postprandial glycemic levels. Protein-bound polysaccharide (PBPP) in pumpkin tends to lower hyperglycemia in rats and is usually dose-dependent [32]. In 2019, an in vivo study was conducted. Both pumpkin polysaccharide (PPE) and pumpkin polysaccharide hydrolysate (PPE-H) showed their hypoglycemic effect to lower fasting blood sugar levels of rats with DM-2. The diabetes-friendly nature of PPE-H has facilitated the decrease in oxidative stress and stimulated the endogenous GLP-1 secretion [33].

Figure 2 illustrates the mechanism of pumpkin polysaccharide hydrolysate in the treatment of DM-2.

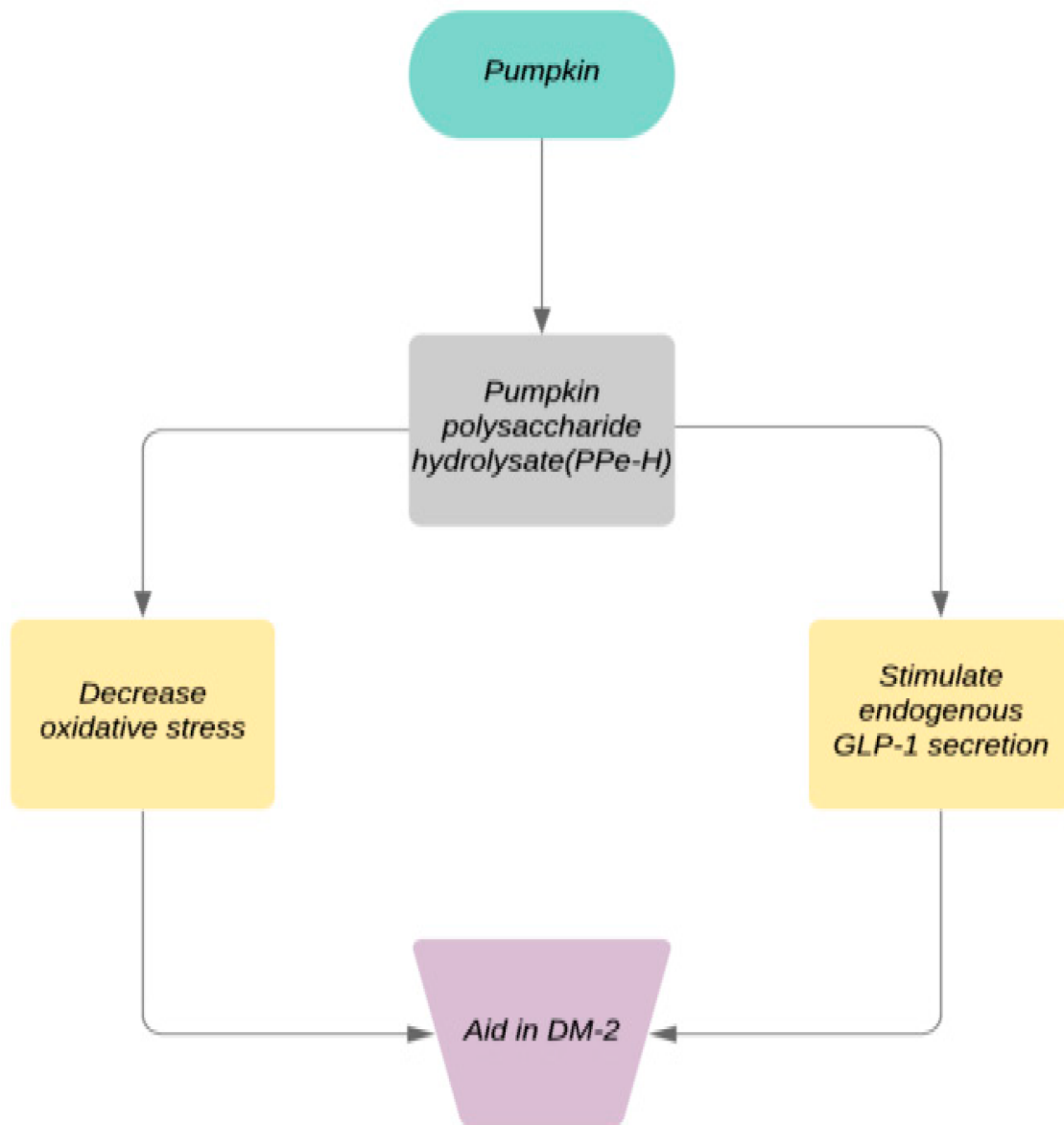


Figure 2. Mechanism of pumpkin polysaccharide hydrolysate in the treatment of DM-2.

Pumpkin regulates the blood glucose level by promoting the discharge of insulin and preventing many of the complications associated with diabetes [34]. Taking this into account, it is stated that pumpkin has antidiabetic properties and can play a protective role against hyperglycemia in diabetic patients. Nevertheless, researchers could not use these data to successfully report the exact mechanism of action of pumpkin against diabetes.

2.2. Anti-Cancerous Properties

A diet rich in oxidants and antioxidants has a significant association with cancer. Diet tends to make the condition worse or better, as cancer is associated with oxidative stress [35]. In 2017, 9.6 million deaths were reported due to all types of cancers. A report by GLOBOCAN estimated that the number of individuals suffering from cancer in 2018 was 18.1 million, and the death rate will be 9.6 million in 2019 [36]. In less developed countries, the rate of

stomach, cervical, and liver cancer is high, while in developed countries, breast, lung, and prostate cancer is more common [37][38].

Pumpkin seeds are a major source of phytoestrogen, such as lignans and isoflavones. Phytoestrogen tends to bind with estrogen receptors (ER) in the female body [39]. A study was conducted to investigate the association between breast cancer and pumpkin seed extract containing phytoestrogens. It was reported that the production of estradiol in MCF7, BeWo, and Jeg3 cells increased, and the reduction in ER- α was observed in MCF7-cells [40]. Essentially, 2S albumins which are proteins present within the seeds of pumpkin, have been reported in a study to have anti-cancerous properties, particularly in the case of breast cancer. MCF7-cells were treated with protein at two different concentrations (10 and 30 μ M). The results obtained by DNA showed fragmentation assays and acridine orange staining, in which 2S albumins from pumpkin seeds have the tendency to cause apoptosis in MCF7-cell lines [41].

2.3. Neuroprotective Properties

Malnutrition is a common issue worldwide, affecting children with limited calorie and protein(s) intake. Malnutrition usually results in behavioral disorders [42]. It is reported that protein-energy malnutrition (PEM) gives rise to free radical production, usually through lipid peroxidation [43]. Lipid peroxidation is a risk factor associated with brain damage. Free radicals production, such as reactive oxygen species (ROS) damages the brain cells, resulting in severe harmful consequences of PEM [44][45]. In a recent study, the leaves of pumpkin (fluted pumpkin) were used to investigate the brain-protective effect of this herb in PEM-induced rats due to the high antioxidant composition [46]. The seed protein was clearly observed and fluted pumpkin leaves joined together to prevent oxidative damage to brain cells due to PEM.

Organic compounds known as aflatoxins have substantial toxic effects, such as carcinogenic, mutagenic, and hepatotoxic. In addition, they contribute to lipid peroxidation, thus affecting the brain [47]. In 2013, research was conducted to investigate the effect of pumpkin seed oil on aflatoxins-induced toxicity in the brain and other organs. It was reported that pumpkin seed oil has the tendency to treat aflatoxins-induced harmful effects in brain tissues [48].

Depression is the most common brain disorder and is specified as a state in which one loses interest, pleasure, sleep, and eating patterns are disturbed. Similarly, in mood swings, the sufferers may feel guilty and ashamed. In addition, they have poor interest/concentration in daily tasks. According to the 2015 World Health Organization statistics, people suffering from depression were more than 300 million [49]. In a study on fluted pumpkin leaves, it was reported that they can be a useful tool in treating depression and convulsions due to their muscle relaxant properties, particularly in hydroethanolic leaf extract [50]. Moreover, another report demonstrated the antidepressant effects of pumpkin in supporting the treatment of depression [51].

2.4. Liver Disease Preventive Properties

In the past, several researchers reported the liver-protective effects of pumpkin. In 2005, a study was conducted on male Sprague Dawley rats, which were administered a low protein diet for 5 days to produce liver dysfunction.

Thereafter, they were administered CCl₄ injections, which resulted in significantly higher levels of four liver enzymes; aspartate transaminase (AST), alkaline phosphatase (ALP), alanine transaminase (ALT), and lactate dehydrogenase (LD). One group was administered with pumpkin seed protein isolate, which lowered the level of both aforementioned enzymes, suggesting the beneficial role of pumpkin in treating liver dysregulation [52]. In a similar study which was carried out a year later (2006), the same results were reported in addition to antioxidative effects [53]. In another study performed on rats with CCl₄, the same hepatoprotective effect of pumpkin seeds protein isolate was mainly reported by enhancing antioxidant activity and decreasing liver enzymes [54]. In a similar study, acetaminophen was used rather than CCl₄ to produce liver injury, and the results were the same as reported earlier [55]. Another research, which was conducted to understand the effect of aqueous leaf extract of fluted pumpkin on anemia, also reported the same results. In this case, 50 mg/kg of aqueous leaf extract of fluted pumpkin has the tendency to regulate ALT and AST [56]. All of these researches support the fact that pumpkin seed protein isolates have the tendency to attenuate the high level of liver enzymes (ALT, AST, ALP, LD) when liver injury is due to a low protein diet or malnutrition. In 2015, Farid et al. reported the same alterations in these liver enzymes with the use of pumpkin [57].

Non-alcoholic fatty liver disease (NAFLD) further leads to atherosclerosis, and CVD is a major health issue worldwide that leads to mortality and morbidity [58]. To cure the NAFLD as well as the onset of NAFLD, intake of fats and the type of fat present in one's diet play an important role [59][60]. As mentioned above, pumpkin seed oil is rich in unsaturated fatty acids that comprise about 80% of enriched phytochemicals [61].

2.5. CVD Preventive Properties

Pumpkin affects serum lipid levels directly and can also affect them indirectly. A research was conducted on Lohmann Brown Lite hens, and they were administered with a diet based on flaxseed and pumpkin oil. It was reported that eggs laid by the hens with a pumpkin diet had the highest MUFA content, lower PUFA, lower myristic acid, and other saturated fatty acids content [62]. However, further investigation is required as the earlier increase in myristic acid content was reported in eggs after pumpkin supplementation [63].

When the body is in hypercholesterolemic situation, dysfunctioning of the endothelial layer occurs, leading to the enhanced level of vascular cell adhesion molecule (VCAM). This occurs due to the activation of reactive oxygen species (ROS), which reduces nitric oxide formation and stops LDL oxidation. Due to the lower levels of nitric oxide (NO), oxidation of LDL will occur, which is responsible for all this VCAM enhancement mechanism [64]. Pumpkin seed powder contains 2.6% arginine, which is the precursor of NO, associated with BP maintenance, apoptosis, myocardial function, and inflammatory response [65]. An in vivo study designed to investigate the effect of pumpkin seed extract (mainly arginine) reported that pumpkin seed extract supplementation in rats with hyperlipidemia could enhance the expression of NO production due to the presence of arginine. Moreover, due to the production of NO, oxidation of LDL is attenuated, leading to the decreased expression of VCAM [66]. Therefore, it can be stated that modifying the lifestyle and adapting the regular use of pumpkins can be a useful dietary strategy to treat hypercholesterolemia.

2.6. Other Health-Related Properties

In addition to all of the aforementioned properties, pumpkin has been reported to play an important role in inflammatory diseases, such as arthritis due to its anti-inflammatory properties [67][68][69].

The worldwide male population above 50 years mostly suffers through an outgrowth of stromal and epithelial cells, usually in the periurethral area and in the transition zone [70][71]. Many researches support the claim that pumpkin seed extract has also been reported to overcome lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH), such as saw palmetto and prazosin [72][73]. In addition to treating LUTS, pumpkin administered for a whole month at a 14 mg/kg dose is a really useful strategy in controlling testosterone-induced hyperplasia [17]. Nevertheless, the data are not sufficient, and further researches are required as many consequences of pumpkin intake, in this case, are neglected in these researches.

Currently, although antimicrobial drugs are available, the focus of scientists is to develop dietary strategies to treat these infections as the use of these antimicrobes can lead to drug resistance. At a concentration of 2% (v/v), pumpkin seed oil has the tendency to treat *Staphylococcus aureus*, *Salmonella enterica*, *Escherichia coli*, *Klebsiella pneumonia*, *Acinetobacter baumannii*, *Candida albicans*, and *Serratia marcescens* [27]. Three hundred and seventy five milligrams of pumpkin seed oil can be useful to treat *Mycosphaerella arachidis*, *Fusarium oxysporum*, and *Botrytis cinerea* [74]. Similarly, proteins from pumpkin (>2 mM) in their purified form can control fungal growth [75]. Likewise, yeast growth has been known to be inhibited by three types of pumpkin proteins named MAP11, MAP4, and MAP2. However, MAP2 and MAP4 are not very useful in treating Gram-negative bacteria [76]. Therefore, pumpkin is a food of great antimicrobial properties and its use should be encouraged by people living in areas where they are more susceptible to any kind of microbial infection.

Pumpkin seeds have also shown anti-ulcerative properties by protecting gastric mucosa in a dose-dependent manner [77]. Wound healing through more effective and cost effective strategies is a constant focus of researchers, as medicines seem to be insufficient for the healing process [78][79]. High amounts of plant sterols, tocopherols, and PUFA present in pumpkin seed oil positively affect wound healing [14]. Similar findings that are related to pumpkin peel are also reported [80].

During the past years, male reproduction has been affected due to changes in lifestyle and some tragedies [81]. As pumpkins tend to attenuate lipid peroxidation and lower oxidative stress, it is a valuable tool to improve testicular properties and enhance reproduction [82][83]. A recent study conducted on fluted pumpkin seed (FPS) extract reported that 40 days of supplementation of 40 mg/kg bodyweight of FPS extract could enhance the number of spermatids, spermatocytes, and spermatogonia as well as protect against oxidative cell damage [84]. Therefore, FPS extract can be used as spermatocytes activator after chemotherapy. However, the effect is still uncertain, thus further investigation is required to understand the effect of pumpkin on serum parameters and testes [85].

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