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A REVIEW ON PUMPKIN SEEDS IN PROMOTING PROSTATE HEALTH

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ABSTRACT

Pumpkin seeds offer some unique health benefits for the prostate especially for men with Benign Prostate Hypertrophy (BPH). The oil in pumpkin seeds can help in preventing the hormones from triggering multiplication of prostate cells. BPH is a condition that commonly affects men after 50 years of age. It involves the enlargement of the prostate gland. Advanced age is a risk factor for an enlarged prostate. One of the factor that contribute to BPH is over stimulation of the prostate cells by testosterone and its conversion product, Dihydro testosterone (DHT). DHT builds up in the prostate and causes it to grow. Studies reveal that pumpkin seeds contain protective compounds called phytosterols that helps in shrinking the prostate. The phytochemicals in the pumpkin seeds reduce the effects of DHT on the prostate. This may also block the conversion of testosterone into DHT. The carotenoids and the omega-3 fats found in the pumpkin seeds are also being studies for their potential benefits on prostate. The fact that pumpkin seeds serve as a good source of zinc may contribute to the role of pumpkin seeds in support of the prostate.

KEYWORDS: Pumpkin, Prostate, Benign Prostate Hypertrophy (BPH), Dihydro Testosterone (DHT), Phytosterols, Testosterone.

INTRODUCTION

The prostate is a gland that only men have. It is about the size of a walnut and located below the neck of the bladder and wraps around the urethra. The prostate makes a milky fluid, which is part of semen. This fluid feeds the sperm. It is normal for the prostate gland to get bigger as men get older. For some men this can cause bladder problems. The changes to the

prostate gland happen over many years. Poor bladder control can also happen due to other health issues.

Benign prostatic hyperplasia (BPH) is considered a public health problem that develops after the age of 40 and has high morbidity and low mortality rate. It ranges in prevalence from over 50% at 60 years of age to as high as 90% by 85 years of age. BPH is a noncancerous enlargement of the prostate gland caused by proliferation of both stromal and epithelial cells. The main underlying mechanism is the change in prostatic androgen metabolism.[1,2] The conversion rate of testosterone to dihydrotestosterone (DHT) by 5α-reductase increases within the prostate, which results in prostatic accumulation of DHT that causes cell proliferation. The voiding dysfunction that appears from prostate gland enlargement and bladder outlet obstruction (BOO) has been genetically termed as the lower urinary tract symptoms (LUTS). The problems associated with BPH are usually progressive and considerably affect the quality of life (QoL). Many herbal medicines have been used for the treatment of numerous chronic and severe diseases.[3] Traditional drugs are relatively safe, easily available and affordable, less toxic with limited side effects compared to synthetic drugs. For such reasons, traditional and complementary medicines have seen an upsurge in their popularity for the treatment of different diseases.[4,5]

The male lower urinary tract symptoms (LUTS) are mostly associated with BPH and they are very common with the ageing population. Male LUTS etiology except BPH involves age-related bladder dysfunction, malignant prostatic diseases, and urethral diseases.[6,7] Clinical manifestations of LUTS include urinary frequency, urgency (storage symptoms), poor flow, hesitancy, straining (voiding symptoms), and incomplete bladder emptying (post-voiding symptoms). BPH is a histological diagnosis and is characterized by an increased number of stromal and epithelial cells within the transition zone of the prostate (represents only 5% of prostatic volume), with further development of BPH within the more proximal periurethral area of the prostate (nodular hyperplasia).[5] The symptoms occur when the enlarged prostate gland compresses the urethra which increases urine flow resistance, and some- times it is associated with the inflammation. This clinical picture is called “prostatism.”

Many herbal medicines have been used for the treatment of numerous chronic and severe diseases. Traditional drugs are relatively safe, easily available and affordable, less toxic with limited side effects compared to synthetic drugs. For such reasons, traditional and complementary medicines have seen an upsurge in their popularity for the treatment of

different diseases. Although phytotherapy is widely used in most countries, only few plants received scientific or medical trust.[8] 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. The **scientific name** for **pumpkins** is Cucurbita pepo, with "pepo" meaning "to ripen in the sun." ***Cucurbita*** is a genus of herbaceous vines in the gourd family, Cucurbitaceae, also known as cucurbits.

Pumpkin (C. pepo L.), a member of Cucur- bitaceae family is an herbaceous, monoecious, annual plant. Most Cucurbita species are creeping or climbing vines that are compact or semi-shrub with five rigid, slightly angular stems. The plant stem produces tendrils to help it climb adjacent plants and structures or extend along the ground. In some species, tendrils are branched or they are simple and little developed. It contains several phyto-constituents belonging to the categories of alkaloids, flavonoids, and palmitic, oleic and linoleic acids. Various important medicinal properties of pumpkin includes anti-diabetic, antioxidant, anti-carcinogenic, anti-inflammatory etc.[9]

The most important part of pumpkin is its low-fat and protein-rich seeds. The second most important part is its fruit. 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. Edible oil is also obtained from the seed of pumpkin which is rich in oleic acid. 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. The fruits are a good source of carotenoids and g-aminobutyric acid. Pumpkin seeds are valued for their high protein content and useful amounts of the essential fatty acid, linoleic acid.[10]

Pumpkin seeds contain remarkably high proportions of essential amino acids. Pumpkin seeds also contain relatively large amount of various essential micro-elements such as K, Cr and Na. 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, non-essential fatty acid and proteins have been isolated. Various hypoglycemic polysaccharides have been characterized from fruit pulps of pumpkin plants. D-chiro-Inositol in pumpkin has been identified as an insulin secretor and sensitizer. Various antibiotic

components including antifungal components have been characterized from various parts of pumpkin plants. Various anti-fungal proteins, such as a- and b-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 characterized.[11]

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. 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. 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. 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.

Pumpkin seeds or orthophosphate supplementation at 60mg/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. 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. Pumpkin may ease depression too, because the seeds contain L-tryptophan, which raises levels of ‘happy’ serotonin in the brain. 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 arecanut and pumpkin seeds gave a better result than when either extract was given alone.[12]

An anti-helminthic effect was reported at the minimum inhibitory concentration of 23g pumpkin seed in 100ml distilled water in preclinical studies. 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. Analgesia and anti-inflammation activities were observed with the head of the pumpkin stem.[24,25]

Protein isolate from pumpkin seeds could inhibit trypsin and activated Hageman factor, a serine protease involved in blood coagulation. A dietetic formula made of pumpkin, rice, chicken and vegetable oils was found to be beneficial for children with diarrhea. Pumpkin has been used for various cosmetic applications such as skin scrubber, body masque, body butter, massage oil, massage lotion and dry facial masque.

Mechanism

Studies reveal that pumpkin seeds contain protective compounds called phytosterols that helps in shrinking the prostate. Beta-Sitosterol is a plant fat found in Pumpkin Seed Oil.[23] Beta-sitosterol is believed to inhibit the enzyme involved in the coversion of testosterone to dihydrotestosterone which can promote excessive prostate growth. Another reason for pumpkin seed oil's remarkable benefits is the high content of unadulterated parent Omega 6 (Linoleic Acid) an essential fatty acid. Omega 6 has been identified to ease symptoms of benign enlargement and decrease prostate cancer risk. Omega 6 affects many functions including production of sexual hormones giving the body a chance to correct any imbalances, correlating to the same effects of beta-sitosterol. Essential fatty acids in the correct ratios (2:1 - 1:1, Omega 6:Omega 3) also produce the body's natural steroids including anti-inflammatories as well as helping to supply oxygen to cells so they do not turn cancerous. Zinc is another nutrient found in the pumpkin seeds that might improve prostate function.[13]

STUDIES

Various clinical studies have been done in determining the benefits of pumpkin seeds on prostate health.

Gossell-Williams et al; examined pumpkin seed oil on testosterone-induced hyperplasia of the prostate of Sprague-Dawley rats. Hyper- plasia was induced by subcutaneous administra-tion of testosterone (0.3 mg/100 g of body weight) for 20 days. Oral administration of either

pumpkin seed oil (2.0 and 4.0 mg/100 g of body weight) or corn oil (vehicle) was given for 20 days. On day 21, they measured prostate weight/rat body weight (prostate size ratio). Researchers observed that testosterone significantly increased prostate size ratio that was reduced in rats fed with pumpkin seed oil at 2.0 mg/100 g of body weight.

Abdel-Rahman investigated the chemical composition of pumpkin seeds and its effect on citral-induced hyperplasia of the prostate in Wistar rats. Fifty adult Wistar male rats were divided into five groups: negative control group that have no BPH and fed on basal diet, positive group rats have BPH and fed on basal diet only, the remaining groups had BPH and were fed on different level of pumpkin seeds. Four weeks later, all rats were sacrificed and results indicated that pumpkin seed can relieve the signs of BPH. Researchers concluded that pumpkin seed in dose- dependent manner can inhibit citral-induced hy- perplasia of the ventral prostate lobe as observed in reducing protein-binding prostate levels, weight of ventral prostate lobe and improve histology of testis.[14]

Tsai et al. reported the effects of pumpkin seed oil alone or combined with Phytosterol-F on testosterone/prazosin-induced (T-P) prostate growth in forty adult Wistar rats. The rats were divided into five groups: a control group (treated with vehicle only), a group treated with T-P, and two groups of T-P-treated rats, one of them received orally pumpkin seed oil alone and other group received orally pumpkin seed oil combined with Phytosterol-F. They concluded that pumpkin seed oil alone or combined with Phytosterol-F can block the T-P-induced increases in prostate size ratio.

Vahlensieck et al. performed a rando- mized, partially blinded, placebo-controlled, para- llel-group trial that investigated the efficacy of pumpkin seeds in 1.431 men with BPH/LUTS.[22] Subjects randomly received the seeds (5 g b.i.d.), capsules with the seeds ethanol extract (500 mg b.i.d.), or matching placebo. The primary response criterion was a decrease in (International Prostate Symptom Score) IPSS of ≥5 points from baseline after 12 months. Secondary outcome measures included QoL, IPSS and nocturia. After 12 months, the response rate did not differ between pumpkin seed extract and placebo. Twelve-month pumpkin seed treatment led to a clinically relevant reduction of IPSS compared to placebo.[16]

Shirvan et al. performed the clinical trial study in 2011-2012. They included 100 patients with BPH who were randomly divided into two equal groups receiving pumpkin seed oil (prostafit) and prazosin (alpha1-blocker). QoL and IPSS questionnaire were filled. Prostae

specific antigen (PSA) level, uro- flowmetry and prostate volume were measured at baseline, 3 and 6 months after the medication. IPSS had significant differences at baseline and 6 months after the treatment in both groups. QoL was also better in both groups. PSA level did not change after the treatment. They concluded that prostafit was an effective and safe treatment in BPH but not as much effective as prazosin.[17]

Coulson et al. evaluated the efficacy and safety of Prostate EZE Max (herbal preparation containing C. pepo L., Epilobium parviflorum, Lycopene, Pygeum africanum and Serenoa re-pens) in medically diagnosed BPH in a short-term phase II randomized double-blind placebo con- trolled clinical trial. The trial included 57 males aged 40-80 years. They received three-month treatment with either herbal preparation (n=32), or a matched placebo capsule (n=25). The out- come was shown as IPSS. There was a significant reduction in IPSS in the active group compared to 8% for the placebo group, during the three-month intervention.

Hong et al. investigated the role of complementary and alternative medicine in the prevention and treatment of BPH. For this pur- pose, a randomized, double-blind, placebo-con- trolled trial was performed over 12 months on 47 BPH patients. Subjects received eithersweet po-tato (Ipomoea batatas) starch (group A, pla- cebo), pumpkin seed oil (group B), saw palmetto (Serenoa repens) oil (group C), or pumpkin seed oil plus saw palmetto oil (group D). IPSS improved in groups B, C and D (after 3 months) and quality of life score was reduced in groups B, C (after 3 months), and D (after 6 months). PSA was re- duced in group D. There was no difference in pro- state volume in the all groups. Therapeutic effici- ency was not improved by a combination of pumpkin seed oil and saw palmetto oil. They sug- gested that administrations of the seed oil and saw palmetto oil are safe and may be effective as complementary medicine treatments for BPH.[18]

Friederich et al. reported a clinical trial in 245 patients suffering from BPH who were taking pumpkin seed extract for 12 weeks (1-2 capsules Prosta Fink Forte per day). Urinary sym-ptoms were recorded by IPSS, and the influence on QoL has been recorded by a QoL questionnaire (LQ Index). The patients' IPSS decreased by 41.4%, and QoL improved by 46. 1% during therapy.

A 2009 study in Korea on the "Effects of pumpkin seed oil and saw palmetto oil in Korean men with symptomatic benign prostatic hyperplasia" has shown pumpkin seed oil to have improvements of "statistical significance" to the maximal urinary flow rate after just 6 months

as opposed to 12 months for saw palmetto. The patients were taking just 320mg (0.32 grams - less than ½ ml) per day of pumpkin seed oil.[20]

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 analyze various bioactive components from plant and food components; however, very few components have been isolated and characterized from pumpkin. Therefore it might be a good area to explore in this field to isolate, characterize and evaluate various components of pumpkin from different parts, for medicinal functionality.

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