PERIODICUM BIOLOGORUM
VOL. 126, No 3–4, 177–185, 2024
DOI: 10.18054/pb.v126i3-4.32801

UDC 57:61
CODEN PDBIAD
ISSN 0031-5362

Original research article

Effect of *Urtica dioica* root hydroalcoholic extract on testosterone and high-calorie diet-induced benign prostate hypertrophy (BPH) in mice

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Keywords: benign prostatic hypertrophy; *Urtica dioica*; testosterone; high-calorie diet; prostate-specific antigen.

Abstract

Background and purpose*: Benign prostatic hypertrophy (BPH) is one of the most common pathologies affecting the urogenital system of the elderly man.* Urtica dioica*, a plant rich in antioxidants, is used in traditional medicine to treat BPH urinary symptoms. This study aims to evaluate the effects of hydroalcoholic extract from* Urtica dioica *roots on benign prostatic hyperplasia (BPH) induced by testosterone and a high-calorie diet.*

Material and methods: *Antioxidant activity of plant root extract and polyphenol assay were performed.* In vivo *experiments included serum biochemical assays and histological analysis of the murine prostate tissue. A population of 16 male mice divided into 4 groups; a control group (group 1), a group 2 receiving an intraperitoneal injection of testosterone (0.5 mL / week) and a high calorie diet (HCD), group 3 received testosterone, HCD and 0.2 mL of the* Urtica dioica *root hydroalcoholic extract (14.8 mg / mL) and a group 4 received HCD and the extract.*

Results: *The inhibition rate and the polyphenol content were respectively 21.3 % and 60.3 µg / mL gallic acid. The body weight of the mice (group 2) was 41.15 ± 1.62 g, in contrast to the group 3 which weighed 36.64 ± 1.38 g. A decrease in blood glucose in group 3 (0.84 ± 0.13 g / L) was observed compared to group 2 (1.09 ± 0.32 g / L). Prostate-specific antigen (PSA) was increased in group 2 (0.25 ng / mL) and decreased in group 3 (0.18 ng / mL). In group 2, prostatic glands and fibro-muscular tissue exhibited an enlarged appearance whereas animals treated with* Urtica dioica *extract had narrower glands and acini of regular shape.*

Conclusion: Urtica dioica *root hydroalcoholic extract demonstrated a beneficial effect on testosterone and high-calorie diet-induced BPH in mice. The treatment reduced prostate enlargement, improved blood glucose levels, and decreased PSA levels, suggesting potential anti-inflammatory or metabolic regulatory properties. However, the exact mechanisms underlying these effects remain unclear and require further investigation.*

Received September 14, 2024
Revised January 15, 2025
Accepted January 16, 2025

INTRODUCTION

The most elderly people are affected by pathologies as they age. Prostatic pathologies can have a direct or indirect impact on sexuality for reproductive purposes. If the various sexual functions can be altered, their impact varies greatly according to age *(1)*. Thus, the consequences on fertility due to ejaculation disorders are much more serious in young

subjects (of childbearing age) than after 50 years *(2)*. Benign prostatic hyperplasia (BPH), or prostatic adenoma, generally affects men over the age of 50. More than 50 % of men aged 60 are affected, and 90 % of those with age more than 80 years *(3)*. This gland of the male reproductive system, which produces sperm, grows so large that it presses on the urethral canal and the bladder, causing difficulty in urinating *(4)*. Benign prostatic hyperplasia is characterized by a proliferation of cells leading to an increase in the volume of the prostate gland. Hyperplasia describes a pathological process. The excessive growth of cells is linked to hormonal changes (testosterone and dihydrotestosterone). Benign prostatic hyperplasia is a medical term often used in human pathology. Benign prostatic hypertrophy refers to an increase in the size of cells without necessarily an increase in the number of cells. In both cases, the symptoms are similar, such as obstructive urinary disorders, and is common in men from the age of 50. In animal studies, it is preferable to use the term hypertrophy instead of hyperplasia. This term is reserved for human health.

The use of drugs (synthetic chemicals), to treat these pathologies, has shown its limits and most drugs induce undesirable side effects after excessive consumption. For example, certain drugs over time attack regulatory metabolic organs including kidney and liver tissue which would expose patients to the risks of cirrhosis, hemodialysis, hyperglycemia, and hormonal disorders *(5)*. The growing focus on long-term well-being and natural health, in contrast to the discomfort caused by industrial chemical drugs, has led the scientific community to explore more affordable alternatives, aiming to shift patients away from the reliance on conventional medicine. This paper highlights the potential of local medicinal plants in treating benign prostatic hypertrophy (BPH), a condition increasingly common due to modern western diets and other risk factors such as genetics and environmental influences. It emphasizes the importance of the Mediterranean diet, rich in vegetables, fruits, fish, and olive oil, which contain beneficial compounds like polyphenols, flavonoids, alkaloids, tannins, and terpenes, proven effective in various studies *(6)*. BPH can be treated naturally with a medicinal plant including nettle (*Urtica dioica*). The present study is focused on this plant species which is locally present in different areas of our region growing in ambient climatic conditions and temperature. *Urtica dioica* is an herb often used for its therapeutic properties. Furthermore, its aerial or underground plant parts (leaves, stem and roots) can be used to prevent and alleviate the pain and symptoms of BPH *(7)*. *Urtica dioica* extract and essential oil are known for their pharmacological, anti-inflammatory, antioxidant and antimicrobial properties *(7–10)*. *Urtica dioica* is a plant rich in vitamins, minerals, polyphenols, flavonoids, alkaloids, terpenes, saponins and tannins providing them medicinal properties *(7, 11, 12)*. The aim of this study was to evaluate the effects of hydroalcoholic *Urtica dioica* root extract on BPH induced in mice by testosterone and a high-calorie diet.

MATERIALS AND METHODS

Phytochemical study

Harvesting *Urtica dioica* roots

The plant material used in this study consisted of the *Urtica dioica* roots, harvested during the autumn season in a depolluted area named Ain Sultan, located in the province of Saida. The *Urtica dioica* roots were dried at room temperature, protected from humidity for an extended period until they were ready for the extract preparation.

Plant identification

Urtica dioica has been identified and authenticated at the Water Resources and Environment Research Laboratory, Department of Biology, Faculty of Nature and Life Sciences, University of Saida, Algeria. The identification of the plant was based on the use of two specialized scientific books, namely *"Encyclopedia of Medicinal Plants"* and *"Aromatic and Medicinal Plants"*.

Urtica dioica root hydroalcoholic extract preparation

The extraction method was a maceration, which consisted of the preparation of a hydroalcoholic extract from the powder of the roots of the *Urtica dioica* plant. Briefly, 150 g of roots were ground into powder using an electric grinder. This powder was then dissolved in a mixture of solvents consisting of a volume of 1400 mL of distilled water and a volume of 600 mL of methanol. The mixture, after stirring, was protected from light for a period of 72 hours, and then filtered through a Wattman No. 1 filter paper. The filtrate was then evaporated using a rotary steamer at 60°C. The hydroalcoholic root extract obtained was dried in an oven for 48 hours. The dry extract was weighed, dissolved in physiological water and then stored at 4°C until use.

Extraction yield

The yield of the extract is defined as being the ratio between the mass of the dry extract obtained after maceration (M') and the mass of the plant material used (M). It is given by the following formula: Yield = (M/M') × 100.

Antioxidative activity of the extract

At room temperature, the DPPH radical exhibits an intense violet color which disappears on contact with a proton-donating substance. This discoloration highlights the antioxidant power of a sample by its ability to trap the free radical and results in a decrease in absorbance at 515 nm. A volume of 50 µl of methanolic solution of the ex-

tract at different concentrations is added to 1.95 ml of the methanolic solution of DPPH (0.025 g/l). At the same time, a negative control is prepared by mixing 50 µl of methanol with 1.95 ml of the methanolic solution of DPPH. The absorbance reading is made against a blank prepared for each concentration at 515 nm after 30 min of incubation in the dark and at room temperature. The results were expressed as percentage inhibition (I%). IC_{50} values were determined graphically by linear regression *(13)*.

$I_{\%}$ = [(Abs control – Abs test)/ Abs control] x 100

Total polyphenol content

Total phenolic compounds were assayed using Folin Ciocalteu's reagent, according to the method of Singleton and Rosi *(14)*. Folin Ciocalteu's reagent consists of a mixture of phosphotungstic acid ($H_3PW_{12}O_{40}$) and phosphomolybdic acid. It is reduced, during the oxidation of phenols, to a mixture of blue oxides of tungsten and molybdenum. The blue color produced is proportional to the amount of polyphenols present in the reaction medium *(15)*.

A volume of 100 µL of the extract at different concentrations is added to 0.5 mL of distilled water and 0.125 mL of Folin-Ciocalteu reagent. The mixture was shaken and incubated for 6 min before adding 1.25 ml of Na_2CO_3 (7 %). The solution was then adjusted with distilled water to a final volume of 3 mL and mixed thoroughly. After incubation in the dark, the absorbance was read at 760 nm against a prepared blank. The total contents of phenolic compounds were expressed in milligrams of gallic acid equivalent per gram of dry residue (mg GAE g-1 DR) on the calibration curve with gallic acid *(15)*.

In vivo *study*

Animal material

The breeding of mice was carried out at the biology department, Faculty of Sciences, University of Saida, Algeria. The maintenance of the animals was carried out in a lighted room 12 hours a day, it is a photoperiod of 12 hours / 24 hours whose temperature was kept constant (22-25 °C). The mice were housed and separated into four plastic cages. They had free access to water and food. Animals were treated in accordance with the principles and guidelines set out in the Care and Use of Experimental Animals Manual. Article 58 of Algerian law 88-08 of 1988 includes a general prohibition of committing 'bad treatments' towards animals. Article 58 also states that the same prohibition applies in relation to animals used in biological, medical and scientific experiments, which experiments are required to be 'limited to cases of strict necessity' *(16)*. Infringement of the provisions in law 88-08 and in the Algerian penal code, referred to above, is punishable by fines and/or imprisonment under articles 415,443, 449 and 457 of the Algerian penal code *(16, 17)*.

Experimental design

A population of sixteen male C57BL/6 mice, 8 weeks old with a weight ranging from 25-29 grams, were divided into 4 groups. Each group consisted of four mice. Each cage was separated into 4 boxes where only one mouse could be housed (Figure 1). This procedure made it possible to control food intake or the amount of food consumed per day. The experimental period was 30 days. The animals were divided as follows:

Group 1: controls received a standard diet (30 g / day), purchased from ONAB (national office for livestock feed).

Group 2: animals were injected intraperitoneally with testosterone (0.5 mL/week), fed with standard diet (30 g/ day) and a high-calorie diet (10 g of chocolate and cheese per day).

Group 3: animals were injected with testosterone (0.5 mL / week), fed with a standard diet (30 g/day) and high calorie diet (10 g of chocolate and cheese) then also were injected intraperitoneally with a 0.2 mL *Urtica dioica* root hydroalcoholic extract three times per week (i.e., 14.8 mg / mL).

Group 4: animals received a standard diet (30 g / day), a high-calorie diet (10 g of chocolate and cheese) and injected intraperitoneally with an *Urtica dioica* root hydroalcoholic extract (14.8 mg / mL) in the same conditions.

Biochemical tests

Blood samples were taken from mice every 10 days for a month. Blood was collected from the retro-orbital sinus of the mice. Blood was collected into heparinized tubes intended for the biochemical assays. Serum assays for glucose, urea, creatinine, cholesterol, glycerides, hepatic transaminases and prostate-specific antigen (PSA) were performed respectively by enzymatic methods with glucose oxidase, urease, colorimetric methods and immunoassay such as ELISA.

Histology

At the end of the experimental period, the animals were anesthetized and then sacrificed. Prostatic tissues were removed for histological study. samples were preserved in 10% formalin solution until use. Histological sections were performed in the Anatomopathology Department of the Center Hospitalier de Nice, France. The technique includes the following steps: the samples were fixed in 10% formaldehyde, dehydration of the samples in successive baths of ethanol, inclusion of the samples in paraffin, after cooling of the paraffin blocks to -20°C (18).

Sections of paraffin-embedded tissue were cut into 4 µm thick slices using a Microm HM 340 E manual microtome (Thermo Scientific, Illkirch). The tissue sections were then stained using the Hematoxylin-Eosin technique.

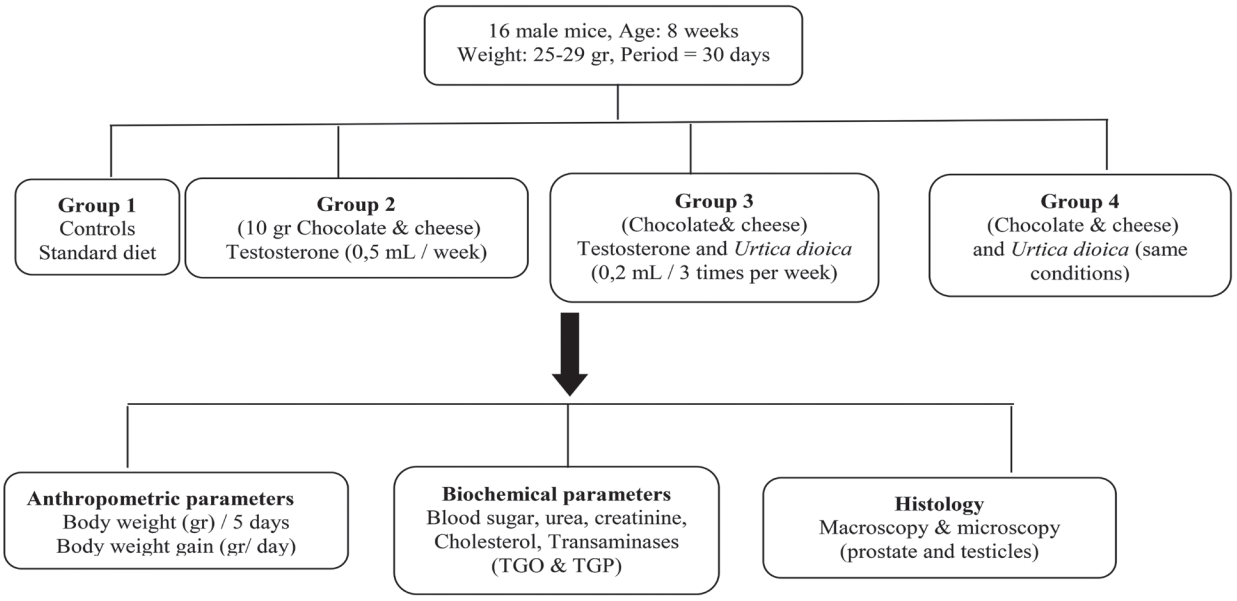


Figure 1. *Experimental design of plant root extract effects on BPH mice.*

Statistical Analysis

Data were expressed as error of mean standard (ESM). To compare the differences between groups, one-way analysis of variance (ANOVA) followed by Tukey test was performed for multiple comparisons. A p-value < 0.05 was considered statistically significant. All analyses were conducted using Sigmaplot (version 11).

RESULTS

Phytochemical study

Yield of the extraction

The maceration technique produced a hydroalcoholic extract from *Urtica dioica* root characterized by a brown color, an aromatic smell and a yield of 9.66 %.

Antioxidant activity

Figure 2 shows that the *Urtica dioica* root crude hydro-methanolic extract and ascorbic acid have inhibitory, oxidizing and DPPH radical-scavenging activities proportional to increasing concentrations of the crude extract and the ascorbic acid. The concentration of the nettle extract analyzed was 14.8 mg/mL which corresponds to an inhibition rate of 21.3% compared to the concentration of ascorbic acid 0.3 mg/mL which has an inhibition rate of 86.6 %.

A concentration of *Urtica dioica* root hydro-methanolic extract of around 50 mg/mL corresponded to an absorbance of 0.38 and a level of total polyphenols of 208.5 µg/mL. Concerning the sample studied, the extract had a concentration of 14.8 mg/mL corresponding to an absorbance of 0.11 and a level of total polyphenols of 60.3 µg/mL (Figure 3).

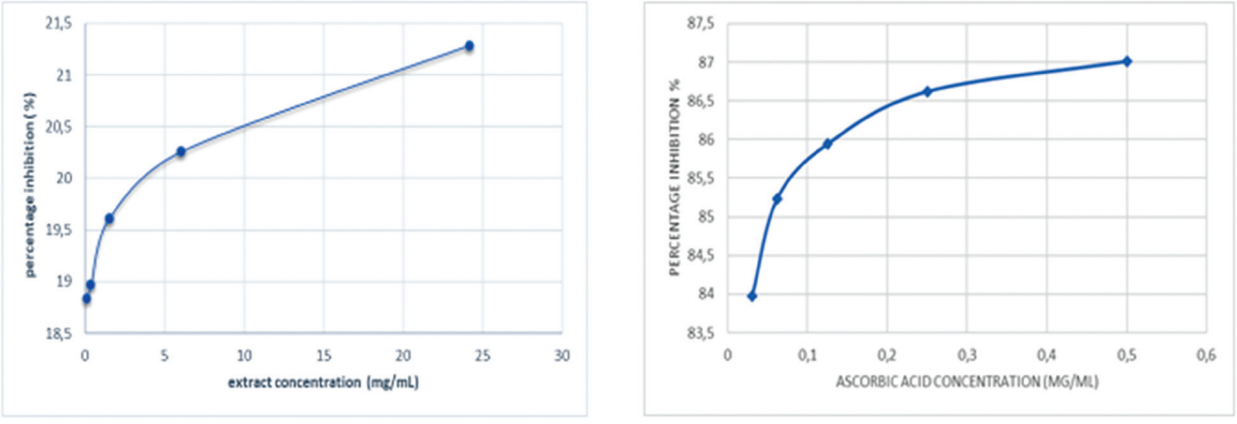


Figure 2. *Antioxidant activity of Urtica dioica root hydroalcoholic extract.*

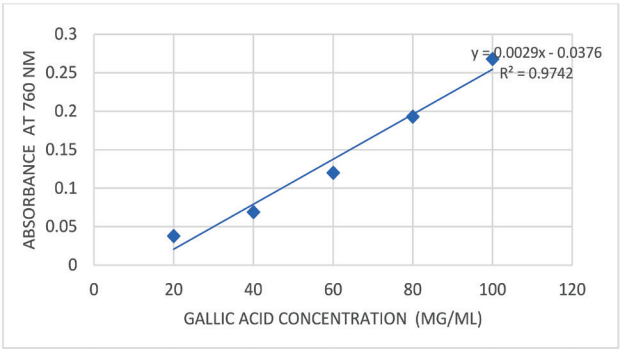


Figure 3. *Total polyphenol content in Urtica dioica root hydroalcoholic extract.*

In vivo *study*

Body weight gain

The results, shown in Table 1, revealed a significant variation in the body weights of the animals in the different groups ($p<0.05$). The weight of mice treated with testosterone (group 2) showed a significant increase in body weight compared to control mice. On the other hand, the weight of the animals (group 3), initially exposed to testosterone and then treated with *Urtica dioica* root hydroalcoholic extract, decreased compared to group 2. Moreover, the mice treated with testosterone (group 2) by intraperitoneal injection, developed a high weight gain unlike the animals treated with testosterone and *Urtica dioica* (or nettle) root hydroalcoholic extract (group 3), while the animals treated only with the plant extract (group 4) had recorded a low weight gain.

Biochemical tests

Biochemical parameters (blood sugar, triglycerides, total cholesterol, urea and creatinine) shown in Table 1 do not have statistical differences between experimental groups. The only two parameters that show statistical significance are hepatic transaminase activities GOT (glutamate oxaloacetate transaminase) and GPT (glutamate oxaloacetate transaminase).

Elevated serum GOT is a sign of liver dysfunction. The treatment of animals with only *Urtica dioica* root hydroalcoholic extract suggested a decrease in the enzymatic activity of this hepatic marker.

The serum assay of the prostatic tumor marker was carried out in the male mice of the different groups studied. Prostate-specific antigen (PSA) was elevated in animals treated only with testosterone (0.25 ng/mL) compared to control animals (0.11 ng/mL) (Table 1). The treatment of animals (groups 3 and 4) with the hydroalcoholic extract of the roots of the Urtica dioica plant resulted in a decrease in PSA compared to the group of animals treated with only testosterone (Table 1).

Histology

Also, macroscopic features of the prostate were analyzed in all experimental groups. During this study, tissue was the target of testosterone, and a high-calorie diet supplemented with chocolate and cheese. The prostate tissue was

Table 1. *Anthropometric and biochemical parameters in control and experimental animal groups.*

Variables studied (average value ± SEM)	Group 1	Group 2	Group 3	Group 4	p-value
Body weight (g)	36.9±0.67	41.15±1.62	36.64±1.38	36.59±0.88	0.031
Body weight gain (g/j)×10-3 (Wi – Wf) / 30 days	0.0±0.0	30±7	27±6	–0.8±0.5	0.97
Blood sugar (mg/dL)	1.28±0.17	1.09±0.32	0.84±0.13	0.96±0.12	0.52
Triglycerides (mg/dL)	1.1±0.1	1.12±0.35	1.36±0.37	1.07±0.28	0.89
Total cholesterol (mg/dL)	1.33±0.17	1.41±0.16	1.41±0.65	1.45±0.02	0.96
GOT (UI/L)	125±1.5	126±24.2	136.5*±19.4	70.5*±6.5	0.006
GPT (UI/L)	35.88±1.04	78.56±11.2	102*±13.23	58.5±3.88	0.009
Urea (g/L)	0.46±0.08	0.38±0.11	0.26±0.11	0.30±0.13	0.63
Creatinine (mg/L)	15.47±1.48	13.36±3.57	10.51±2.12	13.04±2.52	0.63
PSA (ng/mL)	0.11±0.00	0.25±0.001	0.18±0.00	0.10±0.00	–

SEM: standard error of mean, Wi; initial weight, Wf: final weight, GOT: glutamate oxaloacetate transaminase, GPT: glutamate pyruvate transaminase, PSA: prostate specific antigen. Group 1 (controls), group 2 (testosterone + high calorie diet), group 3 (testosterone + high calorie diet + Urtica dioica *extract) and group 4 (high calorie diet* + Urtica dioica *extract). *: Significantly different results*

Table 2. *Morphological characteristics of prostate tissue in different groups of animals.*

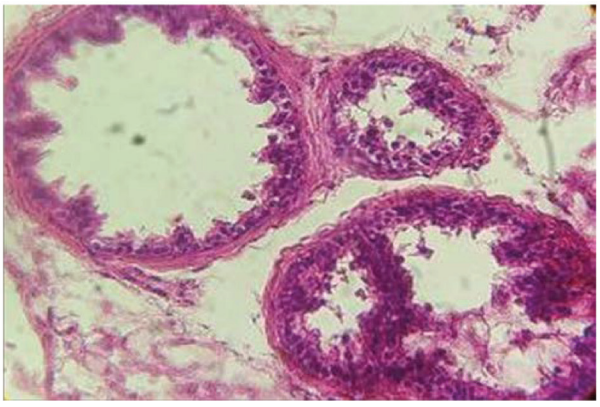
Morphological characteristics of prostate	Group 1	Group 2	Group 3	Group 4	*p*-value
Appearance	Normal. spongy	Hyperplasia. voluminous	Less hyperplastic	Normal	–
Shape	Regular. round	Irregular	More or less regular	Regular	
Color	Redish	Redish	Redish	Redish	–
Size (L×W in cm)	1.5×0.9	2.4×1.1	1.9×0.12	1.7×0.43	–
Tissue weight (g)	0.66±0.012	0.99±0.002	0.70±0.002	0.50±0.001	–
Body weight (g)	39.60±0.67	41.15±1.62	36.64±1.38	36.59±0.88	0.031
Index (TW / BW)×10^{-2}	16.66	24.00	19.10	13.66	–

L: length, W: wide, TW: tissue weight, BW: body weight.

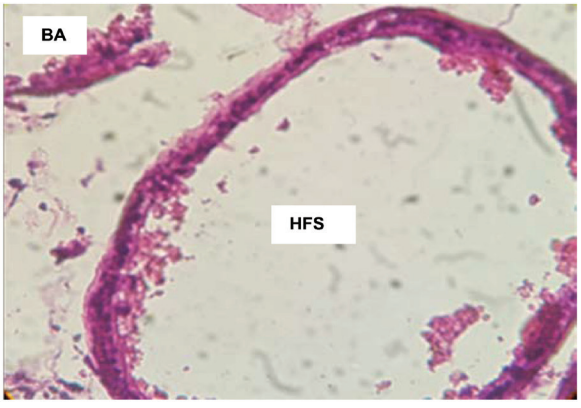
morphologically assessed by determining its weight, size, appearance, and color. These ratings are shown in Table 2. The macroscopic study made it possible to verify whether there were any morphological tissue changes such as the presence of cysts or necroses, edema and vascular congestion, hyperplasia or hypertrophy in the samples taken from the male mice of the different groups.

Finally, a histology of the prostate tissue from all experimental groups was made. Figure 4 shows the microscopic examination of the prostate tissue of control mice and those exposed to testosterone, high calorie diet and then treated with the *Urtica dioica* root hydroalcoholic extract.

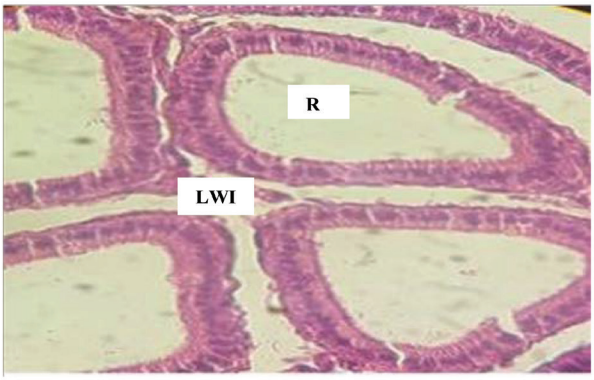
In the group of mice exposed to testosterone and a high-calorie diet (group 2), the prostate showed disorga-



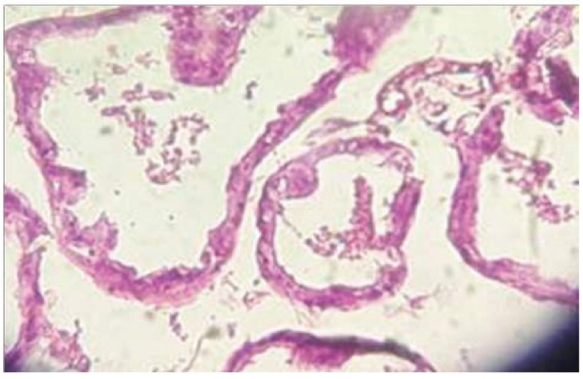
Group 1: Prostatic gland with normal acini (Hem-Eos × 10).



Group 2: Prostatic gland with burst acini (BA) and hypertrophy of the fibrous stroma (HFS). (Hem-Eos × 40).



Group 3: Prostatic acini maintained their regular appearance (RE) and a less wide inter-glandular space (LWIS) (Hem-Eos × 10).



Group 4: normal profile of prostatic acini resembling that of control mice (Hem-Eos × 40).

Figure 4. *Histology of the prostate glands of control and experimental animal groups (HE stain), magnifications ×10 and × 40.*

nized tissue and cellular architecture. In this same group, the prostate glands showed large, hypertrophic, sometimes even burst acini. The fibromuscular tissue, the stroma and the inter-glandular spaces were also large or even hypertrophic (Figure 4). The tissue structure of the prostate was severely compromised. Prostate acini were irregularly shaped and distant from each other, in contrast to the control group, which had a prostate of normal shape and size (Figure 4).

Animals, previously treated with testosterone then treated with the Urtica dioica root hydroalcoholic extract, showed organized tissue and cellular structure. The prostate glands, or acini, were less enlarged. The inter-glandular spaces, or fibromuscular mesenchymal tissue, were narrower compared to group 2. In mice treated only with the nettle root hydroalcoholic extract, the prostate tissue presented a structure and an organization almost identical to that of the controls (Figure 4).

DISCUSSION

Benign prostatic hyperplasia (BPH) is a common public health problem in men over the age of 50 affecting quality of life. The BPH etiology is multifactorial and dominated by the hormonal factor *(19)*, not neglecting the biochemical changes responsible for the development of BPH *(20)*. The secretion of testosterone has great physiological effects on the development of male genital organs (seminal vesicles, prostate and seminiferous tubules) and on the development of male secondary sex characteristics. The biochemical mechanisms underlying the physiological effects of testosterone on the prostate gland are not well understood. In target tissues like the prostate, testosterone does not directly stimulate the growth and development of the gland; instead, its derivative, dihydrotestosterone (DHT), is responsible for this effect. The testicular enzyme (5α-reductase) transforms testosterone into its most active derivative DHT *(21)*.

DHT binds to specific nuclear receptors, which recognize and attach to DNA regulatory sequences, triggering the transcription of messenger RNA (mRNA) that is then translated into proteins.

These proteins trigger mitosis thus increasing cell number and the mass of prostate tissue. Other proteins stimulate cellular metabolism and thus the increase in cell size leading to the BPH appearance *(21)*.

A study, conducted over seven years, assessed the association between dietary factors and the progression of BPH symptoms in 4770 men aged 55 or older with clinical BPH. This study found that regular consumption of milk or milk products such as cheeses that are high in saturated fatty acids appeared to lead to a 31% greater risk of worsening of BPH symptoms *(22, 23)*.

Men who ate red meat daily had a 38% higher risk of experiencing BPH symptom progression compared to those who consumed it once a week. Vegetables appear to play a protective role since men who eat three or more servings of vegetables a day compared to those who eat only one have a 32% lower risk of BPH symptom progression. Vegetables and fruits contain antioxidants, polyphenols, minerals and fiber that may play a beneficial role in the inflammatory processes associated with the progression of BPH *(22)*.

Urtica dioica roots are the parts exploited for the treatment of urinary symptoms of BPH. Root extract composition contains lectin (*Urtica dioica* aglutinin), polysaccharides (glycans, glucogalacturonan and arabinogalactan acid), sterols (β-sitosterol, stigmasterol and campesterol), lignans (secoisolariciresinol-9-O-glucoside, 3,4-divaniltetraidrofuran, neo-olivile) and ceramides (amides of fatty acids with poly-hydroxy-alkylamines) *(23)*. The mechanisms by which the bioactive components of Urtica dioica roots affect prostate cells are not yet clearly understood, although certain pharmacological effects have been proposed *(24)*.

Sex hormone-binding globulin (SHBG), hepatic glycoprotein, on the one hand binds to testosterone or its derivative DHT to transport them and on the other hand SHBG binds to its specific intracellular receptor in the prostate cell. SHBG-testosterone, or SHGB-DHT, complex stimulates the cAMP signaling pathway. This signaling pathway stimulates the synthesis of growth factors that lead to prostatic cell proliferation and possibly the development of BPH *(25)*. *In vitro* study showed the effect of *Urtica dioica* root aqueous extract (10 mg/mL) on a culture of prostate cell membranes taken from BPH patients. This study suggested that the secondary metabolites, lignans, inhibited the binding between SHBG and its prostate receptor. Lignans would seem to affect the interaction of SHBG with its receptor and thus contribute to the slowing down of prostatic cell proliferation *(24)*.

In vivo study, carried out on rats with BPH induced by subcutaneous injection of testosterone, revealed that *Urtica dioica* root alcoholic extract (ethanol) had an inhibitory effect on the activity of the prostatic enzyme 5-α-reductase. Serum prostate-specific antigen (PSA) level and prostate weight (PW) to body weight (BW) ratio were measured. The animals, treated with the extract of the roots, showed a decrease in the ratio and the level of PSA. The decrease in the levels of these two parameters indicates inhibition of 5-α reductase *(26)*. *Urtica dioica* root extract contains various bioactive molecules, including β-sitosterol and scopoletin, which are believed to play a role in inhibiting the activity of the enzyme 5-α reductase, thereby preventing rapid cell growth and an increase in prostate weight and volume *(26)*.

So far, only extracts from *Urtica dioica* roots have shown therapeutic activities against BPH and are widely used as drugs in Europe. Extracts from *Urtica dioica* leaves are used as anti-inflammatory remedies in rheuma-

toid arthritis *(27)*. Previous studies indicate that *Urtica dioica* root components may interfere with several mechanisms involved in the BPH pathogenesis *(28, 29)*. Treatment with *Urtica dioic*a root extracts can reduce prostate volume by 70% and decrease the frequency of urination. While this is not a definitive cure, it significantly improves comfort and quality of life. These studies are in accordance with the results of this present study which showed a decrease in PSA in animals that were treated with *Urtica dioica* root extract. From this, it can be concluded that nettle has a preventive effect against benign prostatic hypertrophy.

CONCLUSION

This study demonstrated that increased prostate weight in an animal model was associated with testosterone and high calorie diet. Previous research has shown that testosterone and obesity in certain animals lead to an increase in prostate volume and weight. It is well established that androgen stimulation (such as with testosterone) can enhance oxidative stress in prostate cells by activating specific metabolic pathways. In contrast, drugs with antiandrogenic effects can reduce the oxidative stress responsible for BPH. The results of this study revealed that the treatment of BPH-affected animals with a hydroalcoholic extract of Urtica dioica root reduced both prostate weight and serum PSA levels. *Urtica dioica* has been shown to have an antioxidant activity contributing to its anti-androgenic activities. This study provides scientific support for future investigation on the treatment of BPH at the cellular and molecular level.

REFERENCES

1. OBEAGU EI, ALUM EU, OBEAGU GU, UGWU OP 2023 Benign Prostatic Hyperplasia: A Review, Eurasian experiment journal of public health (EEJPH), 4 (1): 1–4.
2. KOUDONAS A, ANASTASIADIS A, TSIAKARAS S, LANGAS G, SAVVIDES E, MYKONIATIS I, MEMMOS D 2023 Overview of current pharmacotherapeutic options in benign prostatic hyperplasia. Expert opinion on pharmacotherapy, https://doi.org/10.1080/14656566.2023.2237406
3. ZADVORNYI T, LUKIANOVA N, TETIANA B, KASHUBA O, STAKHOVSKY E, VITRUK Y 2023 Features of the expression of matricellular genes (osteopontin and osteonectin) in benign and malignant tumors of the prostatic gland, Oncology, 25: 47–54. https://doi.org/10.1159/000524567
4. NEPAL S, ASLANI Z, SHI N, TABUNG F 2023 Associations of Dietary Patterns with Colorectal Adenomas in the Prostate, Lung, Colorectal and Ovarian Cancer (PLCO) Cohort, Cancer Epidemiology Biomarkers & Prevention, https://doi.org/10.1158/1055-9965.EPI-23-0143
5. OLUDARE A, IJIMBILI S, OFUASIA G, ANEJO-OKOPI J, WAHEDI J, JASINI O 2023 Prostate Cancer: Causes and Medicinal Plants Used in Africa for Twenty Years (2001–2021), Pharmacognosy Journal, 14: 822–828. https://doi.org/10.5530/pj.2023.14.105
6. BASATI G, GHANADI P, ABBASZADEH S 2020 A review of the most important natural antioxidants and effective medicinal plants in traditional medicine on prostate cancer and its disorders, J Herbmed Pharmacol., 9(2): 112–120. https://doi.org/10.34172/jhp.2020.15
7. BHUSAL KK, KHASU MAGAR S, THAPA R, LAMSAL A, BHANDARI S, MAHARJAN R, SHRESTHA S, SHRESTHA J 2022 Nutritional and pharmacological importance of stinging nettle (Urtica dioica L.): A review, Heliyon, 09717. https://doi.org/10.1016/j.heliyon.2022.e09717
8. MANGANELLI RU, ZACCARO L, TOMEI PE 2005 Antiviral activity in vitro of Urtica dioica L., Parietaria diffusa M. and Sambucus nigra L., J. Ethnopharmacol., 98 (3): 323–327. https://doi.org/10.1016/j.jep.2005.01.025
9. KATAKI MS, MURUGAMANI V, RAJKUMARI A, MEHRA PS, AWASTHI D, YADAV RS 2012 Antioxidant, hepatoprotective, and anthelmintic activities of methanol extract of Urtica dioica L. leaves, Pharmaceut. Crop, 3 (1): 38–46. https://doi.org/10.2174/2210290601203010038
10. FARAHPOUR MR, KHOSHGOZARAN LIDA 2015 Antinociceptive and anti-inflammatory activities of hydroethanolic extract of Urtica dioica., Int. J. Biol. Pharm. Allied Sci., 1:160–170. https://doi.org/10.1234/ijbpas.v1i1.123
11. SAID AAH, OTMANI ISE, DERFOUFI S, BENMOUSSA A 2015 Highlights on nutritional and therapeutic value of stinging nettle (Urtica dioica L.), Int. J. Pharm. Pharmaceut. Sci., 7 (10): 8–14. https://doi.org/10.22159/ijpps.2015v7i10.8245
12. JAN KN, ZARAFSHAN K, SINGH S 2017 Stinging nettle (Urtica dioica L.): a reservoir of nutrition and bioactive components with great functional potential, Food Measure, 11 (2): 423–433. https://doi.org/10.1007/s11694-016-9420-4
13. MOON JK, SHIBAMOTO T 2009 Antioxidant Assays for Plant and Food Components, J. Agric. Food Chem., 57, 1655–1666. https://doi.org/10.1021/jf803537k
14. SINGLETON V L, ROSSI J A 1965 Colorimetry of total phenolics with phosphomolybdic-phosphotungstic acid reagents. American Journal of Enology and Viticulture, 16 (3), 144–158. https://doi.org/10.5344/ajev.1965.16.3.144
15. SERAIRI BEJI R, BEN MANSOUR R, BETTAIEB REBEY I, WANNES WA, JAMELEDDINE S 2018 Does Curcuma longa root powder have an effect against CCl4-induced hepatotoxicity in rats: a protective and curative approach, Food Science and Biotechnology, 28: 181–189. https://doi.org/10.1007/s10068-018-0449-3
16. OFFICIAL JOURNAL OF THE ALGERIAN REPUBLIC 1988 Law No. 88-08 of January 26, 1988 relating to veterinary medicine activities and the protection of animal health.
17. OFFICIAL JOURNAL OF THE ALGERIAN REPUBLIC 1982 Law No. 82-04 of February 13, 1982. Contraventions relating to animals, Algerian Penal Code.
18. HOULOD P 1984. Histopathological Techniques in Medical Research. Paris: Medical Publications.)
19. LI W, WU C, FEBBO PG, OLUMI AF 2007 Stromally expressed c-Jun regulates proliferation of prostate epithelial cells, Am. J. Pathol., 171, 1189–1198. https://doi.org/10.2353/ajpath.2007.070285
20. BOREL JP, RANDOUX A, MAQUART FX, GILLERY P, LEPEUCH C, BELLON G, MONBOISSE JC 1997 Dynamic biochemistry. Edition De Boek & Larcier. Universities of Paris, Brussels.
21. KRISTAL AR, ARNOLD KB, SCHENK JM, NEUHOUSER ML, GOODMAN P, PENSON DF 2008 Dietary patterns, supplement use, and the risk of symptomatic benign prostatic hyperplasia: results from the prostate cancer prevention trial, Am J Epidemiol., 167(8):925–34. https://doi.org/10.1093/aje/kwm389
22. ROEHRBORN CG, PEREZ IO, ROOS EPM, CALOMFIRESCU N, BROTHERTON B, WANG F 2015 Efficacy and safety of a fixed-dose combination of dutasteride and tamsulosin treatment (DuodartR) compared with watchful waiting with initiation of

tamsulosin therapy men with moderately symptomatic benign prostatic hyperplasia: 2-year CONDUCT study results, BJU Int., 116, (3):450–9. https://doi.org/10.1111/bju.13033

23. WICHTL M, ANTON R 2003 Therapeutic plants. 2nd edition. TEC & DOC.
24. HRYB D, KHAN M, ROMAS N, ROSNER W 1995 The Effect of Extracts of the Roots of the Stinging Nettle (Urtica dioica) on the Interaction of SHBG with its Receptor on Human Prostatic Membranes, Planta Med., 61:31–2. https://doi.org/10.1055/s-2006-957993
25. TOSTAIN J, ROSSI D, MARTIN PM 2004 Physiology of androgens in adult men, Prog En Urol., 14:639–60.
26. NAHATA A, DIXIT VK 2012 Ameliorative effects of stinging nettle (Urtica dioica) on testosterone-induced prostatic hyperplasia in rats, Andrologia, 44, (1):396–409. https://doi.org/10.1111/j.1439-0272.2011.01197.x
27. SCHULZE-TANZIL G, BEHNKE B, KLINGELHOEFER S, SCHEID A, SHAKIBAEI M 2002 Effects of the antirheumatic remedy hox alpha – a new stinging nettle leaf extract – on matrix metalloproteinases in human chondrocytes in vitro, Histol. Histopathol., 17: 477–485.
28. ZHANG Q, LI L, LIU L, LI Y, YUAN L, SONG L, WU Z 2008 Effects of the polysaccharide fraction of Urtica fissa on castrated rat prostate hyperplasia induced by testosterone propionate, Phytomedicine, 15: 722–727. https://doi.org/10.1016/j.phymed.2007.12.005
29. MOHAMMADI A, MANSOORI B, AGHAPOUR M, BARADARAN PC, SHAJARI N, DAVUDIAN S, SALEHI S, BARADARAN B 2016 The Herbal Medicine Utrica Dioica Inhibits Proliferation of Colorectal Cancer Cell Line by Inducing Apoptosis and Arrest at the G2/M Phase. J Gastrointest Canc., https://doi.org/10.1007/s12029-016-9819-3