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Extended Abstract
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Pharma Sci - Beneficial effect of a multifunctional polyphytocompound in experimental prostatic hyperplasia in rats- Francesco Marotta- ReGenera Research Group for Aging Intervention and San Babila Clinic

Francesco Marotta
ReGenera Research Group for Aging Intervention and San Babila Clinic, Italy

Abstract

Introduction: Benign Prostatic Hyperplasia (BPH) is a slowly progressing process of micro and macro nodular appearance characterized by hyperplastic epithelial modifications together with stromal growth. This process has a multifactorial etiology and represents the commonest cause of Lower Urinary Tract Symptoms (LUTS) in the aging male. It has been reported that about 90% of men between 45 and 80 years old complain of some degree of LUTS (3 mcWary). More precisely, it seems that by the age of 50 50% of men may show the symptoms related with BPH and in those aged above 70 years this condition is the most significant cause of bladder outflow obstruction. From the histological viewpoint, the process which starts from the transitional or periurethral zone determines hyperplasia of glandular and stromal tissue with papillary buds and increased smooth muscle, lymphocytes and ducts. The consequent prostate enlargement will bring about urethral constriction with following weak urinary stream, incomplete bladder emptying, nocturia, dysuria up to overt bladder outlet obstruction. Thus, BPH-related LUTS can have a significant impact on quality of life and should not be underestimated. Hormones Effect the development and progression of BPH since the development and growth of the prostate gland very closely depends on androgen receptor stimulation. Indeed, especially during aging process, prostate is mainly influence by Dihydrotestosterone (DHT), i.e., an active metabolite generated by the enzymatic conversion of testosterone by steroid 5α-reductase although other metabolites may play a role in health and disease. Long before surgery may be required, well-known pharmacotherapeutic options are currently employed such as 5-alpha-reductase inhibitors, alpha-adrenergic antagonists, anticholinergic agents and combination therapy. Although these treatments have enabled consistent benefits, their use is associated to a different degree of side ejects such as decreased libido, erectile dysfunction gynecomastia and poor ejaculatory function. This limitation holds particularly relevant when very early cases of BPH are faced or when a tentative "preventive" strategy is planned. Till recently, there is a constant flow of experimental articles, reviews and clinical studies highlighting the role of phytocompounds in their conditions, given also its multi-faced pathophysiological mechanisms. The aim of the current study is to assess of a poly-phytocompound in a model of experimental BPH.

Method: Animals: Adult 8 weeks male Wistar rats (240-290 g) were used throughout the experiments and were housed individually in standard polypropylene cages (three rats/cage) under controlled standard conditions of light (12/24 hours) and temperature (26±1 °C). Food pellets and tap water were provided ad libitum. For experimental purposes animals were fasted overnight but were allowed free access to water. Body weight was measured weekly in all rats. All animal procedures were performed according to approved protocols and in accordance with the Guiding Principles for the Care and Use of Animals, based on the Declaration of Helsinki.

This work is partly presented at World Congress on Advances in Pharmaceutical Sciences

Induction of BPH and treatments: Rats were hosted for 10 days to allow acclimatization and four days prior experiment they were subjected to complete orchiectomy with spermatic cord and blood vessels ligation under anesthesia (i.p., injection of 100 mg/kg body weight of sodium pentobarbital). Aier castration, experimental BPH was reproduced by subcutaneous injection of testosterone (20 mg/kg) for 4 weeks at the same time, rats, under a computerized randomization procedure ensuring a comparable body weight distribution were divided in three groups (15 rats each): (1) Untreated BPH model; (2) BPH plus 100 mg/kg of TR10/ P3795, a poli-phytocompound of potential prostate protective effect (100 mg containing: Serenoa repens extract 56.5%, red clover 26%, pumpkin seed extract 13% and pomegranate extract 4.5%, Andronam, Named, Lesmo, Italy) orally and (3) BPH plus finasteride (0.5 mg/kg body weight) administered orally as positive control group. A third group (4) of sham-operated rats served as control. All compounds were administered to the animals in the morning. Care was taken as to put all the TR10/P3795 or finasteride supplementation in the morning food supply while checking that all was eaten up. Finasteride was stored in an air-tight, dark container at room temperature. The finasteride dosing was prepared in powder at the required concentrations and stored at 4 °C.

Urinary output, blood and prostatic tissue samples: On the day before sacrifice (27^{th} day), all groups were transferred into metabolic cages to measure 3 hours urinary outputs. On the next day (4 weeks study), all animals were fasted overnight. Blood samples were collected in EDTA and centrifuged at 3000×g for 10 minute; serum was instantly separated and stored at −20 °C. Aier animals were sacrificed, prostate were weighed and stored in 10% bufferedformaldehyde solution. 5 µm thick sections were cut and stained by haematoxylin and eosin for light microscopic examination. Separate aliquots of ventral prostatic tissue were snap frozen at −70 °C until further analysis.

Results: Weight and prostate parameters body weight physiologically increased in sham-operated group and this was comparable to both untreated BPH model and both treatments groups without any significant difference although the Finasteride-group showed to have a trend towards lower weight (data not shown, $p>0.05$). As compared to sham-operated control, prostate weight, weight ratio and volume significantly increased in untreated BPH model ($p<0.05$). Both TR10/P3795- and finasteride-treated groups showed a significant and comparable reduction.

Discussion: Natural compounds maintain a growing popularity in the treatment of Benign Prostatic Hyperplasia (BPH) and related Lower Urinary Tract Symptoms (LUTS) mainly due their overall general acceptance and reported lack of substantial side effects. While the hormonal factor does represent a relevant pathophysiological variable of BPH occurrence and related drugs have been synthesized accordingly, several mechanisms have been advocated for its development. These include, among others, tissue and intracellular redox unbalance. Indeed it is well known that human prostate tissue has a peculiar vulnerability to oxidative DNA damage due to more rapid cell turnover and also to the low activity of superoxide dismutase and catalase and increased endogenous levels of DNA base products, these two variables having being reported as to be inversely correlated in in BPH samples has received further recent confirmations.

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Biography

ReGenera Research Group for Aging Intervention and San Babila Clinic, Italy

fmarchimede@libero.it