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ANTIOXIDANT EFFECT OF THICK EXTRACT FROM SHIITAKE MUSHROOMS ON THE MODEL OF TESTOSTERONE-INDUCED PROSTATIC HYPERPLASIA

Actuality. Benign prostatic hyperplasia (BPH) is a common disease of elderly and senile men, the clinical manifestations of which are lower urinary tract symptoms. The frequency of detection and progression of this disease increases with age. If BPH occurs in only 40% of men after the age of fifty, then at the age of 80, 90% of men suffer from this pathology. Prescribing drug therapy is not always justified. In the end, the positive effect of pharmacotherapy may not occur and, in the future, surgical intervention will be required. Therefore, it is urgent to find and create new effective drugs for the prevention and treatment of BPH. Currently, the antioxidant support of testosterone replacement therapy is becoming more and more widespread, with the aim of reducing adverse reactions. Therefore, it is urgent to find and create new effective drugs with antioxidant properties for the prevention and complex treatment of BPH.

The aim of the work was to study the antioxidant properties of a thick extract from Shiitake mushrooms under the conditions of testosterone-induced benign prostatic hyperplasia in white rats.

Material and methods. Antioxidant activity of a thick extract from Shiitake mushrooms was studied on a model of testosterone-induced prostate hyperplasia. Shiitake extract was administered intragastrically to white rats daily for 21 days at a dose of 150 mg/kg of animal body weight. Testosterone propionate was injected subcutaneously at a dose of 3 mg/kg according to the same scheme as the studied extract. "Prostatophyt" was chosen as a reference drug, which was administered intragastrically daily for 21 days in a dilution

of 1:10 at a dose of 1 ml/100 g of rat body weight. Antioxidant effect of a thick extract from Shiitake mushrooms was studied according to the following biochemical parameters: activity of acid and alkaline phosphatase, the content of TBA-active products and reduced glutathione, the value of the phosphatase index.

Research results. Subcutaneous injections of testosterone at a dose of 3 mg/kg resulted in a probable increase in the content of TBA-active products and a decrease in the content of reduced glutathione in the serum and prostate homogenate of affected rats. An increase in activity of alkaline phosphatase was also observed in blood serum and prostate homogenate of animals relative to control. The activity of acid phosphatase under the influence of testosterone increased in blood serum and decreased in prostate homogenate of affected animals. Inhibition of the peroxidation processes and improvement of the antioxidant system of the animal body work were observed when a thick extract of Shiitake mushrooms was used against the background of testosterone.

Conclusion. The effectiveness of a thick extract from Shiitake mushrooms under the conditions of simulated hyperplasia of the prostate gland has been proven. The positive effect of the studied extract in this pathology is due to its antioxidant effect, since Shiitake mushrooms contain polysaccharides, in particular lentinan, which exhibits pronounced antitumor activity, steroid compounds and vitamins

Key words: Shiitake mushrooms, thick extract, prostatic hyperplasia, antioxidant action.

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АНТИОКСИДАНТНА ДІЯ ГУСТОГО ЕКСТРАКТУ З ГРИБІВ ШІЇТАКЕ НА МОДЕЛІ ТЕСТОСТЕРОН-ІНДУКОВАНОЇ ГІПЕРПЛАЗІЇ ПЕРЕДМІХУРОВОЇ ЗАЛОЗИ

Актуальність. Доброякісна гіперплазія передміхурової залози (ДГПЗ) є поширеним захворюванням чоловіків похилого та старечого віку, клінічними проявами якого є симптоми нижніх сечових шляхів. Частота виявлення та прогресування даного захворювання збільшуються з віком. Якщо після п'ятдесяти років ДГПЗ зустрічається лише у 40% чоловіків, то

у віці старше 80 років уже 90% чоловіків страждають на дану патологію. Призначення медикаментозної терапії не завжди є обґрунтованим. Позитивний ефект фармакотерапії у кінцевому підсумку може не настати, і надалі буде потрібне оперативне втручання. Нині все більшого поширення набуває антиоксидантний супровід замісної тестостеронової терапії з метою зниження побічних реакцій. Тому актуальним є пошук та створення нових ефективних препаратів з антиоксидантними властивостями для профілактики та комплексного лікування ДГПЗ.

Мета дослідження – вивчення антиоксидантних властивостей густого екстракту з грибів шиїтаке за умов тестостерон-індукованої доброякісної гіперплазії передміхурової залози у білих щурів.

Матеріал і методи. Антиоксидантну активність густого екстракту з грибів шиїтаке вивчали на моделі тестостерон-індукованої гіперплазії передміхурової залози. Екстракт шиїтаке білим щурам вводили внутрішньошлунково щоденно протягом 21 доби в дозі 150 мг/кг маси тіла тварини. Тестостерону пропіонат вводили підшкірно в дозі 3 мг/кг за тією ж схемою, що і досліджуваній екстракт. Референс-препаратом було обрано «Простатофіт», який вводили внутрішньошлунково щоденно протягом 21 доби в розведенні 1:10 у дозі 1мл/100 г маси тіла щура. Антиоксидантну дію густого екстракту з грибів шиїтаке вивчали за такими біохімічними показниками: активністю кислої та лужної фосфатази, умістом ТБК-активних продуктів та відновленого глутатіону, величиною фосфатазного індексу (КФ/ЛФ).

Результати дослідження. Підшкірні ін'єкції тестостерону в дозі 3 мг/кг призвели до вірогідного підвищення вмісту ТБК-активних продуктів та зниження вмісту відновленого глутатіону у сироватці крові та гомогенаті простати уражених щурів. Також спостерігали підвищення активності лужної фосфатази у сироватці крові та гомогенаті простати тварин відносно контролю. Активність кислої фосфатази під впливом тестостерону зросла у сироватці крові та знизилась у гомогенаті простати уражених тварин. Під час застосування на тлі тестостерону густого екстракту грибів шиїтаке спостерігали пригнічення процесів перекисного окиснення та покращання роботи антиоксидантної системи організму тварин.

Висновок. Доведена ефективність густого екстракту з грибів шиїтаке за умов модельованої гіперплазії передміхурової залози. Позитивний вплив досліджуваного екстракту за даної патології зумовлений його антиоксидантною дією, оскільки гриби шиїтаке містять у своєму складі полісахариди, зокрема лентинан, який виявляє виражену протипухлинну активність, стероїдні сполуки та вітаміни.

Ключові слова: гриби шиїтаке, густий екстракт, гіперплазія передміхурової залози, антиоксидантна дія.

Introduction. Actuality. Among the diseases of male genitourinary system, prostatitis and benign prostatic hyperplasia (BPH) take first place. Usually, the provocateur of prostatitis is an infection that affects the prostate gland. Prostatitis can appear at any age, but it is more common in men aged 30–50 and can have quite unpleasant and painful symptoms (Onoja, 2023; Shakir Saleh, 2022). BPG differs from prostatitis in that it is almost painless. This is a benign growth of prostate tissue, which is also called hyperplasia. The number of patients with BPH is constantly increasing. This pathology is the most common disease of the genitourinary system in men (Brechka, 2021; Brechka, 2019). The main symptoms of benign prostatic hyperplasia (BPH) are the weakening of sexual function, frequent urination, leakage of urine during the day, difficulty in urination, as the enlarged tissues of the gland strongly narrow the urinary canal, urinary retention may occur. Pathology develops due to hormonal disorders and aging of the body, that is, usually already in adulthood (Zaichenko, 2019; Herasymets, 2023a).

Correct treatment of BPH is aimed, first of all, at alleviating the symptoms of the lower urinary tract, improving the patient's quality of life and preventing the development of complications associated with prostate adenoma. A wide variety of drugs are used for the treatment of BPH, the effectiveness of which remains insufficient (Brechka, 2021; Brechka, 2019). Treatment of prostate adenoma, which is carried out already in the late stages, involves surgical intervention, the use of both open and endoscopic or transurethral operations (Brechka, 2021, Shchokina, 2017).

Prostate protectors are widely used for the complex treatment of BPH (Epstein, 2021). These are drugs that normalize the stromal-epithelial relationships in the prostate during its age-related morphogenesis. Natural prostate protectors deserve special attention, because the risk of developing side effects is minimal, and the presence of various biologically active substances provides a complex effect on the pathogenetic links of the disease (Zaichenko, 2019; Herasymets, 2023b; Liu, 2024). Therefore, the creation of new prostate protectors of natural origin is promising. Testosterone is a hormone that can affect many aspects of the body, including metabolism and oxidative stress. Antioxidant supplementation may be a useful component of testosterone replacement therapy to reduce possible side effects.

Reishi, maitake and Shiitake mushrooms exhibit an extremely wide spectrum of pharmacological activity. There are data confirming their antioxidant, antiproliferative and anti-inflammatory properties (Herasymets, 2021; Herasymets, 2023b). The object of this study was Shiitake mushrooms (*Lentinula edodes*). They are used in folk medicine to strengthen the immune system, lower blood cholesterol and treat prostate cancer. Today, shiitake is popular all over the world due to its taste qualities, various pharmacological properties and ability to grow both on natural logs and on artificial substrate (Tamang, 2022; Xu, 2020).

Shiitake mushrooms have a positive effect on the work of almost all systems of the human body. Their antioxidant, anti-inflammatory and oncoprotective properties have been confirmed (Spim, 2021; Tamang, 2022). Shiitake mushrooms are also effective in the fight against

various oncopathologies as part of complex therapy. They are also used in the treatment of hypertension, prostatitis, diabetes, polyarthritis and hepatitis. In Japan, it is recommended to use Shiitake mushrooms for those who have a precancerous condition (Tamang, 2022; Xu, 2020).

The aim of the work was to study the antioxidant properties of a thick extract from Shiitake mushrooms under the conditions of simulated benign prostatic hyperplasia in rats.

Material and methods. The object of our research was a thick extract from Shiitake mushrooms. The choice of shiitake mushrooms for the study of their potential antioxidant action in testosterone-induced BPH in rats is due to several factors:

1. The content of biologically active substances: polysaccharides, steroid compounds, amino acids, vitamins and minerals, which may have potential benefits for the prevention and treatment of BPH.

2. Popular in traditional medicine. Shiitake mushrooms are widely used in eastern countries in the treatment of cancer, hepatitis, prostate adenoma, and heart disease.

3. Previous studies. Based on the data of other researchers and the results of our own experiments, which confirm that shiitake mushrooms exhibit pharmacological properties useful for the therapy of prostate adenoma, which may cause further interest in this field.

The choice of research methods is determined by the achievement of specific scientific goals, namely, the study of the potential antioxidant effect in testosterone-induced prostate hyperplasia. With this pathology, the activity of organ-specific enzymes increases, therefore, to confirm the proposed hypothesis, we investigated the activity of acid and alkaline phosphatase, the content of TBA-active products and reduced glutathione, the value of the phosphatase index (AP/ALP).

The sequence of our scientific experiment is determined by a clear definition of the purpose and direction of the research, the study of literary sources on the chosen topic, the development of a hypothesis, the definition of methods and tools for data collection and analysis.

The research stages are:

1. Selection of male white rats for BPH modeling.

2. Division of animals into 7 groups: control, control pathology and groups that received Shiitake mushrooms extract and Prostatophyt to correct the induced pathology.

3. Subcutaneous administration of testosterone propionate for 21 days.

4. Intragastric administration of a thick extract from Shiitake mushrooms and the reference drug for 21 days.

5. Euthanasia of animals on the 15th and 22nd days of the experiment. Sampling of blood, prostate glands and seminal vesicles.

6. Conducting a study of biochemical indicators in blood serum and animal prostate homogenate.

The antioxidative effect of thick extract from Shiitake mushrooms on the model of testosterone-induced BPH was studied according to the recommendations of good laboratory practice (GLP) and bioethics in accordance with the "European Convention for the Protection of Vertebrate Animals Used for Research and Other Scientific Purposes" (Gross, 2015). The study was conducted in 2021 year. Our research was approved by the Ethics Commission of Ternopil National Medical University (excerpt from protocol No. 72 dated January 6, 2023).

All raw materials were purchased from the private enterprise "Mykhailovsky A. V." (Shiitake mushrooms were grown in Donetsk and Kyiv regions). Thick extract of shiitake was obtained by extraction with 40% ethanol in the raw material-extractant ratio of 1:10, which was established experimentally, taking into account the absorption coefficient of the extractant. To obtain thick shiitake extract, the raw materials were extracted with a suitable solvent for 2 hours while heating to 90 °C to intensify the extraction process. The yield of the extract was 46.9% (Burda, 2016).

Standardization of the extract according to steroid compounds was carried out on 5 series according to the requirements of the State Pharmacopoeia of Ukraine (table 1).

The dominant compound in the studied mushrooms was sitostenone (1.95 mg/kg). The presence of polysaccharides, carboxylic acids, phenolic substances, compounds of terpene nature was established using chemical reactions, thin-layer chromatography, gas chromatography and high-performance liquid chromatography. According to the results of the study of the elemental composition of the studied raw materials, the presence of 19 macro- and microelements was established (Burda, 2016).

Experiments were conducted on 56 white male rats weighing 200–250 g. Rats were kept in one room at a constant temperature of 19–23 °C on a balanced standard diet in the vivarium of the Ternopil National Medical University. Daily monitoring of the general condition, body weight, and mortality was carried out. The fluctuation of the massometric indicator was insignificant. Experimental animals were randomized by random sampling. During the experiment, the experimental rats were provided with constant access to food and water. Feeding was carried out with grain mixtures (corn, winter wheat, oats), carrots, table beets and bread were given.

The experimental animals were divided into 7 groups of 8 rats each: 1st – animals that were given the

appropriate amount of purified water every day (for 21 days), control (C); 2nd – rats injected subcutaneously with testosterone propionate solution, control pathology (CP), 15th day of the study; 3rd – animals that were subcutaneously injected with testosterone propionate solution, CP, 22nd day; 4th – rats that received a Shiitake mushrooms thick extract (SMTE) simultaneously with subcutaneous injection of testosterone propionate, 15th day; 5th – animals that received a SMTE simultaneously with subcutaneous injection of testosterone propionate, 22nd day; 6th – rats, which were given intragastrically a reference drug “Prostatophyt” simultaneously with subcutaneous injection of testosterone propionate, 15th day; 7th – animals that received intragastric administration of the reference drug “Prostatophyt” simultaneously with subcutaneous administration of testosterone propionate, 22nd day (Herasymets, 2023a).

BPH was simulated by injecting a solution of testosterone propionate at a dose of 3 mg/kg subcutaneously for 21 days. SMTE was administered intragastrically to experimental rats daily at a dose of 150 mg/kg of the animal's body weight simultaneously with subcutaneous injection of testosterone for 21 days. A dose of 150 mg/kg of rat's body weight was established by our previous studies as conditionally therapeutic. "Prostatophyt" was cho-

sen as a reference drug (manufacturer – LLC "Eim", scientific and production pharmaceutical company, Kharkiv, Ukraine) in a dilution of 1:10 at a dose of 1 ml/100 g of the animal's body weight, which was administered intragastrically according to the same according to the same scheme as *Shiitake mushrooms* extract.

Animals were taken out of the experiment, blood, prostate glands (PG) and seminal vesicles (SV) were collected on the 15th and 22nd days after the start of testosterone administration. The relative mass of PG and SV was determined.

Blood was taken from the heart of animals, centrifuged at 3000 rpm for 30 minutes. The resulting blood serum (supernatant) was used for research. The prostate gland (500 mg) was used to obtain a homogenate using a Silent Crusher S magnetic homogenizer after pre-perfusion with 4.5 ml of physiological saline.

The development of BPH is accompanied by a change in biochemical indicators in the animal's body (Herasymets, 2023a; Makodrai, 2021). In this regard, we investigated the content of TBA-active products (TBA-AP), reduced glutathione (GSH), activity of acid (AP) and alkaline phosphatase (ALP), calculated the phosphatase index (Vlizlo, 2012).

The principle of the TBA-AP determination method: in an acidic medium at high temperature, malondialdehyde reacts

Table 1

Standardization parameters of shiitake thick extract in accordance with the requirements of the State Pharmacopoeia of Ukraine

Series number	Description	Solubility	Identification	Dry residue	The content of heavy metals	Microbiological purity	The sum of steroid compounds
180516	Viscous mass of brown color with a weak characteristic smell.	Easily soluble in 40% ethanol, soluble in water, 50% ethanol, practically insoluble in 96% ethanol and other organic solvents.	Steroid compounds. When adding a 1% solution of p-dimethylaminobenzaldehyde in a 4 N ethanolic solution of hydrochloric acid and subsequent heating, a pink color is formed. The absorption spectrum of the test solution, obtained as indicated in the paragraph on the quantitative determination of steroid compounds, in the region from 450 nm to 600 nm should have a maximum at a wavelength of 518 ± 3 nm.	Not less than 70% 75%	Not more than 0,01%.	In 1 g of extract, the presence of no more than 1000 bacteria and 100 yeasts and molds (in total) is allowed. The presence of bacteria is not allowed Escherichia coli, Pseudomonas aeruginosa and Staphylococcus aureus, genus of bacteria Salmonella	Not less than 0,15%
170316	Meets the requirements	Meets the requirements	Meets the requirements		Meets the requirements	Відповідає	0,18%
201116	Meets the requirements	Meets the requirements	Meets the requirements	81%	Meets the requirements	Meets the requirements	0,16%
270217	Meets the requirements	Meets the requirements	Meets the requirements	77%	Meets the requirements	Meets the requirements	0,18%
210317	Meets the requirements	Meets the requirements	Meets the requirements	79%	Meets the requirements	Meets the requirements	0,17%

with thiobarbituric acid, forming a red colored complex with an absorption maximum at a wavelength of 532 nm. To determine the content of reduced glutathione, a method was used, the principle of which is the interaction of 5,5-dithiobis (2-nitrobenzoic) acid (Ellman's reagent) with free SH-groups of reduced glutathione with the formation of a yellow thionitrophenyl anion, the amount of which is directly proportional to the content of SH-groups. The method of determining the activity of alkaline phosphatase is based on the property of the enzyme to hydrolyze the ether bond in β -glycerophosphate with cleavage of phosphate acid. Phosphorus is determined colorimetrically by reaction with a molybdenum reagent in the presence of an eikonogen reducing agent or ascorbic acid. The product of the reaction is molybdenum blue, the color intensity of which is directly proportional to the amount of phosphorus in the sample, which characterizes the activity of the enzyme. The principle of the method of AP determining: acid phosphatase catalyses the hydrolysis of naphthyl phosphate. The naphthyl produced, reacts with the fast red TR salt to produce an azo dye. The increase in absorbance due to the formation of the azo dye is directly proportional to the concentration of acid phosphatase in the sample (Vlizlo, 2012).

Statistical data analysis was performed using STATISTICA 13 (TIBCO Software Inc., 2018). Parametric and non-parametric methods of evaluating the obtained data were used for statistical processing of the results. For all indicators, the arithmetic mean of the sample (M) and the error of the arithmetic mean (m) were calculated. The probability of the difference in values between independent quantitative values was determined by the Mann-Whitney test. The difference between values was considered probable at $p < 0.05$.

Research results and discussion. Research works of recent years confirm the relevance of new medicinal products of natural origin creation for the prevention and treatment of liver diseases, diseases of cardiovascular and immune systems, cancer and BPH (Makodrai, 2021). Experimental and clinical studies confirm the feasibility of using drugs of natural origin with antioxidant properties in the complex treatment of prostate adenoma.

They are especially effective in the early stages of the disease (Zaichenko, 2019; Brechka, 2019).

It was established experimentally that probable changes in the relative mass of androgen-dependent organs occurred when modeling testosterone-induced benign hyperplasia of the prostate gland in white rats (Zaichenko, 2019). In particular, the relative mass of PG increased by 52 % and 77%, and the relative mass of SV increased by 81% and 125% compared to the control on the 15th and 22nd days of the experiment (table 2).

The development of BPH in white rats was confirmed by histological studies (fig. 1, 2, 3).

The parenchymal component of PG of rats in the control group was represented by numerous alveolar-tubular glands. The basement membrane was lined with a layer of secretory cells – high prismatic epithelium, which together formed folds protruding into the lumen of the glands. Exfoliated epitheliocytes were present in the lumen of the glands, which is a normal process of cell removal. The lumens of the glands were filled with a discharge of various tincture properties. The stroma of PG was represented by connective tissue cords that departed from the organ capsule and smooth myocytes with a large number of blood micro vessels. Venules were full-blooded (fig. 1).

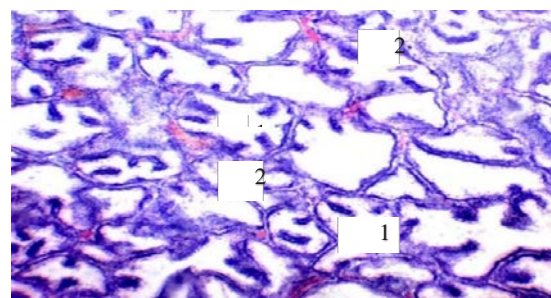


Fig. 1. Prostate gland of a rat from the control group. The glands are lined with columnar epithelium and form numerous folds (1). Blood vessels are congested (2). Stained with hematoxylin and eosin. $\times 100$

Table 2

The impact of Shiitake ushroom extract on the relative mass of reproductive system organs under conditions of simulated BPH (M \pm m; n=56)

Group of animals/Index	Relative weight of organs, g/100 g of body weight			
	PG		SV	
	15th day	22th day	15th day	22th day
C	0,31 \pm 0,02	0,31 \pm 0,02	0,48 \pm 0,03	0,48 \pm 0,03
CP	0,47 \pm 0,03*	0,55 \pm 0,06*	0,87 \pm 0,03*	1,08 \pm 0,05*
CP+SMTE	0,40 \pm 0,03	0,36 \pm 0,03**	0,65 \pm 0,05**	0,59 \pm 0,04**
CP+Prostatophyt	0,34 \pm 0,02**	0,35 \pm 0,03**	0,55 \pm 0,02**	0,54 \pm 0,04**

Note. Here and in the following tables: * – probable changes between the indicator of control and testosterone-affected animals; ** – probable changes between the indicator of testosterone-affected and treated animals; $p < 0,05$; *** – probable changes between the parameters of affected animals treated with SMTE and Prostatophyt.

The affected animals PG tissues histological analysis revealed significant structural changes compared to the control group. Significantly expanded and deformed lumens of the glands were observed. Epithelium located on the basement membrane was represented by cubic or flattened cells. The reversion of the nuclei from the basal part of the cells to the apical part was observed. A decrease in the number of basal cells was detected. At the same time, binucleated epitheliocytes appeared. Number of folds was significantly reduced, as well as the height of the preserved ones. The secretion is unevenly distributed, there were many lumens of the glands that do not contain discharge (fig. 2).

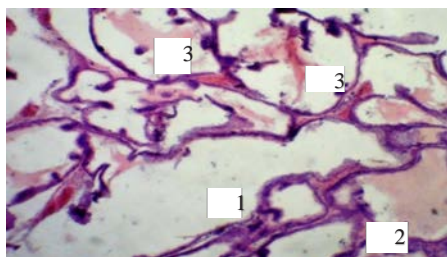


Fig. 2. Prostate gland of a rat with simulated BPH. Cystic transformation of the glands (1), flattening of the epithelial lining (2), and uneven distribution of secretion (3). Stained with hematoxylin and eosin. ×200

The stroma of the gland was mainly represented by fibrous connective tissue with a significantly reduced content of smooth muscle cells. The vessels of the hemomicrocirculatory channel were full of blood, the perivascular stroma was loosened by edema. There was an increase in the number of cellular elements, especially lymphocytes and fibroblasts (fig. 3).

The use of SMTE and Prostatophyte for 21 days in order to correct the lesion of the PG caused a decrease in the relative mass of the PG by 1.2 and 1.4 times on the 15th day of the study and by 1.5 and 1.6 times on the 22nd day of the experiment, respectively, relative to CP group. Administration of shiitake extract and Prostatophyte to white rats caused statistically significant changes in the relative mass of SV relative to CP. Thus, by the end of the experiment, a decrease in the relative

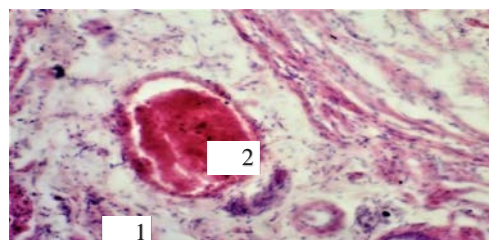


Fig. 3. Interstitial stroma of the prostate gland of a rat with simulated BPH. Edema, infiltration by lymphocytes and fibroblasts (1). Congested venule (2). Stained with hematoxylin and eosin. ×200

weight of the SV was observed by 1.8 and 2.0 times relative to the affected animals after the use of SMTE and the reference drug. There were no significant differences between the effects of shiitake mushroom extract and the comparison drug.

Probable changes were revealed in the activities of acid and alkaline phosphatase in blood serum and prostate homogenate of rats with simulated hyperplasia of the prostate gland after the use of SMTE and the comparison drug.

It was established that when benign prostatic hyperplasia was modeled by the introduction of testosterone propionate, systemic disturbances appeared, which were manifested by changes in the biochemical parameters of blood serum and prostate homogenate of animals. In particular, a probable increase in the activity of acid and alkaline phosphatase was observed in the blood serum of white rats compared to the control. An increase in the activity of phosphatases indicates the development of the inflammatory process in this pathology. AP and ALP activity increased in the prostate homogenate of affected animals; changes are probable (tables 3, 4). So, the activity of AP increased by 2.8 times and ALP – by 2.4 times by the end of the experiment compared to indicators of the control group.

The introduction of a thick extract from Shiitake mushrooms and Prostatophyte contributed to the normalization of phosphatase activity in the blood serum of animals: the activity of AP decreased on the

Table 3

The impact of Shiitake mushroom extract on biochemical parameters in rat blood serum in a model of testosterone-induced prostate hyperplasia, 15th day (M±m; n=56)

Index/Group of animals	C	CP	CP+SMTE	CP+Prostatophyt
AP, nmol/l*hour	6,70±0,38	12,84±0,63*	7,68±0,32**	7,18±0,36**
ALP, nmol/l*hour	10,45±0,36	18,05±0,55*	13,19±0,69**	11,21±0,39**/**
AP/ALP	0,64±0,02	0,72±0,05*	0,58±0,01**	0,64±0,03
TBA-AP, μmol/l	2,06±0,11	3,37±0,16*	2,84±0,17	2,55±0,14**
GSH, mmol/l	1,75±0,06	0,96±0,05*	1,48±0,02**	1,61±0,03**/**

15th day of the study under the influence of SMTE by 1.7 times, under the influence of the comparison drug – by 1.8 times; ALP activity – by 1.4 and 1.6 times, respectively, compared to the control pathology group. A 2.1-fold and 2.5-fold decrease in AP activity, and a 1.9- and 2.2-fold decrease in ALP activity were observed in affected animals on the 22nd day of the use of shiitake extract and prostatophyte, respectively. The AP/ALP ratio increased by 1.5 times in the control pathology group compared to the control, which indicates the development of the inflammatory process in PG (Shchokina, 2017). A probable decrease in the phosphatase index was noted in blood serum relative to CP under the influence of the studied extract and the comparison drug on the 22nd day of the study. Probable differences between the comparison drug and SMSE were noted regarding the activity of ALP and the content of GSH in the blood serum of animals on the 15th day of the experiment, on the 22nd day, probable differences were recorded regarding the activity of AP and the content of TBA-AP.

A probable decrease in AP activity was observed in the prostate homogenate of the affected rats under the conditions of PG testosterone-induced hyperplasia by 32% and 55% relative to the control group on 15th and 22nd days of the study, indicating PG damage. A probable increase in ALP activity was revealed in the animal prostate homogenate by 56% and 90% on the 15th and 22nd days of the experiment compared to the control (tables 5, 6). The phosphatase index decreased by 4.1 times in the prostate homogenate of affected animals under the influence of testosterone compared to the control by the end of the study.

The activity of AP increased by 1.9 times and the activity of ALP decreased by 1.6 times under the influ-

ence of SMTE on the 22nd day of the experiment relative to the affected animals. Prostatophyte significantly increased the activity of AP by 2.1 times and decreased the activity of ALP by 1.8 times relative to the CP group. The AP/ALP ratio increased by 2.9 and 3.6 times under the influence of studied extract and comparison drug respectively, relative to the affected rats (table 6), which indicates the ability of the drugs to stabilize membranes of the PG acini.

The development of testosterone-induced hyperplasia of PG was accompanied by the activation of lipid peroxidation processes, which is confirmed by a 1.6-fold increase in the content of TBA-AP in blood serum already on the 15th day of the experiment, and a 1.8-fold decrease in the level of GSH in CP group animals compared to the indicators of C group (table 3). The largest deviations of the studied parameters from the norm were observed on the 22nd day after the start of experiment

The introduction of SMTE contributed to a decrease in the content of TBA-AP in the blood serum by 1.2 and 1.4 times, an increase in the level of GSH by 1.5 and 1.8 times on the 15th and 22nd days of the study, respectively, relative to the affected animals (table 4, 5). The use of Prostatophyte in parallel with testosterone propionate also contributed to a probable decrease in the content of TBA-AP. Thus, the largest decrease in the content of TBA-AP in the blood serum of rats was observed on the 22nd day of the study by 2 times and the increase in the level of GSH by 2.1 times, respectively, relative to the CP group.

The level of TBA-AP increased by 2.1 times in the prostate homogenate of the affected animals by the end

Table 4

The impact of Shiitake mushroom extract on biochemical parameters in rat blood serum in a model of testosterone-induced prostate hyperplasia, 22th day, (M±m; n=56)

Index/Group of animals	C	CP	CP+SMTE	CP+Prostatophyt
AP, nmol/l*hour	6,70±0,38	19,07±0,66*	9,21±0,63**	7,70±0,32**/**
ALP, nmol/l*hour	10,45±0,36	25,27±1,10*	13,27±0,87**	11,45±0,35**
AP/ALP	0,64±0,02	0,76±0,03*	0,69±0,01**	0,67±0,02**
TBA-AP, μmol/l	2,06±0,11	4,55±0,24*	3,22±0,16**	2,30±0,10**/**
GSH, mmol/l	1,75±0,06	0,73±0,04*	1,32±0,06**	1,53±0,07**

Table 5

The impact of Shiitake mushroom extract on biochemical parameters in prostate homogenate of rats in a model of testosterone-induced prostate hyperplasia, 15th day, (M±m; n=56)

Index/Group of animals	C	CP	CP+SMTE	CP+Prostatophyt
AP, nmol/kg*hour	20,20±0,34	13,83±0,46*	17,03±0,40**	18,69±0,35**/**
ALP, nmol/kg*hour	23,59±0,89	36,75±1,26*	26,95±1,07**	25,38±0,86**
AP/ALP	0,87±0,04	0,38±0,02*	0,64±0,01**	0,74±0,04**/**
TBA-AP, μmol/kg	13,44±0,82	22,41±1,12*	17,31±0,75**	15,26±0,60**
GSH, mmol/kg	1,26±0,06	0,77±0,03*	1,05±0,03**	1,16±0,03**/**

Table 6

The impact of Shiitake mushroom extract on biochemical parameters in prostate homogenate of rats in a model of testosterone-induced prostate hyperplasia, 22th day, (M±m; n=56)

Index/Group of animals	C	CP	CP+SMTE	CP+Prostatophyt
AP, nmol/kg*hour	20,20±0,34	9,10±0,37*	17,00±0,78**	18,98±0,27**/**
ALP, nmol/kg*hour	23,59±0,89	44,75±2,23*	28,41±1,16**	25,27±1,11**
AP/ALP	0,87±0,04	0,21±0,01*	0,60±0,010**	0,76±0,03**/**
TBA-AP, μmol/kg	13,44±0,82	27,96±0,97*	17,70±0,58**	14,58±0,62**/**
GSH, mmol/kg	1,26±0,06	0,55±0,05*	0,95±0,06**	1,17±0,05**/**

of the experiment, the content of GSH decreased by 2.3 times compared to the control (table 6). The use of SMTE and Prostatophyte contributed to a decrease in the content of TBA-AP in the homogenate of the prostate of animals with simulated benign hyperplasia on the 22nd day of the study by 1.6 and 1.9 times, respectively, compared to the parameters of the control pathology. By the end of the experiment, the content of GSH increased by 1.7 times in the homogenate of the animals' prostate under the influence of SMTE, under the influence of comparison drug – by 2.1 times relative to CP (table 5). As can be seen from tables 5 and 6, the comparison drug showed probably greater effectiveness in normalizing some of the studied parameters in the prostate homogenate than SMTE.

The results of our study are consistent with the works of other scientists who modeled BPH and observed similar changes in biochemical parameters. (Zaichenko, 2019; Makodrai, 2021; Brechka, 2021).

The use of SMTE effectively affected the antioxidant/prooxidant balance in the animal's body. This is confirmed by a probable decrease in the content of TBA-AP, an increase in the content of GSH and the normalization of phosphatase activities in blood serum and prostate homogenate of rats with testosterone-induced BPH. The reference preparation caused similar changes in biochemical parameters.

All the revealed results of the SMTE corrective effect on the modeled pathology confirm its antioxidant properties and give reason to consider the studied extract effective for restoring the function of PG. The effectiveness of the

shiitake mushroom extract was almost at the level of the comparator drug. The study extract may expand the range of BPH treatments and reduce the side effects of conventional therapy. The advantage of SMTE is monocomponentity, since most drugs of natural origin, in particular, the comparison drug, are multicomponent, which increases the risk of allergic reactions to their individual components.

Conclusions

SMTE had a positive effect on the state of the prostate gland of rats injected subcutaneously with testosterone propionate to simulate BPH. This is evidenced by probable positive changes in the relative mass of androgen-dependent organs, normalization of phosphatase activity, a decrease in the content of TBA-AP and an increase in the content of GSH in blood serum and prostate homogenate of white rats. The use of comparative preparation “Prostatophyte” also caused probable positive changes in the investigated biochemical parameters.

The data of the experimental study confirm the antioxidant properties of the thick extract of Shiitake mushrooms. The prostate protective effect of shiitake extract can be realized through its antioxidant effect. The pharmacological properties of shiitake are probably related to the presence of polysaccharides in their composition, namely lentinan, steroid compounds and vitamins.

The obtained results are a theoretical justification for the feasibility of a suitable drug further development for the complex treatment and prevention of BPH in men.

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Herasymets I. I. – collection and analysis of literary data, research design, experiments conducting, writing the article, summary, editing an article;

Fira L. S. – idea, abstracts, conclusions, editing of the article;

Medvid I. I. – experiments conducting, statistical data processing;

Fira D. B. – participation in writing the article;

Lukanyuk M. I. – experiments conducting.

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