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THE EFFECTS OF *PISTACIA ATLANTICA* ON TESTOSTERONE-INDUCED BENIGN PROSTATIC HYPERPLASIA IN RATS

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ABSTRACT

Benign prostatic hyperplasia (BPH) is a chronic urological disorder. The aim of this study was evaluation the effects of of Pistacia Atlantica on testosterone- induced benign prostatic hyperplasia in wistar male rats. **Materials and Methods:** Hydroalcoholic extract of Pistacia Atlantica was prepared by maceration method. Forty rats were prepared and divided into four groups with 10 animals in each group. BPH induces through daily subcutaneous injection of 3mgkg^{-1} testosterone enantat (TE) dissolved in corn oil, for 35 days. Pistacia atlantica extract was administered daily by oral gavage at doses of 250 and 500 mg / kg along with the TE injection for 35 days. The negative control received daily 1ml / kg of corn oil via subcutaneous injection and 1ml / kg normal saline by oral gavage. At the end of the experiment blood was collected by heart puncture under light chloroform anesthesia and finally all rats were sacrificed and prostate gland was removed. serum was collected immediately by centrifuge for of testosterone, PSA(prostate specific antigen) and blood urea concentration. The data are expressed as mean ±SD. and analyzed by one-way ANOVA. **Results:** Daily administration of 250 and 500mg /kg of pistacia atlantica extract led to marked decreases in the serum PSA and the serum testosterone levels in the treated groups compared to positive group .Insignificant decrease was reported in the blood urea concentrationin the treated groups compared to positive group. **Conclusion**:Pistacia atlantica extract effectively inhibits the development of BPH induced by testosterone in a rat model.

KEYWORDS: benign prostatic hyperplasia, testosterone, prostate, pistacia atlantica.

INTRODUCTION

Benign prostatic hyperplasia is a histological disease characterized by an increased number of epithelial cells and stromal cells within prostate. [1] BPH has high prevalence that 40% of men 50-60 years of age and 90% of men 80-90 years of age have been diagnosed with BPH. [2] Androgens and aging have been involved in the progression of BPH, but the cellular and molecular mechanisms underlying the pathogenesis of BPH are still not fully known. [3]

Several factors including hormons, dietary factors, inflammatory mediators, and oxidative stress have been more important for the BPH development. [4] Clinical studies suggest that inflammation may be a central mechanism in prostate enlargement and BPH development. [5] Some evidence suggested that oxidative stress may be involved in the pathogenesis of BPH. [6] BPH symptoms include frequency, urgency, nocturia, sense of incomplete bladder emptying, decreased force of steam and interruption of steam. [7,8] Recently, 5 alpha reductase inhibitors and alpha blockers are available for treating BPH. These drugs createthe unfavorable effects such as damage of muscle growth and myopathy, dizziness, loss of libido and erectile dysfunction. The use of herbal compound for treating BPH refer to ancient times. The major factor that has led to the popularity of herbal treatments that these agents have fewer side effects and less toxic and also, because they are available and cheap. The mechanism of action of plant compounds mainly include anti-inflammatory, hormonal and change of growth factor pathways. [8,9] *Pistacia atlantica* is a pistachio species of the *Anacardiaceae* family, including eleven species. There are three species in Iran. These species include *pistacia vera*, *pistacia atlantica* and *pistacia khinguk*. The *pistacia atlantica* is considered as a stimulant due to diuretic properties and hypertention, coughs, sore throats, eczema used to treat, stomachaches, kidney stones and jaundice . [10-12] Due to the strong anti-inflammatory properties of this plant and the role of inflammation processes in the pathogenesis of benign prostatic hyperplasia, this study was managed to evaluate of the effects of *Pistacia Atlantica* on testosterone- induced benign prostatic hyperplasia.

MATERIALS AND METHODS

2.1. Plant Material and Preparation of the *Pistacia Atlantica* Extract

The *pistacia atlantica* fruits were collected from the mountains Kohgiloyeh &Boyerahmad. Their shells have been separated. They soak in hydroalcoholic solvent which prepare with ethanol (70%v/v) for 24 hours. Then the outcome extracts was filtered with whatman filter paper No.1 and the filtrate was concentrated by rotary evaporator system. The250 and 500mg /kg of the *pistacia atlantica* extract have been used. [13]

2.2. Animals

Male wistar rats weighting 180-220 gram were purchased from Shiraz, Iran. They were housed in polypropylene cages and were fed on standard pellet diet.The animals were allowed to adaptation to the laboratory condition for 7 days before the experiment. [14]

2.3. Animal Grouping and Treatment

Rats were divided into four groups with 10 animals in each group. Prostatic hyperplasia was induced by subcutaneous injection of 3mgkg^{-1} testosterone enantat for 35 days in all the groups except the negative control group. The negative control received daily 1mgkg^{-1} of corn oil by subcutaneous injection and 1mgkg^{-1} normal salin by oral gavage. The positive control received daily 3mgkg^{-1} testosterone enantat via subcutaneous injection .The treatment groups received the *Pistacia atlantica* extract at 250 and 500 mgkg^{-1} body weight by gavage for 35 days. All the animals were sacrificed after 35 days. Blood was collected by heart puncture under light chloroform anesthesia and serum was collected immediately by centrifuge.

2.4. Measurement of Serum Testosterone Concentration

Testosterone levels of animals of each group were measured using kayman chemicals ACE^{TM} EIA kits.

2.5. Measurement of Serum PSA Concentration

Prostate specific antigen levels were measured to find the extent of hyperplasia induced in the prostate using PSA ELISA kit. [15]

2.6. Measurement of Blood Urea Levels

Blood urea levels were measured using the colorimetric method.

Statistical Analysis

The data are expressed as mean ± SD . The difference among means has been analyzed by One-way ANOVA. A value of $P < 0.05$ was considered as statistically significant

RESULTS

3.1. Effect of *Pistacia Atlantica* Extract on Testosterone Levels in the Serum

Figure 1 showed the summary of serum testosterone levels. In the animals with prostatic hyperplasia, testosterone levels were elevated. Daily administration of 250 and 500mg /kg of *pistacia atlantica* extract were led to decreasing in the testosterone serum levels.

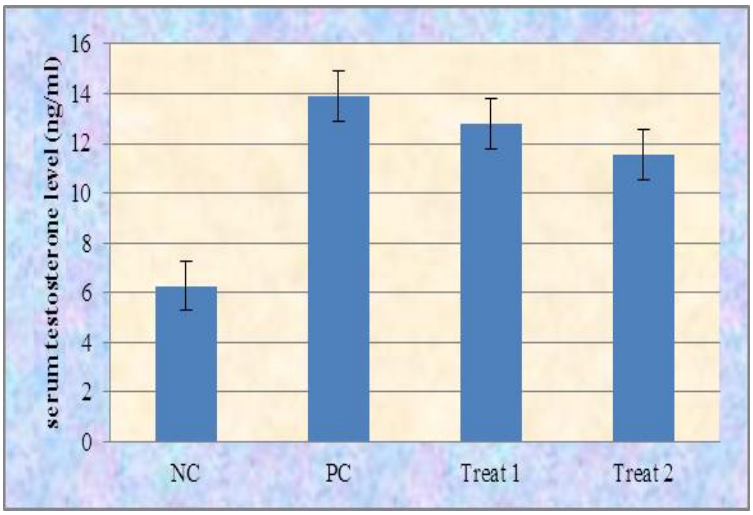

Fig-1.Mean serum testosterone levels of various groups in hormonal induction of benign prostatic hyperplasia in rats.

NC=negative control, PC = Positive control, treat = treatment

3.2. Effect of *pistacia atlantica* extract on PSA levels in the serum

Figure 2 showed the serum PSA levels in the treated and controlled groups. Subcutaneous injection of 3mgkg^{-1}testosterone was caused elevation of PSA levels in the positive control group. In the animal groups which treated with 250 and 500mgkg^{-1}*pistacia atlantica* extract were occurred decrease in serum PSA level compared to the positive control. The serum PSA levels in the treated groups with 500and 250mgkg^{-1} extract were incresed compared to the negative control.

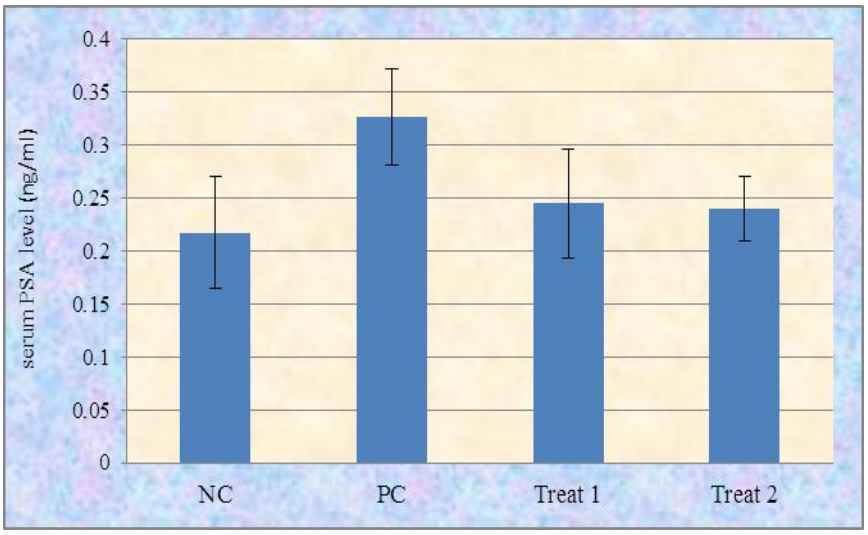

Fig- 2.Mean serum prostate specific antigen (PSA) levels of various groupsin hormonal induction of benign prostatic hyperplasia in rats.

NC=negative control, PC = Positive control, treat = treatment

3.3. Effect of *pistacia atlantica* extract on blood urea levels in the serum

Figure 3 showed the summary of blood urea levels in the groups. Daily administration of 500mgkg^{-1} and 250mgkg^{-1}*pistacia atlantica* extract for 35 days induced a decrease in the blood urea levels compared to the positive control.

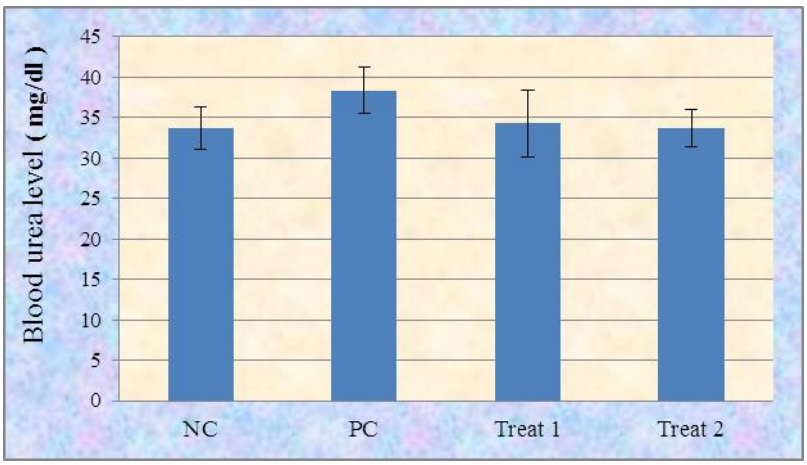

Fig- 3.Mean blood urea levels of various groupsin hormonal induction of benign prostatic hyperplasia in rats.

NC=negative control, PC = Positive control, treat = treatment

DISSCUTION

The benign prostatic hyperplasia etiology in humans depends to several factors. There are some limitations on BPH induction in the animal models. However, the effects of

testosterone on prostate growth documented and has been used to assess the effects of many treatments. [14] Prostate specific antigen is a protein produced by prostate cells. Serum PSA levels increase abnormally in patients with benign prostatic hyperplasia and prostatitis. Therefore reduaction of the serum PSA level can show protective effectson benign prostatic hyperplasia. In this study the serum PSA levels in treated with *pistacia atlantica* extract groups decreased compared to treated with testosterone group. Subcutaneous injection of testosterone led to increasing of serum testosterone levels in the treated with testosterone group. While the serum testosterone levels in the treated with *pistacia atlantica* extract groups showed significant decrease compared to treated with positive group. The blood urea levels is a biochemical parameter that increases in renal disorders. Benign prostatic hyperplasia clinically includes lower urinary tract symptom and prostate enlargement.BPH symptoms range from minimal bother to urinary retention and renal failure. [15] The results of this study show that the blood urea levels in the treated with *pistacia atlantica* extract decrease compared to treated with testosterone group.

CONCLUSION

The data presented here show that in rats, that *pistacia atlantica* extract has the recovery effect in rats with BPH.

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