

ЕКСПЕРИМЕНТАЛЬНІ ДОСЛІДЖЕННЯ**VITAMIN D AND SAW PALMETTO FRUIT EXTRACT
IN EXPERIMENTAL PROSTATE PATHOLOGY**

I. O. Bielkina¹, N. P. Smolienko¹, Ye. M. Korenieva¹, I. O. Marakhovskiy¹,
N. O. Tkachenko², O. S. Protsenko², R. Ye. Blahoveshchenskiy³,
V. O. Bondarenko¹, K. V. Misiura¹

¹ *SI «V. Danilevsky Institute for Endocrine Pathology Problems of the NAMS of Ukraine»,
Kharkiv, Ukraine;*

² *V. N. Karazin Kharkiv National University, Kharkiv, Ukraine;*

³ *Kharkiv National Medical University, Kharkiv, Ukraine*

inna_bel@i.ua

Benign prostatic hyperplasia (BPH) is a serious urological problem that significantly reduces the quality of life of men. The prevalence of BPH increases steadily with age: from 20% in men aged 40, to 70% in men aged 60, and up to 90% in men aged 90. These prevalence rates are caused by both natural aging processes and the influence of external influences such as stress, adverse environmental factors, and living conditions. These factors may contribute to the early onset of BPH in younger men, causing a decrease in androgen secretion, metabolic disorders and dys hormonal conditions [1–3]. BPH is a disease caused by the proliferation of stromal and epithelial cells in the prostate transition zone and periurethral region, which leads to prostate enlargement, inflammation,

fibrosis and changes in smooth muscle activity, urethral compression, and a common cause of lower urinary tract symptoms (LUTS) in men [3, 4]. These symptoms include frequent and difficult urination, nocturia, a feeling of incomplete bladder emptying and urgency [5, 6]. In addition, BPH can lead to complications such as urinary tract infections due to urinary stasis, urolithiasis, and acute renal failure [3].

The impact of BPH on reproductive function deserves special attention. The disease can lead to decreased libido, erectile dysfunction, ejaculation disorders, and disorders of spermatogenesis. The decrease in testosterone (T) levels, which is often observed in patients with BPH, also contributes to the development of erectile dysfunction [7]. Inflammatory processes ac-

* The work was carried out within the frameworks of the research of the SI «V. Danilevsky Institute for Endocrine Pathology Problems of the National Academy of Medical Sciences of Ukraine»: «The determination of role of D-hormone in the prophylaxis of benign prostatic hyperplasia and substantiating of methods of correction of reproductive system pathologies induced by benign prostatic hyperplasia» (State registration number 0122U200369).

The institution that finances the study is the National Academy of Medical Sciences of Ukraine.

The authors assume responsibility for the published work.

The authors guarantee absence of competing interests and their own financial interest when carrying out the research and writing the article.

The manuscript was received by the editorial staff 13.05.2025.



This work is licensed under a Creative Commons Attribution 4.0 International License.



companying BPH often aggravate symptoms and contribute to the development of prostatitis, vesiculitis, and urethritis, thereby increasing the risk of reproductive disorders [2]. Some patients may develop depression, stress, sleep disturbances, and decreased physical activity, which leads to a deterioration in the overall quality of life not only of the patients but also of their partners [7]. Thus, BPH is not only a urological problem, but also a serious medical and social issue that affects various aspects of health and quality of life.

The pathogenesis of BPH is a complex and incompletely understood process that is likely multifactorial, involving on age-related changes, hormonal imbalances, chronic inflammation, and oxidative stress.

With age, men experience a decrease in male sex hormone levels, an increase in estrogens and prolactin (PRL). Hormonal imbalance resulting from a disrupted ratio of T to estradiol (E_2) synthesis increases the number of androgen receptors in the prostate and inhibits androgen metabolism [8, 9]. Increased 5α -reductase activity leads to excessive production of dihydrotestosterone (DHT), which promotes glandular cell hyperplasia, angiogenesis, and oxidative stress [4, 9]. PRL stimulates the proliferation of prostate epithelial cells and acts as a suppressor of apoptosis, promoting hyperplasia [1].

Chronic inflammation of the prostate also plays an important role in the development and progression of BPH by activating proinflammatory cytokines and signaling pathways such as NF- κ B and STAT3. This promotes abnormal cell proliferation and disease progression [6, 8]. Increased expression of growth factors such as TGF- β 1 promotes proliferation of prostate stromal and epithelial cells. Oxidative stress enhances inflammatory processes, and insufficient activity of antioxidant systems impairs the regulation of cell proliferation [10].

Treatment of BPH includes three main approaches: watchful waiting, medication therapy, and surgery. The choice of method depends on the severity of symptoms, the presence of complications, and the impact of the disease on the patient's quality of life [5].

Active surveillance is recommended for mild symptoms or moderate manifestations

that do not affect the quality of life. Drug therapy is the main method of conservative treatment and includes several groups of drugs: α -blockers (tamsulosin, alfuzosin), 5α -reductase inhibitors (finasteride, dutasteride), phosphodiesterase-5 inhibitors (tadalafil, sildenafil, and vardenafil), anticholinergic drugs (tolterodine), β 3-adrenomimetics (mirabegron). However, when prescribing such therapy, a large number of side effects exist. The side effects of α -blockers include dizziness, postural hypotension, lack of ejaculation, a decrease in semen volume, fructose level, and pH, affecting not only the prostate but also other organs of the genitourinary system, in particular the vas deferens and seminal vesicles. Side effects of 5α -reductase inhibitors can include decreased libido, impotence, and gynecomastia [2, 4, 5]. To prevent this, especially in men of reproductive age, phytotherapeutic agents (extracts from pumpkin seeds, saw palmetto (*Serenoa repens*) fruits, etc.) are used.

Surgical interventions are now used less frequently, in cases of ineffectiveness of medical therapy and development of complications. The main invasive methods include transurethral resection of the prostate (TURP), open prostatectomy, laser enucleation and GreenLight laser treatment, thermal therapy and stenting. The main side effect is retrograde ejaculation, which occurs in 70% of patients after TURP. Other complications include infections, bleeding, and reduced fertility [5, 11].

Treatment-related side effects, such as sexual dysfunction, retrograde ejaculation, and reduced fertility, are important factors limiting treatment options. Therefore, there is currently a growing interest in the treatment of BPH in finding agents that do not have the major drawbacks of systemic prostatoprotectors.

The popularity of herbal medicine is due to its relative safety, good tolerability of drugs, favorable pharmacoeconomic profile, and complex effects on the prostate, including anti-inflammatory, antiproliferative, antioxidant, and capillary protective properties. The most studied and popular herbal remedy is the extract of the fruits of the Sabal palm (*Serenoa repens* or Saw palmetto). Studies have shown that the extract of *Serenoa repens* has an effect similar to alpha-blockers and 5α -reductase inhibitors in

improving urinary symptoms, increasing urine flow rate and reducing prostate volume, is well tolerated and has no negative effect on sexual function, including sexual interest, erection quality, orgasm achievement, and ejaculation [4, 6].

The role of vitamin D in recent years has expanded beyond its traditional role in bone and mineral metabolism, and more and more studies indicate its important role in male reproductive health, including its impact on BPH. Vitamin D receptors (VDR) are expressed in various cells of the reproductive organs, including the testes, epididymis, seminal vesicles, prostate, and spermatozoa [2, 8]. Its deficiency, which is a global problem, is associated with an increase in prostate volume, worsening of urinary symptoms, impaired spermatogenesis, the development of androgen deficiency, impaired erectile and ejaculatory components of the copulatory cycle, a decrease in the number and quality of spermatozoa, and reduced

fertility [2, 8]. Some studies have shown that increasing vitamin D intake can reduce prostate inflammation and growth, lower prostate-specific antigen (PSA) levels, and improve BPH symptoms, making vitamin D a promising tool in the treatment of BPH and supporting male reproductive health.

Thus, the complexity of the etiopathogenesis of BPH means that the effectiveness of the therapy is often limited by side effects and contraindications. In this regard, the search for and development of new prostatoprotectors containing several active pharmaceutical ingredients that can simultaneously affect different links in the pathogenesis of BPH and lack adverse effects during long-term use is a highly relevant and pressing issue.

The **aim** of the study was to evaluate the effects of vitamin D and saw palmetto fruit extract on prostate mass, sex hormone levels, and sexual behavior under experimental conditions of prostate pathology.

MATERIALS AND METHODS

The studies were conducted in accordance with the National «General Principles for Animal Research Ethics» (Ukraine, 2001), which are aligned with the provisions of the «European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes» (Strasbourg, 1986). Experimental animals (white outbred rats) were kept in standard vivarium conditions with natural lighting and a diet recommended for this species of animal, with free access to drinking water.

Prostate pathology (BPH) was induced by administering sulpiride solution at a dose of 40 mg/kg b.w. to 12-month-old male rats for 30 days (BPH group). Animals of the control group were received 0.9% sodium chloride solution intramuscularly daily. For correction, starting from day 31, male rats were given per os vitamin D₃ at a dose of 4000 IU for 21 days (BPH + vit. D group); saw palmetto fruit extract (*Serenoa repens*) at a dose of 35 mg/kg b.w. (BPH + Ref group); or vitamin D₃ and saw palmetto fruit extract in the same doses (BPH + vit. D + Ref group).

To gain sexual experience and develop stereotypical responses, each male was placed

once a week with a receptive female for 15 min. The baseline was the parameters of the fourth test, which were characterized by relatively stable indicators and were taken as 100%. Rats that reached ejaculation during the test were considered sexually active. The sexual behavior of the experimental animals was studied during mating with an ovariectomized receptive female for 15 min at dusk according to the quantitative and temporal indicators of mounts, intromissions and ejaculations. The receptivity of ovariectomized females was achieved by sequential administration of an oil solution of estradiol benzoate (10 µg per animal) for 48 h and progesterone (500 µg per animal) for 4–5 h before testing.

After the course administration of the studied substances, the mass of the reproductive organs and the levels of sex hormones (T, E₂) in the blood serum were determined using reagent kits for enzyme-linked immunosorbent assay, the measurements were performed using a Stat FAX-3200 ELISA analyzer.

Statistical analysis was performed using the Shapiro-Wilk test to test for normal distribution of quantitative data. Data are presented as arithmetic mean (\bar{X}) and its error ($\pm S_{\bar{x}}$). The

null hypothesis of no difference between groups was tested using the Student's t-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data, and

the χ^2 test was used for comparative analysis of relative values. Differences between groups were considered statistically significant at a statistical significance level of $p < 0.05$.

RESULTS AND THEIR DISCUSSION

Under conditions of experimental prostate pathology, the mass of the ventral part of the prostate increased by 28.9% to (838.2 ± 34.3) mg. While the combined administration of vitamin D and Sabal palm fruit extract resulted in the normalization of its mass to (654.0 ± 26.4) mg, which was almost equal to the control group (649.8 ± 21.3) mg. No differences were observed in the mass of other organs of the reproductive system.

Analysis of sex hormone levels revealed that the administration of sulpiride in the modeling of BPH led to a decrease in the level of total T by 1.66 times, which led to a violation of the ratio of sex hormones. The T/E_2 ratio in rats administered sulpiride was 1.53 times lower than in the Control (Table 1).

When using corrective substances, the T concentration was normalized. In the group receiving the reference drug, the T level increased by 1.4 times compared to the group of animals with experimental pathology, approaching the Control level. In the group of rats receiving vitamin D together with the reference drug, the T level increased 1.48 times compared to the BPH group, approaching the Control level. The T/E_2 ratio increased almost one and a half times (see Table 1).

The sexual behavior of rats with experimentally induced benign prostatic hyperplasia was characterized by a 1.6-fold increase in the rate

of courtship behavior compared to the Control group. In these animals, the time of onset of copulation was prolonged by 4.1 times, while their number decreased almost twofold. Sulpiride-induced BPH led to a 4.8-fold prolongation of the time when males began to mate directly. Intromissions were observed 2.7 times less often compared to the Control group. None of the males in this group had ejaculation (Table 2).

Correction of BPH with the reference drug reduced the latency period of mountings by 2.7 times and the latency period of intromissions by 1.7 times, and also reduced the number of courtship behavior by 1.9 times, compared with the BPH group (see Table 2).

Co-administration of vitamin D₃ with the reference drug to male rats with BPH led to statistically significant changes in both copulatory and courtship behavior, bringing the values closer to the values of the Control group. In animals of the BPH+vit.D+Ref group, the number of female anogenital sniffing events decreased by 1.7 times, compared with the BPH group. In these animals, the latency period of mountings decreased by 3.3 times and the latency period of intromissions by 4.4 times, compared with the BPH group. At the same time, the number of mounts and intromissions increased by 2.2 and 2.9 times, respectively. Ejaculations occurred in 40% of males in this group (see Table 2).

Table 1

Levels of sex hormones in the serum of male rats, $n = 5, \bar{X} \pm S_{\bar{x}}$

Group	Parameter		
	Testosterone, nmol/L	Estradiol, nmol/L	T/E_2 , arbitrary units (a.u.)
Control	$10,96 \pm 0,93$	$0,24 \pm 0,01$	$45,13 \pm 4,32$
BPH	$6,60 \pm 1,01^*$	$0,26 \pm 0,01$	$25,21 \pm 3,59^*$
BPH+Ref	$9,24 \pm 0,47^\#$	$0,27 \pm 0,02$	$35,22 \pm 2,88$
BPH+vit. D	$8,77 \pm 0,37$	$0,26 \pm 0,02$	$34,33 \pm 2,87$
BPH + vit. D + Ref	$9,76 \pm 0,77^\#$	$0,26 \pm 0,01$	$37,46 \pm 1,43^\#$

Note:

* statistically significant differences from Control group ($p < 0.05$).

statistically significant differences from BPH group ($p < 0.05$).

Table 2

Sexual behavior of male rats, n = 5, $\bar{X} \pm S_{\bar{x}}$

Parameter		Group				
		Control	BPH	BPH + Ref	BPH + vit.D	BPH + vit.D + Ref
Mounts:	number	5,8 ± 0,7	3,0 ± 0,5*	5,2 ± 0,9	5,4 ± 1,3	6,6 ± 0,6 [#]
	latency, s	46,0 ± 22,1	192,0 ± 23,7*	71,0 ± 7,8 [#]	179,0 ± 45,2*	58,0 ± 22,7 [#]
Intromissions:	number	12,0 ± 1,1	4,4 ± 0,5*	6,4 ± 1,0*	5,8 ± 1,2*	12,8 ± 0,7 [#]
	latency, s	95,0 ± 23,8	459,0 ± 60,1*	266,0 ± 29,6* [#]	314,0 ± 37,5*	104,0 ± 26,4 [#]
Ejaculations:	number	1	0	0,2 ± 0,2	0,2 ± 0,2	0,4 ± 0,2
	latency, s	467,0 ± 42,9	—	600	720	837,5 ± 27,5
Sniffing of female		9,4 ± 1,4	15,0 ± 1,5*	8,0 ± 0,7 [#]	11,8 ± 0,6	9,0 ± 0,6 [#]

Note:

* statistically significant differences from Control group (p < 0.05).

[#] statistically significant differences from BPH group (p < 0.05).

The prostate plays a central role in andrology, participating in the regulation of fertility and sexual function. Its function directly depends on hormonal balance, and its change underlies the pathogenesis of BPH. With age, men experience a decrease in T levels, while the levels of estrogens, PRL, and FSH remain stable or increase. This imbalance leads to an increase in aromatase activity, which promotes the conversion of T to E₂. Estrogens, in turn, increase the expression of androgen receptors and enhance the effect of DHT, the active metabolite of T, on the prostate, stimulating hyperplasia and hypertrophy of its cells [4, 8].

The administration of sulpiride, a specific dopamine receptor antagonist, stimulates PRL production and reduces luteinizing hormone (LH) production, which leads to an imbalance in the levels and ratio of sex hormones and the development of BPH [1, 2], which is also confirmed by our results.

Various forms of sexual dysfunction, including decreased libido, erectile dysfunction, and ejaculatory dysfunction, may be observed in BPH. The pathophysiological mechanisms of these disorders are associated with hormonal imbalance, alteration of the NO — cGMP signaling pathway, hyperactivation of the RhoA-ROCK signaling pathway, and hyperactivation of the autonomic nervous system [11].

Our results show that hormonal dysregulation leads to pathological growth of the prostate, and deterioration of sexual function, as supported by data in the literature. T plays

a key role in maintaining sexual function, regulating the motivational and copulatory components of sexual behavior, both through reduction to DHT and through aromatization to E₂. T regulates courtship behavior in rats, which corresponds to libido in humans. T content also affects erections to some extent. DHT is a peripheral stimulant of sexual activity, which ensures ejaculation. E₂ primarily affects mounts and to some extent intromissions and ejaculation in rodents. T deficiency leads to decreased libido and erectile dysfunction, while increased estrogen levels are associated with impaired spermatogenesis and decreased ejaculate quality [12, 13].

The administration of the studied substances led to the normalization of prostate mass and sex hormone ratios, as well as improved sexual behavior, findings supported by both experimental and clinical studies. The obtained results of the positive effect of the extract of the fruits of the Sabal palm on BPH are confirmed by data from the literature. In clinical studies, during treatment with *Serenoa repens*, a decrease in the volume of the prostate, improvement of urodynamic parameters and urinary symptoms in men with BPH were observed [4, 6]. Experimental studies have shown that the extract of the fruits of the Sabal palm led to an increase in the level of T, the ratio of T/E₂ and the normalization of DHT/T, as well as reduced prostate growth and hyperplasia [14]. Furthermore, Sabal palm fruit extract demonstrates a beneficial effect on sexual function.

Thus, in a study involving men with BPH or chronic non-infectious prostatitis, it was shown that *Serenoa repens* not only improves symptoms of LUTS, but also has a positive effect on erectile function, increasing the International Index of Erectile Function. In addition, pooled data from three randomized, double-blind studies demonstrated that *Serenoa repens* does not have a negative effect on sexual desire, erection quality, orgasm, and ejaculation, unlike α -blockers (tamsulosin) and 5- α -reductase inhibitors (finasteride) [6]. And long-term therapy with *Serenoa repens* in patients with BPH contributed to the restoration of erectile function and the continuation of sexual intercourse [15].

Such positive changes can be explained by the anti-inflammatory, antiproliferative activity of the fruits of the Sabal palm, which target the key pathophysiological mechanisms of BPH. Thus, *Serenoa repens* decreases the level of pro-inflammatory cytokines (interleukin-1 β and tumor necrosis factor- α), attenuates immune cell infiltration (CD45+), inhibits the activity of phospholipase A2 and the production of 5-lipoxygenase metabolites, leading to an increased Bax/Bcl-2 ratio, a marker of apoptosis, and increases the activity of caspase-3, which has been demonstrated both in vitro and in vivo [4, 6, 15].

Serenoa repens also affects the hormonal background by inhibiting the activity of 5 α -reductase isoforms 1 and 2, which reduces the conversion of T to DHT without interfering with PSA expression, inhibits the binding of DHT to androgen receptors, reducing DHT levels and increasing T levels, maintaining androgen balance. It also inhibits the nuclear estrogen receptors, reduces epidermal growth factor levels, preventing its stimulating effect on prostate growth [4, 6, 15, 16].

Regarding vitamin D, its positive effect on reducing prostate volume and improving BPH symptoms observed in clinical studies may be due to its antiproliferative, anti-inflammatory, and antioxidant properties. Thus, it has been shown that vitamin D has an inhibitory effect on the RhoA/ROCK pathway, blocks TGF- β signaling, and attenuates the activity of Des(1-3) IGF-I, which reduces prostate cell proliferation. The anti-inflammatory effect of vitamin D is associated with its ability to reduce the expres-

sion of COX-2 and the production of prostaglandin E2, inhibit NF- κ B and STAT3 signaling, resulting in decreased secretion of inflammatory cytokines [8, 10, 16, 17]. The antioxidant effect of vitamin D is due to increased expression of Nrf2, which reduces oxidative stress in prostate tissues [10, 18].

Vitamin D also influences the balance of sex hormones. Clinical studies (17 randomized controlled trials) have shown that vitamin D intake increased total T levels in men [19], a finding that correlates with our results. When men received vitamin D for 1 year, a significant increase in the level of total, bioactive and free T was observed, along with a reduction in E₂ levels [20]. Also, *in vitro* experiments, it was also shown that in Leydig cells, the addition of vitamin D increased the expression of genes encoding steroidogenic enzymes involved in the production of androgens and their precursors, increased the activity of mitochondrial dehydrogenase, which indicating its effect on the energy metabolism essential for T synthesis, and the addition of vitamin D together with LH led to a significantly greater increase in the synthesis of T in vitro compared to the addition of LH alone [21].

Vitamin D acts on sexual function both indirectly — by increasing T levels and normalizing the sex hormone ratio — and directly, by regulating endothelial function and inflammation [12, 13, 22]. T affects both central and peripheral mechanisms in the regulation of male sexual function: centrally, it promotes the release of neurotransmitters such as dopamine, oxytocin and nitric oxide (NO), which are involved in the processes of motivation, pleasure and arousal [23]. Peripherally, T acts as a co-modulator of the erectile process: it modulates the structure and innervation of trabecular smooth muscle cells of the vessels of the penis and the fibroelastic properties of the corpus cavernosum, enhances the activity of NO synthase, contributing to the release of NO and expansion of the corpus cavernosum [24, 25]. Vitamin D directly influences endothelial function through its regulation of vascular stiffness, nitric oxide production, and vascular permeability, as well as through its modulation of inflammatory processes and antioxidant protection of endothelial cells against oxidative

stress [22, 26]. Clinical studies have shown improvements in erectile function following vitamin D therapy [20, 26].

Therefore, the positive effects of vitamin D and saw palmetto fruit extract on sex hormone

balance, sexual behavior, and prostate volume reduction in BPH may be due to their combined effects on different mechanisms involved in the pathogenesis of BPH.

CONCLUSIONS

1. Experimental sulpiride-induced prostatic hyperplasia is accompanied by an increase in the mass of the prostate, an imbalance of hormonal ratios, and suppression of sexual behavior parameters.
2. The combined use of vitamin D and saw palmetto fruit extract corrects benign prostatic

hyperplasia, promotes normalization of prostate mass, an increase in testosterone levels, and restores the ratio of sex hormones, and improves both the courtship and copulatory components of the sexual behavior in rats.

REFERENCES

1. Zheng C, Luo Y, Chen Y, et al. *Experim Ther Med* 2020; 19(4): 2551-2562. <https://doi.org/10.3892/etm.2020.8521>.
2. Brechka NM, Bondarenko VO, Shcherbak OV, Korenieva YM. *Wiadomosci Lekarskie* 2024;77(1): 135-143. <https://doi.org/10.36740/wlek202401117>.
3. Awedew AF, Han H, Abbasi B, et al. *The Lancet Healthy Longevity* 2022;3(11): e754-e776. [https://doi.org/10.1016/S2666-7568\(22\)00213-6](https://doi.org/10.1016/S2666-7568(22)00213-6).
4. Pender GC, Ombaka JH, Mwitari PG, Guyah B. *Int J Sci Res Arch* 2024;11(2): 049-074. <https://doi.org/10.30574/ijrsra.2024.11.2.0381>.
5. Nastanova 00246. Dobrojakisna giperplazija pered-mihurovoi' zalozy (DGPZ), 2017: 10 p, available at: <https://guidelines.moz.gov.ua/documents/3132>
6. Blair HA. *Drugs & Aging* 2022;39(3): 235-243. <https://doi.org/10.1007/s40266-022-00924-3>.
7. Bruskewitz RC. *Rev Urol* 2003;5(2): 72-80, available at: <https://reviewsinurology.com/issues/vol/5/no/2/quality-of-life-and-sexual-function-in-patients-with-benign-prostatic-hyperplasia>
8. Zendeudel A, Ansari M, Khatami F, et al. *Clin Nutr* 2021;40(5): 3325-3331. <https://doi.org/10.1016/j.clnu.2020.11.005>.
9. Angrimani DS, Brito MM, Rui BR, et al. *Sci Reports* 2020;10(1): 14834. <https://doi.org/10.1038/s41598-020-71691-7>.
10. Chen Y, Xu H, Liu C, et al. *Disease Markers* 2021;2021(1): 4029470. <https://doi.org/10.1155/2021/4029470>.
11. Couteau N, Duquesne I, Frédéric P, et al. *J Clin Med* 2021;10(24): 5788. <https://doi.org/10.3390/jcm10245788>.
12. Zhuang B, Zhuang C, Jiang Y, et al. *Andrology* 2024; 2024: 1-13. <https://doi.org/10.1111/andr.13778>.
13. Corona G, Maggi M. *Rev Endocrine Metab Dis* 2022; 23(6): 1159-1172. <https://doi.org/10.1007/s11154-022-09748-3>.
14. Van Coppenolle F. *The Prostate* 2000;43(1): 49-58. [https://doi.org/10.1002/\(SICI\)1097-0045\(20000401\)43:1<49::AID-PROS7>3.0.CO;2-J](https://doi.org/10.1002/(SICI)1097-0045(20000401)43:1<49::AID-PROS7>3.0.CO;2-J)
15. Geavlete P, Multescu R, Geavlete B. *Ther Adv Urol* 2011; 3(4): 193-198. <https://doi.org/10.1177/1756287211418725>.
16. Chung A, Kini M, Hartigan SM, et al. *Academic Press* 2021: 107-111. <https://doi.org/10.1016/B978-0-12-819765-3.00008-X>.
17. Espinosa G, Esposito R, Kazzazi A, Djavan B. *Can J Urol* 2013;20(4): 6820-6825, available at: https://canjurol.com/html/free-articles/V20I4_03F_DrEspinosa.pdf
18. Vázquez-Lorente H, Herrera-Quintana L, Jiménez-Sánchez L, et al. *Antioxidants* 2024;13(8): 996. <https://doi.org/10.3390/antiox13080996>.
19. Abu-Zaid A, Saleh SA, Adly HM, et al. *Diseases* 2024; 12(10): 228. <https://doi.org/10.3390/diseases12100228>.
20. Canguven O, Talib RA, El Ansari W, et al. *The Aging Male* 2017;20(1): 9-16. <https://doi.org/10.1080/13685538.2016.1271783>.
21. Huang Y, Jin H, Chen J, et al. *Animal Reprod Sci* 2015;158: 109-114. <https://doi.org/10.1016/j.anireprosci.2015.05.008>.
22. Crafa A, Cannarella R, Barbagallo F, et al. *Biomolecules* 2023;13(6): 930. <https://doi.org/10.3390/biom13060930>.
23. Corona G, Isidori AM, Aversa A, et al. *J Sex Med* 2016;13(3): 317-337. <https://doi.org/10.1016/j.jsxm.2016.01.007>.
24. Chen Z, Jiang J, Jiang R. *J Sex Med* 2024;21(8): 663-670. <https://doi.org/10.1093/jsxmed/qdae071>.
25. Yafi FA, Jenkins L, Albersen M, et al. *Nature Rev Dis Primers* 2016; 2(1): 1-20. <https://doi.org/10.1038/nrdp.2016.3>.
26. Tirabassi G, Sudano M, Salvio G, et al. *Int J Endocrinol* 2018;2018(1): 3720813. <https://doi.org/10.1155/2018/3720813>.

VITAMIN D AND SAW PALMETTO FRUIT EXTRACT
IN EXPERIMENTAL PROSTATE PATHOLOGY

I. O. Bielkina¹, N. P. Smolienko¹, Ye. M. Korenieva¹, I. O. Marakhovskiy¹,
N. O. Tkachenko², O. S. Protsenko², R. Ye. Blahoveshchenskiy³,
V. O. Bondarenko¹, K. V. Misiura¹

¹SI «V. Danilevsky Institute for Endocrine Pathology Problems of the NAMS of Ukraine»,
Kharkiv, Ukraine;

²V. N. Karazin Kharkiv National University, Kharkiv, Ukraine;

³Kharkiv National Medical University, Kharkiv, Ukraine
inna_bel@i.ua

Benign prostatic hyperplasia (BPH) is a serious problem that significantly reduces the quality of life of men, so the search for new prostatoprotectors is highly relevant. The aim: to evaluate the effect of vitamin D and saw palmetto fruit extract on prostate mass, sex hormone levels, and sexual behavior under experimental conditions of prostate pathology.

Materials and methods. Prostate pathology was induced by administration of sulphiride solution at a dose of 40 mg/kg b.w. to 12-month-old male white outbred rats for 30 days (BPH group). For correction, the following treatments were administered for 21 days per os: vitamin D₃ at a dose of 4000 IU (BPH + vit. D group); Sabal palm fruit extract at a dose of 35 mg/kg b.w. (BPH + Ref group); or vitamin D₃ and Sabal palm fruit extract at the same doses (BPH + vit. D + Ref group) were administered together. Sexual behavior, genital organ mass, and serum testosterone (T) and estradiol (E₂) levels were determined. The probability of differences in mean values was determined by Student's t test. The χ^2 test was used for comparative analysis of relative values. Differences were considered significant at $p < 0.05$.

Results. In the BPH group, the prostate mass increased, and in the BPH + Vit. D + Ref group, the organ mass normalized. Serum total T levels in the BPH group decreased by 1.66 times, and the T/E₂ ratio was 1.53 times lower than in the control group. When using corrective substances, the T concentration normalized. The T/E₂ ratio increased by 1.5 times. In the BPH group, both the courtship and copulatory components of sexual behavior were impaired, and no male in this group ejaculated. In the BPH+Ref group, the latency period for the onset of mounts (by 2.7 times) and intromissions (by 1.7 times) decreased, the number of courtship behaviors decreased by 1.9 times, compared to the BPH group. In animals in the BPH+vit. D+Ref group, the latency period for mounts decreased by 3.3 times, intromissions — by 4.4 times, the number of mounts and intromissions increased by 2.2 and 2.9 times compared to the BPH group. Ejaculations were recorded in 40% of males in this group.

Conclusions. Experimental sulphiride-induced prostatic hyperplasia is accompanied by an increase in the mass of prostate, an imbalance of hormonal ratios, and suppression of sexual behavior parameters. The combined use of vitamin D and saw palmetto fruit extract corrects benign prostatic hyperplasia, promotes normalization of prostate mass, an increase in testosterone levels, and restores the ratio of sex hormones, and improves both the courtship and copulatory components of the sexual behavior in rats.

Key words: benign prostatic hyperplasia, vitamin D, saw palmetto fruit extract, male rats, testosterone, sexual behavior.

**ЗАСТОСУВАННЯ ВІТАМІНУ D ТА ЕКСТРАКТУ ПЛОДІВ ПАЛЬМИ САБАЛЬ
ЗА УМОВ ЕКСПЕРИМЕНТАЛЬНОЇ ПАТОЛОГІЇ ПЕРЕДМІХУРОВОЇ ЗАЛОЗИ**

Белкіна І. О.¹, Смоленко Н. П.¹, Коренева Є. М.¹, Мараховський І. О.¹,
Ткаченко Н. О.², Проценко О. С.², Благовещенський Р. Є.³,
Бондаренко В. О.¹, Місюра К. В.¹

¹ ДУ «Інститут проблем ендокринної патології ім. В. Я. Данилевського НАМН України»,
м. Харків, Україна;

² Харківський національний університет імені В. Н. Каразіна, м. Харків, Україна;

³ Харківський національний медичний університет, м. Харків, Україна
inna_bel@i.ua

Доброякісна гіперплазія передміхурової залози (ДГПЗ) являє собою серйозну проблему, що значно знижує якість життя чоловіків, тому пошук нових простатопротекторів є надзвичайно актуальним. Мета: визначити вплив вітаміну D та екстракту плодів пальми Сабаль на масу простати, рівень статевих гормонів та статеву поведінку за умов експериментальної патології передміхурової залози.

Матеріали та методи. Патологію простати викликали введенням 12 міс. самцям нелінійних білих щурів розчину сульфпіриду у дозі 40 мг/кг м.т. протягом 30 діб (група ДГПЗ). Для корекції протягом 21 діб надавали *per os* вітамін D₃ в дозі 4000 МО (група ДГПЗ + віт. D); екстракт плодів пальми Сабаль у дозі 35 мг/кг м.т. (група ДГПЗ + Реф); або сумісно вітамін D₃ та екстракт плодів пальми Сабаль у тих самих дозах (група ДГПЗ + віт. D + Реф). Визначали статеву поведінку, масу статевих органів, рівні тестостерону (Тс) та естрадіолу (Е₂) у сироватці крові. Вірогідність розбіжностей середніх величин визначали за t критерієм Ст'юдента. При порівняльному аналізі відносних величин використовували критерій χ^2 . Розбіжності вважали значущими при $p < 0,05$.

Результати. У групі ДГПЗ маса простати збільшилась, а в групі ДГПЗ + віт. D + Реф маса органу нормалізувалась. У групі ДГПЗ знижувався рівень загального Тс в 1,66 раза, коефіцієнт Тс/Е₂ був в 1,53 раза менше, ніж у контролі. При застосуванні коригувальних речовин концентрація Тс нормалізувалась. Співвідношення Тс/Е₂ підвищувалось в 1,5 раза. У групі ДГПЗ погіршувалися як залицяльні, так і копулятивні складові статеві поведінки, у жодного самця цієї групи не було еякуляції. У групі ДГПЗ + Реф знижувався латентний період настання садок (у 2,7 раза) та інтромісії (в 1,7 раза), в 1,9 раза знижувалась кількість залицяльної поведінки у порівнянні з групою ДГПЗ. У тварин групи ДГПЗ + віт. D + Реф латентний період садок зменшився в 3,3 раза, інтромісією — в 4,4 раза, кількість садок та інтромісії збільшилась у 2,2 та 2,9 раза проти групи ДГПЗ. Еякуляції реєструвались у 40% самців цієї групи.

Висновки. Експериментальна сульфпірид-індукована гіперплазія передміхурової залози супроводжується збільшенням маси простати, розбалансуванням гормонального співвідношення, пригніченням показників статеві поведінки. Сумісне використання вітаміну D та плодів пальми Сабаль корегує доброякісну гіперплазію передміхурової залози, сприяє нормалізації маси простати, зростанню рівня тестостерону та нормалізації співвідношення статевих гормонів, покращує як залицяльну, так і копулятивну складові статеві поведінки щурів.

Ключові слова: доброякісна гіперплазія передміхурової залози, вітамін D, екстракт плодів пальми Сабаль, самці щурів, тестостерон, статеву поведінку.