



# Investigation of antioxidant and anti-inflammatory properties of burdock thick extracts on the model of benign prostatic hyperplasia (BPHP) in rats

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## ABSTRACT

**Aim:** Benign prostatic hyperplasia (BPHP) is one of the most common diseases in men middle-aged and elderly. In this regard, search and study of new effective and safe medicines with prostatoprotective effect is important and actual. **Methods:** BPHP model reproduced the intraperitoneal administration of sulpiride male rats, 40 mg / kg for 30 days. Thick Burdock extracts at a dose of 75 mg / kg and reference drug prostaplan forte, 35 mg / kg were administered intraperitoneally in a medical mode 31 to day 52 of the study. **Results:** The administration of thick extract of burdock roots contributed to the reliable normalization of acid phosphatase activity in serum of animals, as it is evidenced by the absence of significant differences of indicator of the treated animals from the same indicator in the groups of animals with intact control. The administration of thick extract of burdock roots contributed to a significant inhibition of LPO processes, normalization of reduced glutathione and diene conjugates in the serum levels of thiobarbituric acid active products and reduced glutathione – in the homogenate of the prostate. The effect of the indicators mentioned above thick extract of burdock roots was not significantly inferior to the effect of the drug compared with Prostaplan Forte. Thick extract of burdock leaves inferior to thick extract of burdock roots and the reference drug by normalizing influence on the activity of acid phosphatase, the level of reduced glutathione and diene conjugates in blood serum of the experimental animals. **Conclusions:** The one of the most important components of the mechanism of the prostate protective action of burdock thick extracts in benign hyperplasia of the prostate gland are their anti-inflammatory and antioxidant action which are not inferior to the reference drug Prostaplan Forte.

**KEY WORDS:** Thick burdock extracts; Benign prostatic hyperplasia; Prostatoprotective action.

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Received: April 05, 2016

Accepted: June 01, 2016

Published: ?

## INTRODUCTION

Benign prostatic hyperplasia (BPHP) is one of the most common diseases in men middle-aged and elderly. According to the scientific literature, signs of BPHP are found in 40% of men in the age of 50 years and more than 90% of men over 80 years, and the level of the disease is growing. [1, 2]. In this regard, the search and study of new effective and safe drugs for the BPHP treatment is important and actual.

In recent years there has been a growing interest in drugs of plant origin. Phytotherapeutic drugs have apparent pharmacological activity and the higher level of safety compared to synthetic drugs [3]. Low toxicity allows to use herbal drugs for a long period of time without the risk of serious complications taking into account the age of the patients with BPHP and related diseases. In addition, the herbal drugs are rich in pharmacodynamics that allow simultaneously affect the several pathogenetic links of the disease [2, 3]. The herbal drugs are included in the national and international treatment standards for the BPHP. Nowadays, the nomenclature of domestic prostatoprotective drugs with plant origin is limited.

One of the medicinal plants with potential prostate protective properties is burdock (*Arctium lappa* L.). The analysis of phytochemical composition of the given medicinal raw materials indicates the presence of  $\beta$ -phytosterol,

lignans, inulin, flavonoids [4, 5]. It is also proved that the medicines of burdock have anti-inflammatory, antioxidant and cytotoxic action which are the part of prostatoprotective activity. Based on the foregoing, the aim of this work was to study the effect of thick extracts of burdock roots (TEBR) and leaves, (TEBL) obtained at the Botany Department in the National University of Pharmacy, on the severity of inflammatory processes and antioxidant-prooxidant balance on the model of sulpiride-induced BPHP in rats.

## MATERIALS AND METHODS

The research was executed on 30 adult white male rats weighing 280-320 g that are grown up into nursery vivarium of the central research laboratory NUPh, certified by the State expert center the Ukrainian Ministry of Health (the certificate N 21 from 30.04.2009). "The general ethical principles of animal experiments" (Ukraine, 2001) coordinated with provisions "The European convention on protection of the vertebrate animals used for experimental and other scientific purposes" (Strasbourg, 1986) and the resolution of the First national bioethics congress (Kiev, 2007) were held during the work with animals. The painful procedures were carried out under anesthetic (Thiopental sodium in a dose 80 mg/kg).

Ethics standards confirmed by the Bioethics Commission of the National University of Pharmacy (the protocol N3

from 20.03.2013).

The model of BPHP was reproduced using intraabdominal injection of sulpiride to rats (Eglonil, “Sanofi-Aventis”, France) at a dose of 40 mg/kg for 30 days [6]. TEBL and TEBR at a dose of 75 mg/kg, which was identified in previous screening researches and reference drug - Prostaplant Forte (“Schwabe”, Switz) at a dose of 35 mg/kg [6] was administered intraperitoneally in the treatment regime from 31 to 52 days of the research. On the 53-d day the euthanasia of animals using lethal dose of thiopental anesthesia was performed. Blood and the prostate gland (PG) were taken on the analysis.

Experimental animals were divided into 5 groups (6 rats into each group):

- The 1st group – intact control (healthy animals),
- The 2nd group – control pathology (untreated animals that were being injected intraabdominal sulpiride (Eglonil, “Sanofi-Aventis”, France) of the dose 40 mg/kg in 30 days period),
- The 3rd group – rats that were being injected intraabdominal sulpiride of the dose 40 mg/kg in 30 days period and from the 31st till 52nd day of research (in the therapeutic regime) were being injected intraabdominal thick extract of burdock roots (TEBR) of the dose 75 mg/kg (this dose has been defined in the previous screening researches),
- The 4th group - animals that were being injected intraabdominal sulpiride of the dose 40 mg/kg in 30 days period and from the 31st till 52nd day of research (in the therapeutic regime) were being injected intraabdominal thick extract of burdock leaves (TEBL) of the dose 75 mg/kg (this dose has been defined in the previous screening researches),
- The 5th group - rats that were being injected intraabdominal sulpiride of the dose 40 mg/kg in 30 days period and from the 31st till 52nd day of research (in the therapeutic regime) were being injected intraabdominal referens-drug Prostaplant forte (“Schwabe”, Switzerland) of the dose 35 mg/kg.

The content of TBA-active products (TBA-AP), reduced glutathione (RG), diene conjugates (DC), activity of acid phosphatase (Aph) were determined in serum of blood and in the homogenate of PG. The activity of Aph was determined by A. Bodansky, the content of TBA-AP -

spectrophotometrically by reaction with 2-thiobarbituric acid by the method of I. D. Stalnoy, T.G. Garishvili using biochemical on-boar “Reagent” of domestic production, the level of DC –by the method Platzter Z, etc., the level of RG - by the method of Beutler E. D., ets. [7, 8].

Working with experimental animals we adhered to the “Common ethical principles of animal experiments”, agreed with the provisions of the “European Convention for the protection of vertebrate animals used for experimental and other scientific purposes” (Strasbourg, 1986) and the resolution of the First national Congress on bioethics (Kyiv, 2001).

Taking into account the results in the form of average±standard error, the statistical significance of Bonferroni correction of intergroup differences was calculated by student’s t test.

## RESULTS

In the blood serum of experimental animals in the control group of the pathology, it is noted the significant 1,2 times increase in Aph activity compared with to the same index of intact animals. Wherein, the activity of Aph in homogenate of PG is not changed, with suggests the acinus of the prostate membranes permeability. The leves of TBA-AP and DC in the blood serum of rats of the control pathology group increases in 1.4 and 5.9 times, while the level of RG decreases in 1.9 times (table. 1). The level of TBA-AP in the homogenate of PG is increased in 2,2 times, and the RG content significantly decreases in 1,6 times (table. 2).

Administration of TEBR contributed to a significant decrease in the blood level of animals Aph in 1.2 times, the DC – in 4,4 times, to increase the level of RG – in 1.7 times compared with the corresponding figures in the group of control pathology. On the background of TEBL, the Aph content in the blood of rats is not significantly changed, however, there is a decline in the levels of TBA-AP – in 1.2 times, the DC – in 3.8 times. The level of RG in the blood of experimental animals has increased in 1,9 times. Prostaplant contributed to accurate resultant decrease in the blood levels of Aph, TBA-AP and DC in 1.1, 1.2 and 5.3 times respectively, and the increase in the content of RG in 1.8 times in comparison with the indicators of the control group of pathology (table. 1).

**Table 1.** The effect of burdock thick extracts on the activity of acid phosphatase and indicators of the antioxidant/prooxidant balance in blood serum

Grups of animals, n=6	Aph, n-Mol/s*l	TBA-AP, k-Mol/l	RG, mg%	DC, k-Mol/l
Intact control	191,00±2,00	0,32±0,02	28,80±0,73	0,037±0,004
Control phathology	229,00±8,00*	0,44±0,02*	15,32±0,40*	0,218±0,002*
TEBR	195,00±3,00**	0,42±0,02*	25,43±1,39**	0,049±0,006**
TEBL	220,00±3,00*#&	0,38±0,01*/**	29,54±1,13**#	0,058±0,006*/**
Prostatoplant forte	202,00±2,00***	0,37±0,02**	27,53±0,48**	0,041±0,004**

Note: Statistically significant differences (p < 0.05): \* - with the group of intact control, \*\* - pathology control group; # - with a group TEBR, & - with a group of Prostaplant Forte.

**Table 2.** The effect of burdock thick extracts of on the activity of acid phosphatase and indicators of antioxidant/prooxidant balance in the homogenate of the prostate

Grups of animals, n=6	Aph, n-Mol/s*g	TBA-AP, k-Mol/g	RG, mg%	DC, k-Mol/g
Intact control	599,00±3,81	30,98±2,28	22,06±1,24	0,97±0,62
Control pathology	601,00±15,11	68,59±1,65*	13,68±0,84*	2,54±0,52
TEBR	587,00±7,63	35,90±3,66**	20,79±1,26**	0,96±0,58
TEBL	629,00±4,71*#&	35,26±1,84**	21,88±1,29**	1,00±0,58
Prostatoplant forte	530,00±7,99*/**	32,05±2,71**	23,34±0,73**	0,94±0,59

Note: Statistically significant differences ( $p < 0.05$ ): \* - with the group of intact control, \*\* - pathology control group; # - with a group TEBR, & - with a group of Prostatplant Forte.

Amid of TEBR and TEBL in homogenate of rats PG the content of TBA-AP significantly decreases in 1.9 times, and the RG increased in 1.5 and 1.6 times respectively. The use of Prostatoplant Forte contributed to a significant decrease in the homogenate of PG of Aph and the level of TBA-AP in 1.1 and 2.1 times, respectively. The RG content in the homogenate of prostate increases in 1,7 times (tab. 2).

## DISCUSSION

Sulpiride-induced BPHP is one of the most modern and informative experimental models of BPHP. The mechanism of sulpiride action is associated with blockade of dopamine receptors. The long-term administration of a DOPA-receptors blocker to rats promotes the increase level of prolactin and inhibit the release of gonadotropin hormones. Prolactin is androgen-independent, inhibit apoptosis of prostatic epithelium and contributes to the development of hyperplasia of the prostate gland. The increased level of prolactin also activates the conversion of testosterone to estradiol which also contributes to the activation of proliferative processes in the cells of the PG [6, 9, 10].

A significant increase in activity of Aph in the serum of control pathology group animals showed violation of the functional activity of the PG and indicated the development of the inflammatory process. It is also known that one of the cell damage mechanism is free radical oxidation. An excess of peroxidation products breaks physico-chemical structure of the cell membrane, inhibits their enzyme system inactivates cytoplasmic enzymes, cleaves ATP and amino acids, depolarize DNA strands, and reduces the activity of thiol enzymes which leads to the development of alternative and exudative processes in the body [3, 11]. The results of the research have shown that the development of the pathological process in the prostate gland, which were accompanied by the activation of peroxidation processes and the imbalance of antioxidant and prooxidant systems.

The administration of TEBR contributed to the reliable normalization of Aph activity in serum of animals, as it is evidenced by the absence of significant differences of indicator of the treated animals from the same indicator in the groups of animals with intact control. The use of TEBL hasn't caused significant changes of Aph activity in the rats blood serum in comparison with a similar index of

control pathology group ( $220,00 \pm 3,00$  and  $229,00 \pm 8,00$  in accordance). Thus, TEBR as opposite to TEBL has shown anti-inflammatory action. Both of administrative burdock extracts contributed to significant braking processes of POL, namely, normalization of RG and DC indexes in the serum of blood, levels of TBA-AP and RG – in a gomogenate of prostatic gland (tab. 1, 2).

Under the influence of TEBR the maintenance of RG has significantly increased in the serum of blood in 1,7 times in comparison to the index of control pathology group, the maintenance of DC – has significantly decreased in 4,4 times. On the TBA-AP level in the experimental animals blood serum TEBR hasn't shown significant action (indexes in TEBR group and control pathology group were not differ).

The influation on the above-stated indexes of TEBR was not significantly differ from the comparison drug - Prostatplant forte. TEBL and the Prostatplant forte, as opposite to TEBR significantly reduced the maintenance of TBA-AP in the experimental animals blood serum on average in 1,2 times. TEBL surpassed the referense-drug in the normalizing influence on the recreation of DC level and surpassed TEBR – on the maintenance of RG. All studied drugs significantly normalized the maintenance of TBA-AP and RG in the gomogenate of prostate gland experimental animals, significant distinctions were not recorded according to this group indexes.

## CONCLUSION

Analyzing the results, it can be argued that thick extracts of burdock roots and leaves of burdock on the model of sulpiride-induced benign hyperplasia of prostate in rats reduced the development of inflammatory processes, decreased the activity of peroxidation processes and normalized the antioxidant / prooxidant balance in the organism of the experimental animals. It is possible to assume that important components in the mechanism of prostateprotective activity of burdock thick extracts at the being prostatic hyperplasia are their anti-inflammatory and antioxidant properties.

According to results of the conducted researches, thick extract of burdock roots surpasses thick extract of burdock leaves in expressiveness of anti-inflammatory action that

1 decrease activity of acid phosphatase in the experimental  
2 animals blood serum testifies to. At the same time activity  
3 of this enzyme in the homogenate of prostate gland hasn't  
4 changed, permeability of atsinus membranes of a prostate  
5 hasn't changed yet.

6 On expressiveness of antioxidant action thick extract of  
7 burdock roots yields to thick extract of burdock leaves  
8 (influence on TBA-active products and the reduced  
9 glutathione in the serum of blood ). On expressiveness of  
10 anti-inflammatory and antioxidant action thick extracts  
11 of burdock roots and leaves don't yield to a referens-drug  
12 Prostaplant forte.

13 Anti-inflammatory and antioxidant activity of the studied  
14 extracts can be explained by the fact that lignans, which are  
15 their constituents, namely arctigenin, dimethylhexylamine,  
16 dibenzylideneacetone, as well as polysaccharides, flavonoids,  
17 coumarins, derivatives of carboxylic acids are antioxidants  
18 with anti-inflammatory properties [4, 5, 11, 12].

19 To sum up, the conducted researches prove prospects of  
20 further preclinical studying of pharmacological properties of  
21 the thick extracts of burdock roots and leaves for the purpose  
22 of optimization of BPHP pharmacotherapy.  
23

#### 24 LIST OF ABBREVIATIONS

25 BPHP - benign prostatic hyperplasia; TEBL - thick extract  
26 of burdock leaves; TEBR - thick extract of burdock roots;  
27 APh - acid phosphatase; TBA-AP - thiobarbituric acid active  
28 products; DC - diene conjugates; RG - reduced glutathione.  
29

#### 30 CONFLICT OF INTEREST STATEMENT

31 The authors declare that they have no conflict of interest.  
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Source of Support: Nil, Conflict of Interest: None declared