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Pumpkin Seed Oil: An Alternative Medicine

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Abstract

Pumpkin seed oil has long been considered as an ingredient for its nutritional and medicinal values for the prevention of various ailments, especially for prostate diseases. In addition, several studies have suggested the crucial roles and effectiveness of pumpkin seed oil in the treatment of diabetes, anxiety and even cancer. Pumpkin seed oil is being used in several countries worldwide including North America, Mexico, India and China. This review highlights the characterization, properties and use of pumpkin seed oil from various pumpkin species against several diseases pathophysiologies. We strongly believe that this review will provide overall insights to the chemists, biologists and researchers on the roles of pumpkin seed oil extracts that possess promising biological activities.

Keywords

Pumpkin Seed oil; Alternative medicine; Cancer

INTRODUCTION

Pumpkins including *Cucurbita moschata*, *Cucurbita pepo* and *Cucurbita maxima* are gourd squashes which belong to the genus Cucurbita and the family Cucurbitaceae[1,2]. *Cucurbita maxima* (Japanese name: kabocha) is indigenous to the plateaus of central and south America, but is cultivated throughout the World. Pumpkins were primarily used by native Americans for centuries and later adapted by European. Currently, the United States is the largest production center for pumpkins, followed by Mexico, India and China. Pumpkin is an important leaf and seed vegetable tropical vine of high traditional nutritional and medicinal values[3]. Its fruits, flowers, and seeds have been consumed as vegetables, which are rich in vitamins and antioxidants including A, C, and E. The Extracts of the pumpkin ingredients (rind, flesh, seed oil and defatted seeds meal (DSM) possess various biological activities which can be characterized into antimicrobial, antiviral, cytotoxic and antitumor activities[4].

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CONFLICT OF INTEREST

Authors declare no competing conflicts of interest.

Pumpkin seed, its bioactive components and characteristics

The pumpkin seed oil is dark green in color that contains a high amount of free fatty acids including four dominant fatty acids (oleic, linoleic, palmitic and stearic) are present with the relative distribution of 43.8%, 33.1%, 13.4% and 7.8% respectively, representing 98 ± 0.1% of the total fatty acids amount[4]. The oil content of dry pumpkin seeds is 47.03%. However, the variability of the oil contents in various pumpkin species is predominantly attributed to its broad genetic diversity[5]. Importantly, pumpkin seed oil is used as nutritional supplements for natural source of proteins, essential fatty acids, polyunsaturated fatty acids, omega 3, 6 and 9, carotenes, lutein, vitamins such as carotenoids and β- and γ-tocopherols, phytosterols, chlorophyll, and trace elements, such as zinc and selenium[6,7]. In addition, several triterpenes such as cucurbita-5, 24-dienol, α- and β-amyrin and sterols are present in the seeds and flowers of *Cucurbita maxima* [8–10]. Moreover, three new multiflorane-type triterpenes: 7α-methoxymultiflor-8-ene-3α,29-diol 3-acetate-29-benzoate, 7-oxomultiflor-8-ene-3α,29-diol 3-acetate-29-benzoate and, multiflora-7,9(11)-diene-3α,29-diol 3-p-hydroxybenzoate-29-benzoate were isolated from the seeds of *Cucurbita maxima* along with three known compounds, multiflora-7,9(11)-diene-3α,29-diol 3,29-dibenzoate, multiflora- 7,9 (11)-diene-3α-29-diol 3-benzoate and, multiflora-5, 7, 9(11)-triene-3α,29-diol 3,29-dibenzoate[11]. The essential trace mineral zinc in pumpkin seeds acts as an antioxidant which is attributed to its ability to neutralize free radical generation or directly engross the iron or copper binding sites of lipids, proteins, and DNA molecules[12]. Of significance, pumpkin seed extracts have been used as an adjuvant for immunomodulation, reproductive health and therapeutic purposes for wide ranges of disease conditions[13,14]. In addition, omega 3 and 6 essential fatty acids in pumpkin seed oil are important for healthy brain and body functioning as well as preventing and improving bladder and prostate problems[15].

Pumpkin seed oil and its effects in various physiological processes

Several studies have demonstrated that pumpkin seeds and daily rich diet of zinc can decrease the undesirable side effect of lead contaminants and improve the sexual health status[16]. Pumpkin seeds improve sexual stimulation and intromission and ejaculatory latency[17]. On the other hand, pumpkin plant extract caused a significant reduction in sperm count with primary and secondary abnormalities by producing further zinc and protein[18]. Therefore, pumpkin seed oil but not the plant extract has been used in preclinical studies to explore its role in both the prevention and treatment of infertility in male animal models [18]. Along similar lines, studies by Aghaei et al have demonstrated that pumpkin seed extract could recover the side effects of cyclophosphamide (CP) mediated changes in histology of epididymis and sperm parameters through preventing oxidative stress[19]. The sperm characteristics in CP-treated rats were significantly decreased and biochemical analysis revealed that the administration of pumpkin seed extract significantly enhanced the total antioxidant capacity (TAC)[19]. In addition, pumpkin seed extract remarkably improved the histopathological parameters such as vacuolization, disorganization and separation of epididymal epithelium in CP-treated rats. These finding indicate that the pumpkin seed extract could be used to prevent CP-induced reproductive toxicity[19]. Similarly, Mohammadi et al have shown that administration of ginger and pumpkin seed extract simultaneously increased the number of germ cells in seminiferous tubes and had positive effects on

the recovery of spermatogenesis in adult rats after cyclophosphamide (CP) treatment[20–22]. Studies by Bourre et al have further brought the importance of oleic acid, a monounsaturated fatty acid also present in pumpkin in reducing the susceptibility of the testis and epididymis to lipid Peroxidation[23].

Multiple studies have demonstrated that an antioxidative property of pumpkin seed extract could improve the fertility and help in preventing arteriosclerosis, high blood pressure and heart diseases as well as in stimulating the metabolism of accumulated fats[24–25]. Studies by Bharti et al have provided pharmacological evidence of tocopherol fraction of raw seeds of *Cucurbita pepo L.* as possessing an anti-hyperglycemic property mediated via the interactions of its various components with multiple signaling targets that play crucial roles in diabetes mellitus (DM)[26]. In addition, El-Mosallamy et al have demonstrated the effect of pumpkin seed extract on blood pressure induced by nitric oxide synthase inhibitor N(ω)-nitro-L-arginine methyl ester hydrochloride (L-NAME)[27]. In this study, rats treated with 50 mg/kg/day L-NAME with or without calcium channel blocker, amlodipine and pumpkin seed oil and their effects on the pathological alterations in the heart and aorta induced by L-NAME were evaluated[27]. Authors demonstrated that both pumpkin seed oil and amlodipine treatments protected the rats from L-NAME induced defects in the heart and aorta through the mechanism that could involve the generation of NO suggesting that pumpkin seed oil exhibits an antihypertensive and cardioprotective effects[27].

The effects of pumpkin seed oil have also been investigated in influencing the growth of hairs. Interestingly, studies by cho et al have evaluated the effects of pumpkin seed oil on hair growth in men with androgenetic alopecia[28]. After 24 weeks of treatment, self–rated improvement score and self-rated satisfaction scores in the pumpkin seed oil-treated group were higher compared to the placebo group ($p = 0.013, 0.003$)[28]. The pumpkin seed oil-treated group had more hairs after treatment than at baseline, compared to the placebo group ($p< 0.001$). The mean hairs count increased by 40% in pumpkin seed oil-treated men at 24 weeks compared to 10% in placebo-treated men ($p< 0.001$)[28]. In another study, *Cucurbita maxima* (CM) seed oil has been shown to exhibit antiamnesic activity as indicated by a significant reduction in the latency time in the Morris water maze test and decreased social interaction during trial 2 in the social recognition test[29]. Moreover, CM seed oil treatment have been shown to significantly decrease acetylcholinesterase (AChE) activity and malondialdehyde levels and increase glutathione levels in brain regions[29]. As CM seed oil significantly decreased the expression of proinflammatory cytokine, tumor necrosis factor alpha (TNF-α) in the hippocampus, its effects on the behavior and biochemical parameters was comparable with the rats treated with piracetam[29]. These findings indicate that CM seed oil may exert antiamnesic activity via its ability to inhibit AChE and inflammation as well as its antioxidant activity in the brain[29].

An isocaloric switch from a diet rich in saturated fat to a diet rich in unsaturated fat can attenuate non-alcoholic fatty liver disease (NAFLD) and atherosclerosis development. Given that phytochemical-rich virgin pumpkin seed oil exerts additional anti-inflammatory effects resulting in more pronounced health effects, authors investigated the potential long-term health effects of isocaloric substitution of dietary fat (i.e. partial replacement of saturated by unsaturated fats), as well as putative additional effects of phytochemicals present in

unrefined (virgin) oil on the development of NAFLD and associated atherosclerosis[30]. In a study, Morrison et al used pumpkin seed oil because of its high levels in unsaturated fatty acids and a rich source of phytochemicals. To that end, mice were fed with a western-type diet containing cocoa butter (15% w/w) and cholesterol (1% w/w) for 20 weeks to induce risk factors and disease endpoints. In separate groups, cocoa butter was replaced by refined or virgin pumpkin seed oil. These studies demonstrated that both oils improved dyslipidaemia, with decreased VLDL-cholesterol and triglyceride levels compared to western-type diet, and additional cholesterol-lowering effects were associated with virgin over refined pumpkin seed oil[30]. While refined oil did not affect the plasma inflammatory markers, virgin oil reduced the circulating levels of serum amyloid A and soluble vascular adhesion molecule-1 [30]. The development of NAFLD and atherosclerosis was modestly reduced in refined-oil fed mice and virgin-oil strongly decreased liver steatosis, inflammation, atherosclerotic lesion area and disease severity[30].

In a clinical trial, effects of the pumpkin seed oil from Cucurbita pepo (CP oil) were evaluated in over 2000 men suffering from benign prostate hypertrophy (BPH) [31]. Authors demonstrated that an oral administration of 500–1000mg/day of CP oil for 12 weeks decreased the International Prostate Symptom Scores by 41.4% and more than 96% of the patients had no undesired side effects indicating that CP oil significantly improved the urinary dysfunction in patients[31]. Studies by Gossell-Williams et al have demonstrated that CP oil inhibited testosterone-induced hyperplasia of the prostate in rats[6]. In this study, rats treated with 0.3 mg/100 g body weight of testosterone showed an increase in prostate size ratio which was inhibited by the administration of 2.0 or 4.0 mg/100 g body weight of CP oil[6]. Along similar lines, Nishimura et al have evaluated the effect of another pumpkin seed oil extract of *Cucurbita maxima* (CM oil). In these studies, authors demonstrated that CM oil was safe, well tolerated and was effective in preventing urinary disorders such as Overactive bladder (OAB) and benign prostate hypertrophy (BPH). These effects were attributed to the sitosterols content of the CM oil indicating its potential in the prevention or treatment of urinary disorders including OAB[32].

Phytochemicals (phytosterols) have been used as an alternative or integrative therapy for the relief of lower urinary tract symptoms caused due to a prostatic disease. This problem seems to be growing quickly all over the world, including the Republic of Korea[33]. In this regard, studies by Hong et al determined the effects of pumpkin seed oil and saw palmetto oil in Korean men with symptomatic benign prostatic hyperplasia[34]. These studies demonstrated that patients treated with pumpkin seed oil, saw palmetto oil, or a combination of pumpkin seed oil and saw palmetto oil for over 12 months have improved in BPH symptoms compared to the patients on placebo. While the therapeutic efficacy of a combination of these two oils did not improve, no side effects were reported[34]. These studies suggest that pumpkin seed oil and saw palmetto oil are clinically safe and may be effective as complementary and alternative medicines for the treatment of BPH.

Effects of Pumpkin seed oil in Cancer models

Phytoestrogens are plant compounds that show structural and functional similarities to mammalian estrogens and are able to bind to mammalian estrogen receptors[35].

Phytoestrogens may alter risk of breast cancer by their weak inhibitory effect on aromatase[36]. Importantly, low to high consumption of pumpkin seeds and of soybeans and sunflower were associated with significantly reduced risk of breast cancer[37]. A population-based case control study in German postmenopausal women evaluated the correlation between phytoestrogen-rich foods and dietary lignans with breast cancer risk. The data collected on dietary profiles from 2,884 cases and 5,509 controls using a validated food-frequency questionnaire, which included additional questions related to phytoestrogen-rich foods. The results provided evidence for the reduced postmenopausal breast cancer risk associated with increased consumption of sunflower and pumpkin seeds and soybeans[37]. As increased estradiol production was reported in MCF7, BeWo, and Jeg3 cells in a concentration dependent manner, Richter et al delineated the effects of phytoestrogen extracts isolated from pumpkin seeds on estradiol production and ER/PR expression in breast cancer and trophoblast tumor cells[38]. To that end, MCF-7 cells treated with different concentrations of estradiol (10, 50, and 100 μg/ml) revealed the same pattern of ER and PR expression. However, ERα expression was significantly downregulated, ERβ expression remained unaltered, and PR expression was upregulated[38]. The ERα, ER-β, and PR expression levels in Jeg-3 and BeWo cells did not differ significantly by the treatment of pumpkin seed extract as compared with non-treated cells[38]. Nevertheless, detailed preclinical studies are warranted to further explore the potential role of pumpkin seed's lignans in breast cancer prevention and/or treatment.

Plant novel ribosome-inactivating proteins (RIPs) have been shown to have multiple functions, such as antiviral, antifungal and insecticidal properties. Therefore, they may play important roles in plant defense system, and may have great potential in medicinal or agronomic applications, such as anticancer drugs or antiviral transgenic tobacco[39]. A novel RIP designated as Moschatin has been isolated and characterized from the mature seeds of pumpkin (Cucurbita moschata) [40]. Using the anti-human melanoma McAb Ng76, a novel immunotoxin Moschatin-Ng76 was prepared successfully which efficiently inhibited the growth of targeted melanoma cells M21 with an IC_{50} of 0.04 nM concentration that is 1500 times lower dose than that was observed with free Moschatin[40]. These results indicate that Moschatin could be used as a new and potent chemopreventive agent against melanoma[40].

CONCLUSION

To conclude, these reports from several studies indicate that despite all the benefits from several types of pumpkin seed oil extract (*Cucurbita moschata*, *Cucurbita pepo* and *Cucurbita maxima*) in treatment or prevention of various disease pathogenesis or symptoms, further exploratory studies are warranted to investigate the implications of pumpkin seed oil extract for its preventive and/or therapeutic effects.

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ABBREVIATIONS

CM	*Cucurbita maxima* and *Cucurbita moschata*
CP	C*ucurbita pepo*
CP	cyclophosphamide
TAC	total antioxidant capacity
DM	diabetes mellitus
L -NAME	N(ω)-nitro-L-arginine methyl ester hydrochloride
AChE	Acetylcholinesterase (AChE) activity
NAFLD	non-alcoholic fatty liver disease (NAFLD)
OAB	overactive bladder
BPH	benign prostate hypertrophy

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