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Cactus flower extracts may prove beneficial in benign hyperplasia due to inhibition of 5alpha reductase activity, aromatase activity and lipid peroxidation. Adi Jonas, Gennady Rosen, Daniel Krapt William Bitterman, Ishak Neeman

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Cactus flower extracts may prove beneficial in benign prostatic hyperplasia due to inhibition of 5alpha reductase activity, aromatase activity and lipid peroxidation. Urol Res. 1998;26(4):265-70.

PubMed: **9760000** (<https://pubmed.ncbi.nlm.nih.gov/9760000/>)

DOI: 10.1007/s002400050055
(<https://doi.org/10.1007/s002400050055>)

Abstract:

The cactus flower is deemed to be helpful in benign prostatic hyperplasia (BPH) therapy, although there is no published

information regarding its clinical effect in patients and on the mechanism of its biological activity. The present study evaluated the ability of cactus flower extracts to exert an effect on BPH through possible inhibition of such processes as lipid peroxidation, androgen aromatization and testosterone reduction. Cactus flower extracts indeed inhibited aromatase and 5 α reductase activity in cultured foreskin fibroblasts and also in human placental and prostatic homogenates. The inhibitory activity in both instances was associated with the dichloromethane or ethanol (methanol) extracts, while a marked antioxidative activity was associated with the aqueous extract. The finding that cactus flower extracts interfere concurrently in vitro with aromatase and reductase activity as well as with free radical processes suggests that these substances may prove beneficial in BPH treatment.

Keywords: cactus flowers extracts, 5 α reductase, inhibitor, Aromatase inhibitor, Antioxidants.

Introduction:

Numerous compounds have been tested during the last decade for possible therapeutic and prophylactic effect on benign prostatic hyperplasia (BPH), which is the most common neoplastic disease in the human male. Much efforts has been expended on the formulation of inhibitors prostatic steroids 5 α reductase, aromatase inhibitors, it was reasoned that these could block the conversion of testosterone to the more potent tissue-specific androgen 5 α denydro-testosterone, which is believed to be involved in the etiology of prostatic hyperplasia and prostatic cancer. The prostatic gland is an androgen -sensitive organ and therefor androgen deprivation decreases the size of the prostate. Increasing evidance of involvement of the estrogen in pathogenesis of BPH has led to the initiation of including aromatase inhibition as a medical strategy in clinical trials of BPH. Aromatase inhibitors block the estrogen biosynthetic stemming from the aromatization of androstenedione and testosterone. Phytotherapeutic preparations have been had a long tradition of use in the medical treatment of BPH in Europe and are still commonly used for this purpose. Various plant extracts such as those from *Serenoa repens*, *Sabal* *serrulatae*, *Urtica dioica*, etc. are marketed for the treatment of BPH and are reported to have 5 α reductase inhibitory activity, aromatase inhibitory activity or the ability to modulate the binding of sex hormone-biding globulin to its receptor on membranes. No precise biochemical mode of action has been elucidated for various extracts from plants such as *Pygeum africanum*, *Hypoxis rooperi*, or the rye pollen extracts known as "Cernitin". The purpose of the present

study was to evaluate the 5 α reductase inhibition, aromatase inhibition and antioxidant potential of cactus flower extract known as Opuntia. Opuntia is included in the British Herbal Pharmacopoeia as a medicine with astringent and antihemorrhagic effects, which is indicated for colitis, diarrhea and prostatic hypertrophy.

Discussion:

The cactus flower is deemed helpful in benign prostate hyperplasia therapy (British Herbal Pharmacopoeia, 1983), although there is no published any information regarding its clinical effect on patients or the mechanism of its biological activity. In screening new therapeutic agents for the treatment of BPH we have examined the ability of the cactus flower to ameliorate BPH and this through the inhibition of such processes as lipid peroxidation, androgen aromatization and testosterone reduction. All our experiments with cactus flower extracts were geared to determine the inhibition of aromatase activity in the crude placenta extract and of 5 α reductase activity in crude prostate extract. Ancillary trials were also carried out in cultured human foreskin fibroblasts because the latter were shown to contain a variety of steroid-metabolizing enzymes, including two 5 α reduction isozymes as in human prostate. Moreover, the fibroblasts proved useful for screening aromatase inhibitors. Our results demonstrate that cactus flower extracts contains antioxidants as well as 5 α reductase and aromatase inhibitors. Thus, about 80% of the enzymatic activities of both aromatase and 5 α reductase in crude placenta or prostate extracts were inhibited by our cactus flower extracts, but the properties of subfractions DM3 and DM33 were even greater. Contrariwise, in cultured foreskin fibroblasts only 30% of aromatase activity was inhibited compared with the control. One possible reason for this is the elevated level of androst-4-ene-3,17-dione which transforms to estrogen in the presence of 5 α reductase inhibitor. Androst-4-ene-3,17-dione is the chemical precursor of both testosterone (DHT) and estrogen and inhibition of testosterone transformation to DHT may cause increased androst-4-ene-3,17-dione aromatization. It has already been shown that progesterone, a competitive inhibitor of 5 α reductase, stimulates aromatization of androstenedione without affecting the aromatase complex. Our study demonstrates that in the presence of another 5 α reductase inhibitor namely finasteride, the transformation of androstenedione to estrogen in cultured foreskin fibroblasts is markedly increased. This finding is in agreement with Lin et al, who deduced from their experiments with rat smooth muscle cells that the aromatization pathway of testosterone to estradiol would prevail when DHT formation is inhibited. Accordingly, the relatively weak aromatase inhibitory effect

of cactus flower extract on cultured foreskin fibroblasts, is attributable to the increased aromatization of androst-4-ene-3,17-dione stemming from the concurrent 5 α reductase inhibition. The finding that cactus flower extracts simultaneously interfere in vitro with both aromatase and reductase activities suggests their possible beneficial use in BPH treatment. Indeed, the contributory role of steroid 5 α reductase (and its product DHT) to prostate enlargement has already been confirmed and there is increasing evidence that the inhibition of this enzyme would induce regression of hyperplastic gland. The contribution of estrogen to the pathogenesis of BPH has also been proposed. One such hypothesis conjectures that under the mediation of sex hormone-binding globulin (SHBG), estrogen participates in setting the pace for prostatic growth and function. It is generally assumed that SHBG synthesis is regulated by, and is, in fact, a reflection of the estrogen/androgen ratio. Be that as it may, there is a highly significant fall in plasma testosterone and DHT levels in men over 50 years of age, so that the estrogen/androgen ratio increased. It is not clear as yet whether the in vitro finding on the effect of 5 α reductase inhibitors on androgen aromatization is consistent with the in vivo situation. The reported results regarding the estrogen/androgen ratio in 5 α reductase inhibitor-treated patients have not really resolved this problem, while Volpi et al have reported a bilateral gynecomastia in a 62-year-old man following finasteride treatment, which was probably caused by an increase of the estrogen to androgen ratio. From all the foregoing, however, we feel justified in concluding that the capacity of cactus flower extracts to inhibit aromatase as well as 5 α reductase activity, augurs its usefulness in the treatment of BPH. We further believe that the extremely high effective dose requirement of our cactus extracts and fractions as compared with those of potent synthetic 5 α reductase or aromatase inhibitors, do not reflect the true picture but simply mirror inadequate extraction procedures. We are confident that the further and better fractionation of our cactus extracts will yield a much more highly concentrated product. Another important finding of the present study is the high antioxidant activity of our aqueous plant extract. Numerous previous investigations have shown that lipid peroxides and reactive oxygen species (ROS) (e.g. superoxide radicals, singlet oxygen, hydrogen peroxide, hydroxy radicals) are involved in the regulation of cellular proliferation and in the etiology of a variety of disease, including accelerated aging and prostate cancer. Intracellular ROS are generated spontaneously as a result of oxygen interaction with reducing compounds, or as intermediates of some metabolic reactions. Under normal

conditions, the ROS level in the tissue is controlled by antioxidants and antioxidant enzymes such as glutathion, vitamin C, vitamin E, superoxide dismutase, catalase, glutathion reductase, etc. the augmentation of ROS concentration (oxidative stress) is commonly

associated with increasing age and with several diseases accompanied by tissue inflammation. Recently Ripple et al. demonstrated that the oxidative stress is also increased by androgen treatment in androgen responsive human prostatic carcinoma cells LNCaP. It is proposed that redox alteration may play a key role in a signal transduction pathway important for regulation cell growth. Antioxidants are believed to reduce the risk of prostate cancer. Publications generated sizable evidence that plant antioxidants play an important role in biological systems as agents of antioxidative defense. Hence the ameliorative effect of cactus flower extracts on prostate hyperplasia is likely to be attributable to numerous, as yet unidentified compounds, which inhibits the prostatic 5alpha reductase and aromatase activity and may possible also regulate free radical processes. The full significance of cactus flower extracts in the treatment of BPH is now being evaluated by us in clinical trials.

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The article on Healthline.com reviews the benefits and the main uses of the Sabra cactus flower also known as Nopal, Prickly pear, Opuntia Ficus Indica.

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Dan Palevitch , Gideon Earon & Israel Levin (1993) Treatment of Benign Prostatic Hypertrophy with *Opuntia ficus-indica* (L.) Miller, Journal of Herbs, Spices & Medicinal Plants, 2:1, 45-49, DOI: 10.1300/J044v02n01_06 Goto article summary page>> Abstract: The cactus flower

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