

Medicinal and biological potential of pumpkin: an updated review

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The use of herbal remedies individually or in combination with standard medicines has been used in various medical treatises for the cure of different diseases. Pumpkin is one of the well-known edible plants and has substantial medicinal properties due to the presence of unique natural edible substances. It contains several phyto-constituents belonging to the categories of alkaloids, flavonoids, and palmitic, oleic and linoleic acids. Various important medicinal properties including anti-diabetic, antioxidant, anti-carcinogenic, anti-inflammatory and others have been well documented. The purpose of the present article is to discuss various medicinal and biological potentials of pumpkin that can impart further research developments with this plant for human health benefits.

Pumpkin: Herbal medicine: Anti-diabetic properties: Antioxidants: Anti-carcinogens: Phytochemicals

Introduction

Since ancient times, many herbal medicines in different formulations have been recommended for the treatment of various diseases. Traditional and/or indigenous drugs have special significance of having been tested over a long time, and are relatively safe, easily available and affordable. Many ethno-botanical surveys on medicinal plants used by the local population have been performed in different parts of the world including the USA, China, India, Mexico, Morocco, Saudi Arabia, Taiwan, and Trinidad and Tobago^(1–4), and suggested that several medicinal plants have been used as dietary adjuncts for the treatment of numerous chronic and severe diseases. In India and China, the use of herbal medicines has been commonly practised for a long time as a less expensive way to treat various health problems. The herbal drugs are considered frequently less toxic with limited side effects compared with synthetic drugs^(5,6). For such reasons, traditional and complementary medicines have seen an upsurge in their popularity for the treatment of different diseases. Herbal medicine development is one of the main subjects of studies in the National Center for Complementary and Alternative Medicines, Bethesda, USA which was established in 1998 by the US Government^(7,8). The WHO has also recommended the initiation of studies to identify and characterise new herbal preparations from traditionally known plants and the

development of new effective therapeutic agents, especially in the areas where we lack safe modern drugs to treat chronic diseases^(9,10). In the ongoing search for more effective and safer drugs, attention is being paid to new and safe medicinal herbs or food components^(7,10). Although phyto-therapy continues to be used in several countries as in the past, only a few plants have received scientific or medical scrutiny. Although most of the medicinal plants are safer, still a number of medicinal plants possess some degree of toxicity; therefore it is very important to analyse the traditional therapeutic regimens scientifically and validate their dosing, toxicity and other health consequences, before proper use in human diseased conditions. In the present article we discuss the biological and medicinal potential of a well-known edible plant, pumpkin (genus *Cucurbita*; family Cucurbitaceae). Pumpkin has various health benefits, which are summarised in Fig. 1.

Pumpkin used as a good edible plant

Pumpkin is cultivated from northern Mexico to Argentina and Chile and has spread to Europe (France and Portugal, for example), Asia (India and China) and Western America. Pumpkin is an annual vine or trailing plant and can be cultivated from sea level to high altitudes. It is famous for its edible seeds, fruit and greens⁽¹¹⁾. The most important part of

Abbreviations: MAP, myeloid antimicrobial peptide; MW, molecular weight.

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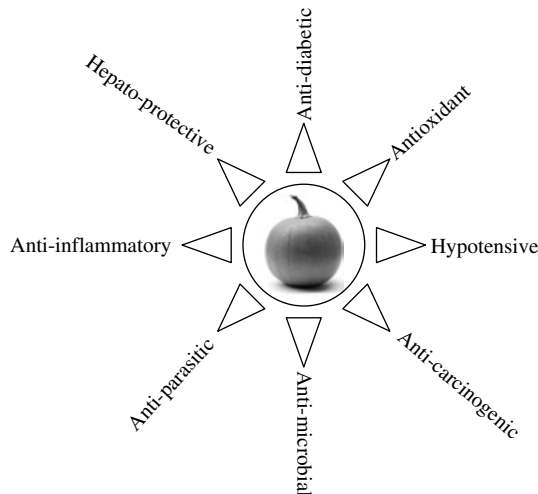


Fig. 1. Medicinal properties of pumpkins.

pumpkin is its low-fat and protein-rich seeds⁽¹²⁾. The second most important part is its fruit. The immature fruit is cooked as a vegetable, while the mature fruit is sweet and used to make confectionery and beverages, sometimes alcoholic. The fruit has a good β -carotene content and has a moderate content of carbohydrates, vitamins and minerals (Table 1). Different parts of the pumpkin plant have been used in the form of various food regimens throughout its distribution area in America. The unripe fruit is eaten as a boiled vegetable, while the flesh of the ripe fruit is used to prepare sweets and soft or slightly alcoholic drinks. Seeds are also greatly valued and in Chiapas, Mexico, they are used with honey to prepare desserts known as palanquetas. Edible oil is also obtained from the seed of pumpkin which is rich in oleic acid. Many varieties of pumpkins are available, and some of them are described elsewhere⁽¹³⁾.

Botanical description

Pumpkin is a creeping or climbing plant, monoecious, annual although persistent for a certain period, giving the impression of being a short-lived perennial, without swollen reserve roots. It is resistant to low temperatures but not to severe frosts. It has five vigorous, slightly angular stems and leaves with 5 to 25 cm petioles that are ovate-cordate to suborbicular-cordate, with or without white spots on the surface and have three to five rounded or obtuse, apiculate lobules, the central one bigger than lateral ones. Male flowers are long and pedicellate and have a campanulate calyx that is 5 to 10 mm long and almost as wide, 5–15 × 1–2 mm linear sepals and a tubular campanulate corolla that is rather broader towards the base, 6 to 12 cm long and yellow to pale orange. They have three stamens. Female flowers have sturdy peduncles, 3 to 5 cm long, an ovoid to elliptical, multilocular ovary, sepals that are occasionally foliaceous and a corolla that is somewhat larger than that of the male flowers. They have a thickened style and three lobate stigmas. The fruit is globose to ovoid-elliptical, with three colour patterns: (1) light or dark green, with or without longitudinal white lines

or stripes towards the apex; (2) minutely spotted white and green; (3) orange, white, cream or flesh white. The flesh is sweet and the seeds are ovate-elliptical, flattened, 15–25 × 7–12 mm, and a dark brown to black or creamy white colour⁽¹⁴⁾.

Table 1. Nutrients in pumpkin*

Constituent(s)	Amount
Water (g/100 g)	89
Protein (g/100 g)	4.0
Fat (g/100 g)	0.2
Carbohydrate (g/100 g)	2.0
Fibre (g/100 g)	2.4
Ca (mg/100 g)	475
P (mg/100 g)	175
Fe (g/100 g)	0.8
β -Carotene (mg/100 g)	1.0
Thiamin (mg/100 g)	0.08
Riboflavin (mg/100 g)	0.06
Niacin (mg/100 g)	0.3
Ascorbic acid (mg/100 g)	80
Al (mg/g dry weight)	9.21
Co (mg/g dry weight)	0.29
Cr (mg/g dry weight)	2.84
Cu (mg/g dry weight)	15.4
K (mg/g dry weight)	5.70
Mg (mg/g dry weight)	5.60
Na (mg/g dry weight)	6.90
Zn (mg/g dry weight)	113
Amino acids (mg/g dry weight)	
Alanine	23.4
Arginine	93.2
Aspartic acid	52.8
Cysteine	6.73
Glutamic acid	104
Glycine	28.3
Histidine	13.8
Isoleucine	23.0
Leucine	40.9
Lysine	22.0
Methionine	12.4
Phenylalanine	31.4
Proline	20.2
Serine	31.7
Threonine	18.4
Tryptophan	15.3
Tyrosine	22.1
Valine	28.2
Fatty acids (mg/g dry weight)	
12:0	0.02
14:0	0.16
14:1	0.07
15:0	0.02
16:0	13.0
16:1n-7	0.17
18:0	7.8
18:1n-9	45.4
18:1n-7	0.98
18:2n-6	31.0
18:3n-6	0.09
18:3n-3	0.19
20:0	0.58
20:1	0.13
22:0	0.16
22:1	0.08
24:0	0.15
24:1	0.09

* The sources of the data in the table were USDA Nutrient Composition Tables, various studies including de Escalada Pla *et al.*⁽⁶⁵⁾ and other websites.

Phytochemistry of pumpkin

Pumpkin has been considered as beneficial to health because it contains various biologically active components such as polysaccharides, *para*-aminobenzoic acid, fixed oils, sterols, proteins and peptides^(15–17). The fruits are a good source of carotenoids and γ -aminobutyric acid^(17,18). Pumpkin seeds (*Cucurbita* spp.) are valued for their high protein content⁽¹⁹⁾ and useful amounts of the essential fatty acid, linoleic acid⁽²⁰⁾. Pumpkin seeds contain remarkably high proportions of essential amino acids⁽²⁰⁾. Pumpkin seeds also contain relatively large amount of various essential micro-elements such as K, Cr and Na (Table 1). Pumpkin seeds are a good source of Mg, Zn, Cu, Mo and Se, etc. From pumpkin leaves and germinated seeds, several phytochemicals such as polysaccharides, phenolic glycosides, NEFA and proteins have been isolated^(21,22). Various hypoglycaemic polysaccharides have been characterised from fruit pulps of pumpkin plants⁽²³⁾. *D*-*chiro*-Inositol in pumpkin has been identified as an insulin secretor and sensitiser⁽²⁴⁾. Various antibiotic components including anti-fungal components have been characterised from various parts of pumpkin plants. Various anti-fungal proteins, such as α - and β -moschins (molecular weight (MW) 12 kDa), myeloid antimicrobial peptide (MAP)-28 (MW 28 kDa), MAP2 (MW 2.2 kDa), MAP4 (MW 4.6 kDa), MAP11 (MW 11.6 kDa) and a peptide (MW 8 kDa) from pumpkin have been isolated and characterised⁽²⁵⁾. The structures of some of these components are represented in Fig. 2.

Medicinal bioactivities of pumpkin

Although pumpkin is a well-known edible plant, most parts of this plant are also used in traditional systems of medicine around the world. Although a large number of compounds have been isolated from pumpkin spp.⁽¹⁵⁾, only some of them have biological activities and medicinal properties, which are described in the following sections. Table 2 summarises the bioactive compounds from pumpkin and their medicinal properties.

Anti-diabetic activity

With the rapidly increasing prevalence of diabetes and its high economic burden in the world population, the scientific community has been called upon to develop new safer and inexpensive medicines for the treatment of diabetes. Herbal medicines fulfil these requirements. Therefore, various studies have been recently conducted to recognise the anti-diabetic potential of herbal formulations; pumpkin is one of them, which is a normally cultivated plant in farms and its fruits are used for human consumption in diabetic conditions^(26,27). Local healers recommend the ingestion of crude aqueous extract of pumpkin fruits for the treatment of type 2 diabetes or non-insulin-dependent diabetes mellitus^(27,28). In various other reports, the pumpkin exhibited acute hypoglycaemic activity (blood sugar lowering) in temporarily hyperglycaemic rabbits, in alloxan-induced diabetic rabbits, and in type 2 diabetic patients^(28–30). Xia & Wang⁽³¹⁾ demonstrated that pumpkin has hypoglycaemic activity like a standard drug (tolbutamide) in healthy animals with temporary hyperglycaemia and in mild diabetic animals, but not in severe diabetic animals. They suggested that these effects might be due to either increased pancreatic insulin secretion from the existing β -cells or insulin release from the bound form. *D*-*chiro*-Inositol was identified in pumpkin (especially in *Cucurbita ficifolia*) and this compound has been considered as an insulin action mediator (insulin sensitiser)⁽³²⁾. However, the detailed mechanism of anti-diabetic action of this component remains to be clarified.

Various other components have also been isolated from pumpkin and analysed for anti-diabetic potential. For example, Kwon *et al.*⁽²⁷⁾ reported that phenolic phytochemicals of pumpkin have anti-diabetic effects in terms of β -glucosidase and α -amylase inhibition. Pumpkin also has hypotensive effects in terms of angiotensin I-converting enzyme-inhibitory activities. Furthermore, Quanhong *et al.*⁽³³⁾ also investigated hypoglycaemic substances from pumpkin, and they isolated protein-bound polysaccharide by activity-guided isolation from water-soluble substances of the pumpkin fruits. When this protein-bound polysaccharide from pumpkin fruits (PBPP) was evaluated for hypoglycaemic activity and effects on serum insulin levels in alloxan diabetic rats, and it was found that PBPP can increase the levels of serum insulin, reduce the blood glucose levels and improve tolerance of glucose in alloxan-induced diabetic animals. By considering all these facts, it can be concluded that pumpkin has potential anti-diabetic properties, which may suggest the inclusion of this plant in anti-diabetic regimens to treat human diabetes. However, further studies in detail are warranted to explore the mechanistic and therapeutic potential of pumpkins for diabetes.

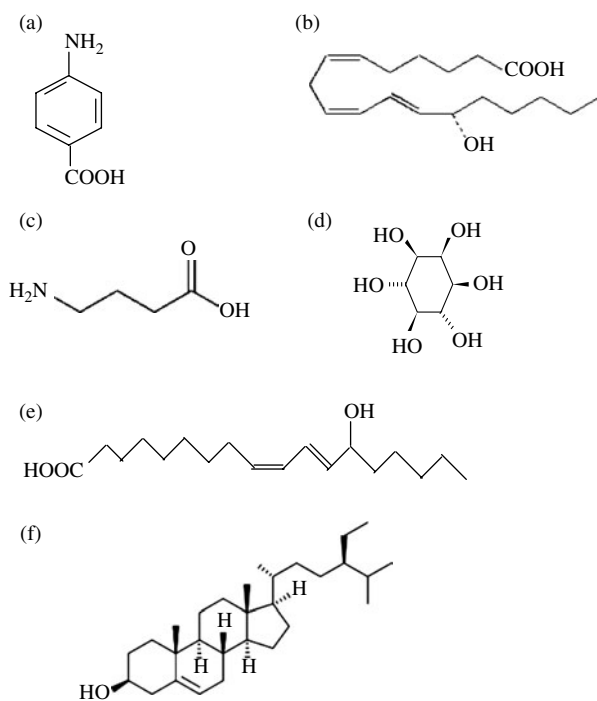


Fig. 2. Structures of some compounds isolated from pumpkins: (a) *para*-aminobenzoic acid; (b) 11*E*-octadecatrienoic acid; (c) γ -aminobutyric acid; (d) *D*-*chiro*-inositol; (e) 13-hydroxy-9*Z*; (f) β -sitosterol.

Table 2. Important bioactive compounds from pumpkin and their biological activities

Pumpkin compound(s)	Source	Biological activity	Major findings	References
D- <i>chiro</i> -Inositol	Seeds	Anti-diabetic	Increase in insulin secretion Increase in β -cell mass	Xia & Wang ⁽²⁶⁾
Phenolic phytochemicals	Fruits	Anti-diabetic	α -Amylase inhibition α -Glucosidase inhibition	Kwon <i>et al.</i> ⁽²⁷⁾
Protein-bound polysaccharide	Fruits	Anti-diabetic	Reduced blood glucose Increased insulin levels	Quanhong <i>et al.</i> ⁽³³⁾
Extract	Fruit	Anti-diabetic and antioxidant	Improved glucose tolerance Reduced blood glucose	Xia & Wang ⁽²⁶⁾
Extract	Fruit	Antioxidant	Increased insulin Reduced TBARS Enhanced SOD, catalase, glutathione functions	Dang ⁽³⁶⁾
Pumpkin polysaccharide	Fruit	Antioxidant	Increased serum and hepatic activities of SOD and GSH-Px Reduced malonaldehyde	Xu ⁽³⁷⁾
Boiled fruit juice	Fruit	Anti-carcinogenic	Reduced malonaldehyde	Ito <i>et al.</i> ⁽⁶⁴⁾
MAP2	Fruits	Anti-carcinogenic	Reduced aberrant cells	Cheong <i>et al.</i> ⁽⁴³⁾
MAP4			Inhibited growth of leukaemia K-562 cell	
Moschatin	Mature seeds	Anti-carcinogenic	Inhibited cell tumour cell growth Works like ribosome-inactivating protein	Xia <i>et al.</i> ⁽⁴⁵⁾
Cucurmosin	Sarcocarp	Anti-carcinogenic	Inhibited cell tumour cell growth Works like ribosome-inactivating protein	Hou <i>et al.</i> ⁽⁴⁶⁾
Peptide (MW 8 kDa)	Seeds	Anti-fungal	Inhibited growth of <i>Botrytis cinerea</i> , <i>Fusarium oxysporum</i> and <i>Mycosphaerella arachidicola</i>	Vassiliou <i>et al.</i> ⁽²⁵⁾

TBARS, thiobarbituric acid-reactive substances; SOD, superoxide dismutase; GSH-Px, glutathione peroxidase; MAP, myeloid antimicrobial peptide; MW, molecular weight.

Antioxidant activity

Oxidative stress has been considered as a hallmark of various chronic diseases and their complications such as diabetes, obesity, CVD and cancer. It is a condition of potentially harmful imbalance between the level of pro-oxidants and antioxidants in favour of the former⁽³⁴⁾. Various extracts of pumpkin have potential antioxidant activity which might play an important role in pre-diabetics, diabetics and individuals with vascular injury. Xia & Wang⁽³¹⁾ demonstrated the hypoglycaemic action of pumpkin (fruit) extract as well as its role as an antioxidant to reveal a mechanism for its cytoprotective (cell-protecting) action in streptozotocin-induced diabetic animals. Pumpkin seeds have a high content of vitamin E (tocopherol; an antioxidant), and pumpkin seed oil has been considered to provide a significant source of vitamin E in Japanese diets⁽³⁵⁾. Dang⁽³⁶⁾ reported that pumpkin extract administration significantly increased the serum and hepatic activities of superoxide dismutase and glutathione peroxidase in mice, and reduced the concentration of malonaldehyde. It has also been found that pumpkin polysaccharide could increase the superoxide dismutase and glutathione peroxidase activity and reduce the malonaldehyde content in tumour-containing mice serum⁽³⁷⁾.

Anti-carcinogenic effect

Cancer is a rapidly growing health problem; it presents the biggest challenge to researchers and medical professionals and has been selected for various prevention and therapeutic

strategies. The dietary intake of many vegetables and fruits has been found to reduce the risk of occurrence of cancer⁽³⁸⁾. Diets high in pumpkin seeds have also been associated with lower risk of gastric, breast, lung and colorectal cancers⁽³⁹⁾. There are also potential health benefits, including anti-carcinogenic effects, to be gained from the various carotenoid pigments found in pumpkin seed oil⁽⁴⁰⁾. The carotenoids from pumpkin fruits have been linked to the prevention of prostate cancer^(40,41). There are still various controversies regarding the use of juices of pumpkin fruits in cancer situations; for example, boiled pumpkin juice significantly suppressed the incidence of aberrant cells while fresh pumpkin juice enhanced it⁽⁴²⁾. It was reported that pumpkin fruit extracts markedly reduced tumour weight in S-180-bearing mice⁽⁴²⁾. Cheong *et al.*⁽⁴³⁾ isolated some basic proteins from pumpkin seeds named MAP2 (MW 2249 Da) and MAP4 (MW 4650 Da), and reported inhibition of the growth of leukemia K-562 cells. Moreover, other proteins from pumpkin seeds were reported to inhibit melanoma proliferation⁽⁴⁴⁾. Xia *et al.*⁽⁴⁵⁾ isolated a novel ribosome-inactivating protein (RIP) called moschatin from the mature seeds of pumpkin (*C. moschata*) and a novel immunotoxin moschatin-Ng76 was prepared successfully which efficiently inhibits the growth of targeted melanoma cells M21 with an IC₅₀ (50% inhibitory concentration) of 0.04 nM, 1500 times lower than that of free moschatin. Recently, Hou *et al.*⁽⁴⁶⁾ isolated a novel type 1 RIP designated cucurmosin 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.

Antimicrobial activity

Diseases caused by bacteria, viruses, fungi and other parasites are major causes of death, disability, and social and economic disruption for millions of individuals. Despite the existence of safe and effective interventions, many individuals lack access to needed preventive and treatment care. Increasing drug resistance in infectious micro-organisms has warranted the development of new drugs against pathogenic micro-organisms. In this regard, natural sources have been considered as the best option to isolate new and novel anti-microbial components. Various broad-spectrum anti-microbial components have been isolated from pumpkins. Pumpkin oil inhibits *Acinetobacter baumannii*, *Aeromonas veronii* biogroup *sobria*, *Candida albicans*, *Enterococcus faecalis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella enterica* subsp. *enterica* serotype *typhimurium*, *Serratia marcescens* and *Staphylococcus aureus* at the concentration of 2.0% (v/v)⁽⁴⁷⁾. A peptide (MW 8 kDa) from pumpkin seeds was proved to inhibit *Botrytis cinerea*, *Fusarium oxysporum* and *Mycosphaerella arachidicola* at a dose of 375 µg and to exert an inhibitory effect on cell-free translation with an IC₅₀ (50% inhibitory concentration) of 1.2 µM⁽²⁵⁾. Purified α-moschin and β-moschin, two proteins with a MW of 12 kDa from fresh brown pumpkin seeds, displayed translation-inhibiting activity with IC₅₀ of 17 µM and 300 nM, respectively⁽²⁴⁾. A significant inhibitory effect of a purified protein (MW 28 kDa) against the fungal growth of *Fusarium oxysporum* was exerted in an agar disc plate at a concentration greater than 2 mM. This protein possessed a synergistic effect with nikkomycin, a chitin synthase inhibitor, for the growth inhibition of *Candida albicans*⁽⁴⁸⁾. Three pumpkin seed basic proteins, MAP2 (MW 2.2 kDa), MAP4 (MW 4.6 kDa) and MAP11 (MW 11.7 kDa), have been shown to inhibit the growth of yeast cells, with MAP11 being the most effective inhibitor. However, MAP2 and MAP4 did not inhibit the growth of the Gram-negative bacterium *E. coli*⁽⁴³⁾. Moreover, it has been reported that phloem exudates from pumpkin fruits possess anti-fungal activities via inhibition of pathogenic fungal proteases⁽⁴⁹⁾. Recently, Park *et al.*⁽⁵⁰⁾ isolated a new protein called Pr-1 from pumpkins which has potential anti-fungal activity, without toxicity for human erythrocytes. It is a thermostable protein that is stable up to 70°C, without showing growth-arresting activity towards *E. coli* or *Staphylococcus aureus*⁽⁵⁰⁾. By considering these facts, it is of great importance that those living in developing countries be encouraged to consume pumpkin, as it protects against organisms that cause infectious diseases in these regions of the world.

Other medicinal effects

Pumpkin-supplemented foods are considered as a good source of anti-inflammatory substances, which can help in many diseases such as arthritis, etc. Fahim *et al.*⁽⁵¹⁾ reported that pumpkin seed oil significantly inhibited adjuvant-induced arthritis in rats, similar to a well-known anti-inflammatory substance called indomethacin. It may well be considered that the supplementation of natural components

with standard drugs might give synergistic, antagonistic and no-change effects (called drug interaction effects) during treatment of diseased conditions. Similarly, Fahim *et al.*⁽⁵¹⁾ tested the drug interaction effects of pumpkin seed oil with indomethacin and they found no effect in the adjuvant-induced arthritis model in rats. Pumpkin seed oil has potential hypotensive activity, as suggested by Zuhair *et al.*⁽⁵²⁾. They also suggested that pumpkin seed oil has a very good drug interaction with hypotensive drugs such as felodipine (Ca antagonist) and captopril (an angiotensin-converting enzyme inhibitor), in regards to enhanced hypotensive potential in hypertensive animal models. Supplementation of pumpkin seed snacks showed a higher level of inhibitor of crystal formation or aggregation which will subsequently reduce the risk of bladder stone disease in the Thailand population⁽⁵³⁾. Pumpkin seeds or orthophosphate supplementation at 60 mg/kg (body weight) per d could reduce the incidence of bladder stones; the longer the supplementation period of pumpkin seeds, the better the results that can be found⁽⁵⁴⁾. It was reported that the oil preparation could remarkably reduce bladder pressure, increase bladder compliance and reduce urethral pressure. Shishigatani pumpkin possessed bio-antimutagenicity from the chloroform and ethyl acetate fractions⁽⁵⁵⁾. Pumpkin may ease depression too, because the seeds contain L-tryptophan, which raises levels of 'happy' serotonin in the brain⁽⁵⁶⁾. The effect of water extracts of pumpkin seeds in the treatment of puppies experimentally infected with heterophyiasis gave promising results, and the combined extracts of areca nut and pumpkin seeds gave a better result than when either extract was given alone⁽⁵⁷⁾. An anti-helminthic effect was reported at the minimum inhibitory concentration of 23 g pumpkin seed in 100 ml distilled water in preclinical studies⁽⁵⁸⁾. The administration of pumpkin seed proteins after CCl₄ intoxication resulted in significantly reduced activity levels of lactate dehydrogenase, alanine transaminase, aspartate transaminase and alkaline phosphatase and hence this protein administration was effective in alleviating the detrimental effects associated with protein malnutrition⁽⁵⁹⁾. Analgesia and anti-inflammation activities were observed with the head of the pumpkin stem⁽⁶⁰⁾. Protein isolate from pumpkin seeds could inhibit trypsin and activated Hageman factor, a serine protease involved in blood coagulation^(61,62). A dietetic formula made of pumpkin, rice, chicken and vegetable oils was found to be beneficial for children with diarrhoea⁽⁶³⁾. Pumpkin has been used for various cosmetic applications such as skin scrubber, body masque, body butter, massage oil, massage lotion and dry facial masque.

Conclusion and future perspectives

Pumpkin is an edible food which can be included in our daily diet that can give various health benefits to improve our overall health. Pumpkin has various effects beneficial to health such as anti-diabetic, anti-carcinogenic, antioxidant and anti-microbial potential. There are other various health-beneficial effects of pumpkin also reported such as inhibition of kidney stone formation, and hypotensive, anti-inflammatory and blood-coagulatory effects. In various studies pumpkin products show synergistic and no-change

effects to treat diseased conditions. Since most of the studies have been done either *in vitro* or in animal models, controlled clinical trials are strongly needed to confirm these health-beneficial effects in human subjects. There are various food products such as snacks, pies, etc available containing pumpkin alone and in combination with other edible supplements such as ginger and various fruits for human consumption. It would be a good idea to follow up the normal consumption effects in human populations of these products in relation to various chronic diseases such as diabetes, cancer and heart diseases. It is very important to analyse various bioactive components from plant and food components; however, very few components have been isolated and characterised from pumpkin. Therefore it might be a good area to explore in this field to isolate, characterise and evaluate various components of pumpkin from different parts, for medicinal functionality.

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