EFFECTS OF *Picralima nitida* STEM BARK ON HEMATOLOGICAL PARAMETERS AND PROSTATE HEALTH IN RATS INDUCED WITH BENIGN PROSTATIC HYPERPLASIA

BY

Onyeka Gloria OJEI (Miss)

LSC2007325

PHYSIOLOGY AND PHARMACOLOGY TECHNIQUE

DEPARTMENT OF SCIENCE LABORATORY TECHNOLOGY

FACULTY OF LIFE SCIENCES

UNIVERSITY OF BENIN

BENIN CITY

NOVEMBER, 2025.

EFFECTS OF *Picralima nitida* STEM BARK ON HEMATOLOGICAL PARAMETERS AND PROSTATE HEALTH IN RATS INDUCED WITH BENIGN PROSTATIC HYPERPLASIA

BY

Onyeka Gloria OJEI (Miss)

LSC2007325

PHYSIOLOGY AND PHARMACOLOGY TECHNIQUE

A PROJECT REPORT SUBMITTED TO THE DEPARTMENT OF SCIENCE LABORATORY TECHNOLOGY, FACULTY OF LIFE SCIENCES IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE AWARD OF BACHELOR OF SCIENCE (HONOURS) DEGREE (B.SC) IN SCIENCE LABORAORY TECHNOLOGY

NOVEMBER, 2025.

CERTIFICATION

THIS IS TO CERTIFY THAT THIS PROJECT WORK CARRIED OUT BY **Onyeka Gloria OJEI** with matriculation number LSC2007325 of the Department of Science Laboratory Technology, Faculty of Life Sciences, University of Benin, Benin city, Edo State, Nigeria.

DR. O.C EKHATOR _____

Project Supervisor Signature and Date

DR P. O. ALONGE _____

Project Coordinator Signature and Date

PROF. J.O. OSARUMWENSE _____

Head of Department Signature and Date

EXTERNAL EXAMINER _____

Signature and Date

DEDICATION

This work is dedicated to God Almighty, whose grace, wisdom, and strength have sustained me throughout this academic journey.

I lovingly dedicate it to my lovely mothers, whose prayers, sacrifices, and unconditional love continue to shape my path. Your encouragements, resilience, and unwavering supports have given me the courage to overcome every challenge. This achievement belongs to you just as much as it belongs to me.

I also dedicate this work to my family and friends, who have stood beside me with patience, motivation, and kindness. Your belief in me has made this journey meaningful.

Thank you all for being my pillars of strength

Last but not the least, I wanna thank me for believing in me, I wanna thank me for doing all this hard work, I wanna thank me for having no days off, I wanna thank me for never quitting, I wanna thank me for always being a giver and trying to give more than I received, I wanna thank me for trying to do more right than wrong, I wanna thank me for just being me at all times

ACKNOWLEDGEMENT

I express my sincere appreciation to my supervisor, Dr. O.C. Ekhator, for his invaluable guidance, steadfast support, and constructive feedback throughout this research project. His expertise and encouragement significantly shaped the direction and quality of this work. I remain deeply grateful for his dedication and mentorship.

My heartfelt gratitude also goes to the Head of Department, Prof. J. O. Osarumwense, whose exemplary leadership and commitment to academic excellence have created a supportive and enriching learning environment. His encouragement and motivation have contributed greatly to my success.

I extend my appreciation to all lecturers of the Department of Science Laboratory Technology for their dedication, mentorship, and the knowledge imparted throughout my program. Your collective contribution has greatly influenced my academic and personal development.

Reflecting on this journey, my heart is filled with gratitude for the love, sacrifice, and unwavering support that have accompanied me from beginning to end. To my incredible mothers, Mrs. Joy Ojo and Mrs. Mercy Unimhen, the steady anchor in my life, your prayers, sacrifices, and unconditional love have been my greatest strength. Every achievement I make stands as a testament to your resilience and belief in me. I am immensely blessed to be your child.

To my wonderful friends and family, thank you for the laughter, encouragement, and support that carried me through difficult moments. Your companionship turned challenges into stepping stones and made this experience truly rewarding. I am grateful for every memory we created together.

This work is a reflection of everyone who stood by me. I am thankful beyond words for the community that surrounds me, the love that sustains me, and the faith that continues to guide me.

CONTENTS

LIST OF TABLES

ABSTRACT

Benign prostatic hyperplasia (BPH) refers to a progressive, non-malignant enlargement of the prostate that is associated with urinary obstruction, hormonal imbalances, oxidative stress, and systemic hematological disruptions. Due to the side effects and high costs of conventional therapies, there is growing interest in medicinal plants such as *Picralima nitida*, which has traditionally been used to treat urinary tract disorders and inflammation. This study investigates the effects of an extract from the stem bark of *Picralima nitida* on hematological parameters and prostate health in male albino rats with testosterone-induced BPH. Fresh stem bark of *Picralima nitida* was collected, shade-dried, pulverized, and extracted using distilled water through decoction. The rats were divided into six (6) groups of five (5) rats each: a normal control group, a BPH-induced control group, a group was given Testosterone Pionate and standard, a group was treated with the standard medication finasteride, and two groups receiving different oral doses of the stem bark extract for a set treatment period. BPH was induced using subcutaneous testosterone propionate. Hematological parameters, including red blood cell (RBC) count, hemoglobin (Hb), packed cell volume (PCV), white blood cell (WBC) count, platelet count, and differential leukocyte indices, were measured using automated hematology procedures. Prostate weight, prostate index, and histopathological examinations were performed to assess prostate architecture and inflammation. The results showed that BPH induction led to a significant decrease in RBC indices and an increase in WBC counts and the prostate index compared to the normal control group. Treatment with the *Picralima nitida* extract significantly improved parameters related to anemia, reduced the elevation of inflammatory leukocyte counts, and resulted in a marked decrease in the prostate index and tissue hyperplasia, similar to the effects of finasteride, in a dose-dependent manner. This study concludes that the stem bark of *Picralima nitida* has promising hematoprotective and anti-BPH effects, supporting its potential as a safe and affordable phytotherapeutic alternative for managing BPH and minimizing associated hematological complications

CHAPTER ONE

INTRODUCTION

1.1 Background of the Study

Benign prostatic hyperplasia (BPH) is a progressive, non-cancerous enlargement of the prostate gland that commonly affects ageing men worldwide. It is largely diagnosed among men above the age of 50 and over 50% of men above 60years experience symptoms related to BPH (Lee et *al.,* 2023). The condition leads to lower urinary tract symptoms (LUTS) such as urinary frequency, urgency, a weak stream and incomplete bladder emptying, all of which can significantly impair social functioning and psychological well-being (Chang et al., 2024). The pathogenesis of benign prostatic hyperplasia (BPH) is closely linked to age-related hormonal alterations, particularly the excessive intraprostatic conversion of testosterone to dihydrotestosterone (DHT) catalyzed by the enzyme 5-α-reductase. DHT binds to androgen receptors in prostatic epithelial and stromal cells, stimulating cell proliferation, reducing apoptosis, and ultimately leading to glandular enlargement and hyperplasia. (Wei *et al.,* 2020). Chronic inflammation and oxidative stress further contribute to gland enlargement and prostate dysfunction (Chan *et al.,* 2023).

Conventional therapies for benign prostatic hyperplasia (BPH), such as α-adrenergic blockers and 5-α-reductase inhibitors, effectively relieve lower urinary tract symptoms but are frequently accompanied by adverse events, including dizziness, orthostatic hypotension, erectile dysfunction and ejaculatory disorders. (Zhou *et al.,* 2025). This challenge has driven increasing scientific interest in medicinal plants as safer and more accessible alternatives, particularly in low-resource settings.

Picralima nitida (Akuamma), a plant native to West and Central Africa, has a long history of use in traditional medicine for treating fever, pain, gastrointestinal disorders and inflammatory conditions (Akinlade *et al.*, 2023). The stem bark of many medicinal plants is rich in bioactive phytochemicals such as alkaloids, flavonoids, phenolic compounds, saponins and glycosides, which exhibit significant anti-inflammatory, antioxidant and cytoprotective effects. These compounds play crucial roles in mitigating oxidative stress and inflammatory responses associated with various pathological conditions (Aremu and Pendota, 2021). These bioactive compounds have shown promising biological actions relevant to prostate health and hematological integrity.

Benign prostatic hyperplasia (BPH) is increasingly recognized to have systemic effects, including alterations in hematological indices such as the platelet-to-lymphocyte ratio (PLR) and systemic immune-inflammation index (SII) driven by chronic inflammatory responses. Consequently, monitoring blood-cell–derived indices plays an important role in assessing disease burden and guiding therapeutic safety and efficacy. (Shi *et al.*, 2024). Considering the limited research on the role of *Picralima nitida* in prostate disorders and blood function, this study investigates its stem bark extract as a potential phytotherapeutic option for managing BPH and associated hematological alterations in testosterone-induced rats. Findings from this research may contribute useful knowledge to natural drug development and improved urologic healthcare.

1.2 Statement of the Problem

Current pharmacological therapies for BPH are effective but associated with adverse effects, high cost, and limited accessibility for many patients in developing countries. Although *Picralima nitida* is widely used in traditional medicine, there is insufficient scientific evidence supporting its effect on prostate health and hematological functions in BPH. This research therefore examines

the efficacy of the aqueous stem bark extract of *Picralima nitida* in reducing BPH-related complications and restoring hematological balance.

1.3 Aim of the Study

To evaluate the effects of aqueous stem bark extract of *Picralima nitida* on hematological parameters and prostate health in testosterone-induced BPH in rats.

1.4 Objectives

1. To induce BPH in male Wistar rats using testosterone propionate.
2. To administer graded doses of aqueous *Picralima nitida* stem bark extract.
3. To assess changes in hematological parameters (RBC, Hb, PCV, WBC and differentials, PLT, PCT).

1.5 Scope of the Study

This research is restricted to:

a. Male Wistar rats
b. Extraction of *Picralima nitida* stem bark using Aqueous extract
c. A treatment period of 21 days following BPH induction
d. Analysis of hematological parameters (RBC, Hb, PCV, WBC, GRAN, LYM, MID, PLT, PCT)

1.6 Significance of the Study

This research highlight the potential of *Picralima nitida* stem bark extracts as a natural remedy, it contributes to the scientific validation of a traditionally used medicinal plant, offering insights into its anti-inflammatory, antioxidant, and prostate-protective effects. The study demonstrates that the

extract can reduce prostate enlargement in BPH-induced rats without causing haematotoxicity, suggesting its safety and therapeutic potential in managing BPH and its associated hematological alterations. If proven effective, the plant could offer a safer, more affordable alternative to current BPH medications, especially in resource limited settings. It could also serve as a basis for the development of novel phytotherapeutic agents with minimal side effects and promotes evidence-based integration of traditional medicine into modern healthcare laying the foundation for future research on the molecular mechanisms, bioactive compound characterization, and clinical evaluation of *Picralima nitida* in the prevention and management of benign prostatic hyperplasia.

CHAPTER TWO

2.0 Benign Prostatic Hyperplasia (BPH): An Overview

Benign Prostatic Hyperplasia (BPH) is a non-malignant, progressive enlargement of the prostate gland caused by hyperplastic proliferation of both stromal and epithelial cells within the transition zone. This condition primarily affects aging males and represents one of the most prevalent urological disorders worldwide. Although BPH is not life-threatening, it significantly affects patients' quality of life through bothersome lower urinary tract symptoms and complications such as acute urinary retention, recurrent urinary tract infections, bladder stones, and renal impairment (McVary, 2024). It is essential to distinguish BPH from prostate cancer, as the two conditions may coexist but differ fundamentally in their pathogenesis, prognosis, and management strategies. Unlike prostate cancer, BPH is not associated with increased mortality but contributes substantially to morbidity and reduced functional capacity in older men.

The prevalence of BPH increases markedly with advancing age. Studies have shown that approximately 50% of men over the age of fifty and up to 90% of men over eighty years exhibit histological evidence of BPH (McVary, 2024). However, only about half of these individuals develop clinically significant symptoms that require medical intervention. Globally, BPH imposes a considerable economic burden on healthcare systems due to the costs associated with long-term management, hospitalization, and surgical procedures. In the United States alone, the annual cost of managing BPH exceeds four billion dollars, encompassing both direct medical expenses and indirect productivity losses (Taub et al., 2006). In sub-Saharan Africa, particularly Nigeria, the prevalence of BPH is also rising as a result of increasing life expectancy, urbanization, and lifestyle changes. Despite this trend, limited access to diagnostic and treatment facilities in rural areas has led to under diagnosis, delayed presentation, and increased disease burden (Chikezie et al., 2024).

The hallmark of BPH is the presence of lower urinary tract symptoms, which typically include increased frequency and urgency of urination, nocturia, weak urinary stream, hesitancy and straining during micturition, intermittent flow, terminal dribbling, and a sensation of incomplete bladder emptying. The severity of these symptoms is commonly evaluated using the International Prostate Symptom Score (IPSS) questionnaire, which rates the degree of symptomatology on a scale from zero to thirty-five, with higher scores indicating more severe disease (McVary, 2024). In addition to these symptoms, patients may develop complications such as acute urinary retention, recurrent urinary tract infections, bladder diverticula, hematuria, and chronic renal failure secondary to prolonged obstruction. These complications often necessitate emergency intervention and significantly increase the likelihood of hospitalization.

BPH profoundly impairs health-related quality of life by disrupting sleep, reducing daytime productivity, and affecting emotional well-being. Nocturia, for instance, contributes to sleep deprivation and fatigue, while frequent urination can restrict social activities and limit travel, particularly among elderly men (Chikezie et al., 2024). Furthermore, sexual dysfunction—including erectile dysfunction and ejaculatory disturbances—is common in men with BPH, especially those receiving pharmacological treatment with alpha-blockers or five-alpha-reductase inhibitors. These adverse effects often lead to psychological distress, decreased self-esteem, and diminished overall quality of life.

The diagnosis of BPH involves a combination of thorough clinical evaluation, physical examination, and diagnostic testing. A digital rectal examination is performed to assess the size, texture, and consistency of the prostate as well as to detect nodules that may suggest malignancy. Measurement of prostate-specific antigen (PSA) levels assists in ruling out prostate cancer and monitoring disease progression. Urinalysis and urine culture are carried out to detect urinary tract

infections or hematuria, while uroflowmetry measures urinary flow rate to evaluate voiding efficiency. Imaging studies such as trans rectal or abdominal ultrasound are used to determine prostate volume, post-void residual urine, and assess the condition of the upper urinary tract. In selected cases, cystoscopy may be performed to visualize the urethra and bladder neck anatomy and to detect possible obstructive lesions. These diagnostic procedures enable clinicians to determine disease severity, identify complications, and establish appropriate management strategies for optimal patient outcomes (McVary, 2024).

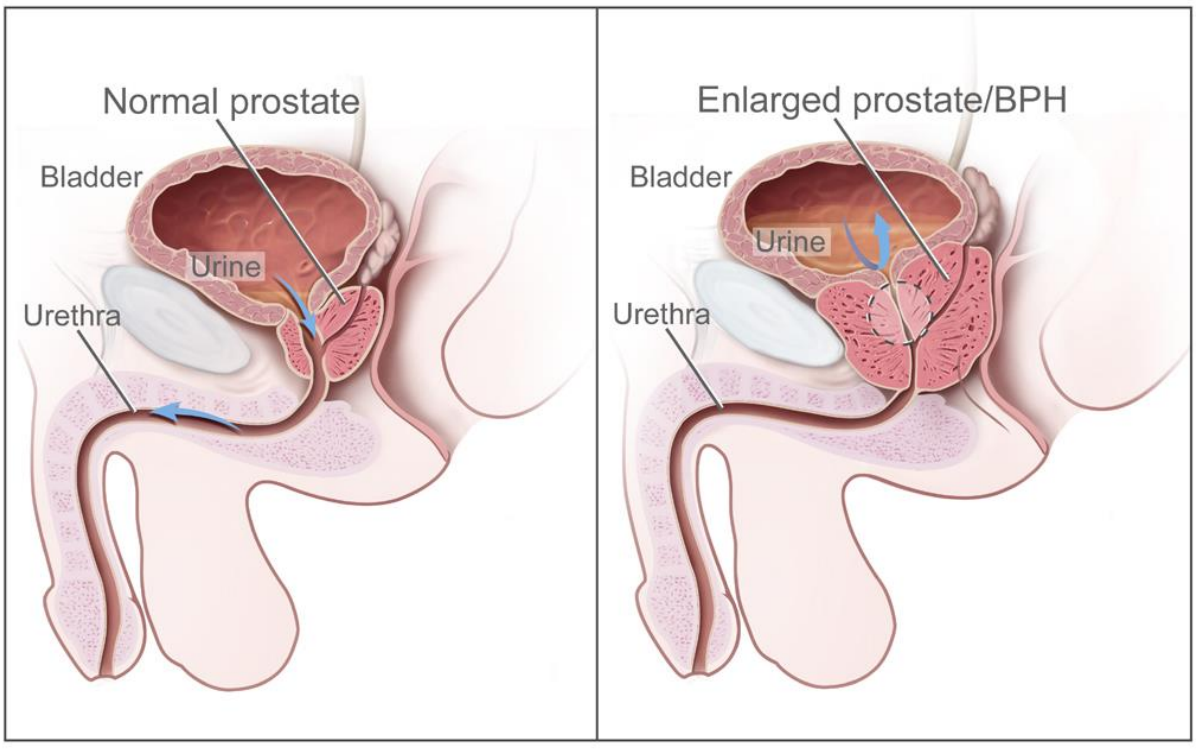


Plate 1: Benign Prostatic Hyperplasia

2.1 Effects of Benign Prostatic Hyperplasia on Hematological Parameters

i. **Effects on Red Blood Cell (RBC) Count**: Chronic obstruction of the urinary tract in BPH may lead to post-renal azotemia and progressive renal insufficiency. The resultant decline in erythropoietin synthesis from the kidneys reduces stimulation of bone marrow erythropoiesis, often culminating in mild to moderate normocytic, normochromic anemia. Furthermore, inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) interfere with iron metabolism and erythroid progenitor cell activity, further suppressing RBC production (Akanbi et al., 2021). Thus, BPH patients, particularly those with long-standing obstruction or associated prostatitis may experience decreased RBC counts.

ii. **Effect on Hemoglobin (Hb) Concentration**: The hemoglobin concentration is often reduced in patients with chronic or complicated BPH. This reduction is primarily secondary to inflammatory anemia and renal hypo function, both of which limit erythropoietic activity and iron utilization. Additionally, oxidative stress within the prostatic micro environment can lead to erythrocyte membrane fragility, promoting hemolysis and subsequent Hb depletion. Studies by Adebayo et al. (2023) reported significant decreases in Hb concentration in testosterone-induced BPH rats, correlating with elevated inflammatory markers and oxidative damage.

iii. **Effect on Packed Cell Volume (PCV):** Packed Cell Volume (PCV), an index of red cell mass, shows a parallel decline with RBC and Hb values in BPH. The reduction reflects decreased erythropoietin activity, chronic inflammatory burden, and in severe cases, hem dilution from fluid retention secondary to renal dysfunction. Conversely, when BPH

coexists with dehydration due to urinary obstruction and retention, transient elevation of PCV may occur. (Liedtke et al., 2024).

iv. **Effect on White Blood Cells (WBC) and Differentials**: The total white blood cell (WBC) count and its differentials provide critical insight into the inflammatory or infectious component of BPH. In uncomplicated BPH, total WBC counts typically remain within normal limits, In BPH with prostatitis or urinary tract infection, a leukocytosis is often observed, primarily neutrophilic, indicating acute inflammatory response and chronic inflammatory states in BPH are marked by a relative increase in lymphocytes and monocytes, reflecting ongoing immune modulation. (McVary 2016).

v. **Effect on Platelet Count (PLT):** The platelet count (PLT) in BPH patients may exhibit variable trends depending on the degree of systemic inflammation. Chronic inflammatory cytokines stimulate thrombopoiesis, resulting in mild thrombocytosis in some patients. Elevated platelet activity and aggregation have been linked to oxidative endothelial injury associated with prostatic inflammation. (McVary 2016). Conversely, in cases of renal impairment secondary to prolonged obstruction, uremic platelet dysfunction may occur, leading to a slight reduction in platelet count and function.

vi. **Effect on Plateletcrit (PCT):** Plateletcrit (PCT) is the volume percentage of platelets in blood which serves as a marker of total platelet mass. Like platelet count, PCT tends to increase modestly in chronic inflammatory states due to enhanced megakaryocytic activity. Elevated PCT has been observed in BPH patients with concurrent systemic inflammation, potentially reflecting platelet hyperactivity and vascular stress. However, excessive PCT elevation may predispose to thrombotic tendencies, necessitating careful clinical and

laboratory monitoring during disease progression and pharmacotherapy (Adesokan et al., 2022).

2.2 Pathophysiology of Benign Prostatic Hyperplasia (BPH)

Benign Prostatic Hyperplasia (BPH) is a non-malignant enlargement of the prostate gland, predominantly affecting aging men. The pathogenesis of BPH is multifactorial, involving complex interactions between hormonal, cellular, molecular, and environmental factors. Understanding these mechanisms is crucial for developing targeted therapeutic strategies.

2.2.1 Hormonal Influences

a. **Androgens and Estrogens:** The prostate remains hormonally responsive throughout life. Dihydrotestosterone (DHT), a potent androgen derived from testosterone through the action of 5α-reductase, plays a pivotal role in prostatic growth. DHT binds to androgen receptors in stromal and epithelial cells, promoting cellular proliferation and inhibiting apoptosis. Additionally, an age-related increase in estrogen levels, coupled with a relative decrease in androgen levels, may contribute to BPH development by altering the balance between stromal and epithelial cell growth (Xu et al., 2024).

b. **Growth Factors:** Insulin-like growth factor 1 (IGF-1) and other growth factors are implicated in BPH pathogenesis. Elevated levels of IGF-1 have been associated with increased prostate volume and severity of lower urinary tract symptoms (LUTS), suggesting a role in prostatic cellular proliferation (Xu et al., 2024).

2.2.2 Cellular and Molecular Mechanisms

a. **Stromal-Epithelial Interactions:** BPH involves the proliferation of both stromal and epithelial cells within the prostate's transition zone. These cellular interactions are regulated by various growth factors and cytokines that promote cellular proliferation and tissue remodeling (Xu et al., 2024).

b. **Inflammation:** Chronic inflammation is a significant contributor to BPH. Histological studies have identified inflammatory cell infiltrates in prostate tissue of men with BPH. These inflammatory cells release cytokines and growth factors that stimulate stromal and epithelial cell proliferation, leading to glandular hyperplasia and fibrosis (Xu et al., 2024).

c. **Oxidative Stress and Autophagy:** Oxidative stress, characterized by an imbalance between reactive oxygen species and antioxidant defenses, has been implicated in BPH. Elevated oxidative stress can damage cellular components, leading to cellular dysfunction and promoting BPH progression. Additionally, impaired autophagy, the process by which cells degrade and recycle damaged components, may exacerbate oxidative damage and contribute to prostatic hyperplasia (Xu et al., 2024).

2.2.3. Mechanical Factors

a. **Bladder Outlet Obstruction:** The enlarged prostate compresses the urethra, leading to bladder outlet obstruction. This obstruction results in increased bladder wall thickness, detrusor muscle hypertrophy, and reduced bladder compliance. Over time, these changes can lead to detrusor over activity, increased urinary frequency, urgency, and nocturia (Xu et al., 2024).

b. **Smooth Muscle Tone:** Increased smooth muscle tone within the prostate and bladder neck contributes to dynamic obstruction. Alpha-1 adrenergic receptors mediate this smooth

muscle contraction, and their blockade can alleviate LUTS by reducing muscle tone (Xu et al., 2024).

2.2.4. Genetic and Environmental Factors

a. **Genetic Predisposition:** Family and twin studies suggest a genetic component in BPH development. Specific genetic polymorphisms related to androgen metabolism, growth factors, and inflammatory pathways have been associated with an increased risk of BPH (Xu et al., 2024).

b. **Environmental Factors:** Lifestyle factors such as diet, physical activity, and obesity have been linked to BPH. High-fat diets, sedentary lifestyles, and obesity are associated with increased prostate volume and severity of LUTS, possibly due to alterations in hormone levels and increased inflammation (Xu et al., 2024).

2.3 Current Pharmacological Management of Benign Prostatic Hyperplasia (BPH)

Pharmacotherapy remains the first-line treatment for moderate to severe lower urinary tract symptoms (LUTS) associated with BPH, particularly for patients who prefer non-surgical options or are not candidates for surgery. The primary goals are to alleviate symptoms, improve quality of life, and reduce the risk of disease progression.

i. **Alpha-Adrenergic Receptor Antagonists (α-blockers):** Alpha-blockers are commonly used as first-line therapy for men with moderate-to-severe LUTS. They function by blocking alpha-1 adrenergic receptors in the smooth muscle of the prostate, bladder neck, and proximal urethra, leading to decreased smooth muscle tone and reduced urethral resistance. This results in improved urinary flow and decreased symptoms such as hesitancy, weak stream, and incomplete bladder emptying. Examples: Tamsulosin,

Alfuzosin, Doxazosin, Silodosin, Naftopidil and Terazosin. These agents are often selected based on patient comorbidities, side-effect profiles, and potential drug interactions. They are effective in providing rapid symptom relief and are generally well-tolerated. (American Urological Association, 2018).

ii. **5-Alpha Reductase Inhibitors (5-ARIs):** 5-ARIs inhibit the enzyme 5-alpha reductase, responsible for converting testosterone into dihydrotestosterone (DHT), a potent androgen that drives prostate cell proliferation. By reducing DHT levels, these medications decrease prostate volume and can reduce the risk of disease progression such as Finasteride and Dutasteride. These are recommended for men with enlarged prostates (>30–40 mL), elevated prostate-specific antigen (PSA) levels (>1.5 ng/mL), or palpable prostate enlargement. Patients should be informed about the delayed onset of action and potential sexual side effects. (Salisbury, 2024).

iii. **Phosphodiesterase-5 Inhibitors (PDE5 inhibitors):** PDE5 inhibitors, such as tadalafil and sildenafil, inhibit the enzyme phosphodiesterase-5, leading to increased levels of cyclic guanosine monophosphate (cGMP). Elevated cGMP levels relax smooth muscle in the prostate and bladder, improving LUTS and erectile function. These agents are particularly beneficial for patients experiencing both BPH-related LUTS and erectile dysfunction. Tadalafil is commonly used, while sildenafil may be considered if tadalafil is not well-tolerated. (Salisbury, 2024).

iv. **Anticholinergics:** Anticholinergic medications block M2 and M3 receptors in the detrusor muscle of the bladder, reducing involuntary bladder contractions and alleviating storage symptoms such as frequency, urgency, and nocturia. Examples includes**:** Solifenacin, Fesoterodine, Darifenacin, Oxybutynin, Propiverine, Tolterodine andTrospium chloride**.**

These are recommended for patients with predominant storage symptoms. However, they should be used with caution if post-void residual (PVR) urine volume is elevated to minimize the risk of acute urinary retention. (Papet and Dupuis, 2024).

v. **Beta-3 Adrenergic Agonists:** Beta-3 adrenergic agonists, such as mirabegron, stimulate beta-3 receptors in the detrusor muscle, increasing cyclic adenosine monophosphate (cAMP) levels and promoting bladder smooth muscle relaxation. This leads to improved storage capacity and reduced symptoms of urgency and frequency. Mirabegron is an alternative for patients with storage symptoms, particularly when anticholinergics are contraindicated or poorly tolerated. (Staskin, 2024; Sumitomo Pharma America, 2024)

vi. **Combination Therapies:** Combination therapies have emerged as a strategic approach to managing LUTS in men with BPH, particularly for those with moderate-to-severe symptoms or those at risk of disease progression. By integrating agents with complementary mechanisms, these therapies aim to address both static and dynamic components of bladder outlet obstruction, while balancing efficacy and tolerability**.**

Common combination therapies include:

- Alpha-blocker + 5-ARI
- Alpha-blocker + PDE5 inhibitor
- Alpha-blocker + Anticholinergic
- Alpha-blocker + Beta-3 agonist

These combinations have been shown to provide superior efficacy over monotherapy in certain cases, particularly with alpha-blockers and 5-ARIs, which significantly reduce disease progression and symptoms. Other combinations, including alpha-blockers with anticholinergics, beta-3

agonists, or PDE5 inhibitors, provide potential benefits for patients with mixed symptom profiles, though evidence remains heterogeneous. (Ganesan, 2024).

2.4 Minimally Invasive Surgical Techniques for Benign Prostatic Hyperplasia (BPH)

Minimally invasive surgical techniques are considered for patients with BPH who are refractory to medical therapy but are not candidates for traditional surgery. These procedures aim to alleviate symptoms, improve quality of life, and reduce the risk of disease progression.

i. **Transurethral Microwave Thermotherapy (TUMT):** Transurethral Microwave Thermotherapy (TUMT) is a minimally invasive procedure that employs microwave energy transmitted through a urethral catheter to thermally ablate hyperplastic prostate tissue. It is typically performed in an outpatient setting under local or regional anesthesia, offering advantages such as minimal bleeding, reduced hospitalization time, and a lower risk of sexual dysfunction compared with surgery (Madersbacher et al., 2000).

ii. **Transurethral Needle Ablation (TUNA):** TUNA employs low-level radiofrequency energy delivered through needles inserted into the prostate via a urethroscopic approach to destroy obstructive tissue. This procedure is suitable for patients with mild to moderate BPH, offering a less invasive option with a lower risk of sexual side effects and shorter recovery time. However, it is less effective than surgery and may require re-treatment. Possible side effects include a burning sensation, temporary urinary retention, or hematuria (Hill et al., 2004).

iii. **Prostatic Urethral Lift (UroLift System):** The UroLift system involves placing tiny permanent implants to lift and hold enlarged prostate tissue away from the urethra, thereby relieving obstruction without cutting, heating, or removing tissue. This procedure preserves

sexual function, offers a quick recovery time, and does not require catheterization. Side effects may include mild pelvic pain, urinary discomfort, migration or erosion of the implant, hematuria, and urgency after the procedure (Sievert et al., 2019).

iv. **Rezūm Water Vapor Therapy:** Rezūm uses natural water vapor (steam) to deliver thermal energy directly into prostate tissue through a handheld device via a cystoscope. The heat destroys excess prostatic cells, leading to the gradual shrinkage of tissues and improving urinary flow. This minimally invasive procedure preserves sexual function and can be performed in an outpatient setting. Side effects may include urinary tract infection, dysuria, hematuria, and short-term urgency. Symptom improvements may take up to 3 months and may require repeat treatments in some cases (Siu et al., 2025).

v. **Laser-Based Ablative Techniques (PVP and HoLEP):** Photo selective Vaporization of the Prostate (PVP) uses a high-powered potassium-titanyl-phosphate (KTP) laser delivered through a fiber inserted via a cystoscope into the urethra, allowing the surgeon to remove the enlarged prostate lobes from within the urethra. Holmium Laser Enucleation of the Prostate (HoLEP) involves the use of a holmium: YAG laser, which accurately cuts and removes the enlarged inner portion of the prostate from its surrounding capsule. The cut tissue is then fragmented and removed from the bladder. These procedures require specialized equipment and training, result in minimal bleeding, and offer rapid recovery. They are suitable for patients on anticoagulants. Side effects may include transient irritative symptoms like burning urination, mild hematuria, retrograde ejaculation, urinary incontinence, urinary tract infection, and dysuria (Tholomier, 2015).

2.5 Surgical Interventions for Benign Prostatic Hyperplasia (BPH)

When medical therapy fails or complications arise, surgical options are considered to alleviate symptoms and improve quality of life in patients with BPH.

2.5.1 Transurethral Resection of the Prostate (TURP): TURP is considered the gold standard for BPH treatment. It involves the removal of prostate tissue using an electrical cutting loop inserted through the urethra. The procedure is performed by inserting a resect scope through the urethra to excise obstructing parts of the prostate using electrocautery, allowing urine to flow freely and reducing post-void residual urine. TURP offers rapid symptom relief and long-term efficacy. However, it requires general or spinal anesthesia and carries the risk of significant intraoperative bleeding. Postoperative complications may include retrograde ejaculation, erectile dysfunction, urinary incontinence, and TURP syndrome due to absorption of irrigation fluids (Mayo Clinic, 2024; Cleveland Clinic, 2025).

2.5.2 Transurethral Incision of the Prostate (TUIP): TUIP involves making small incisions in the prostate and bladder neck to widen the urethral passage. It is typically used in men with smaller prostates and less obstructive tissue burden. No tissue is removed. TUIP provides a lower risk of complications than TURP and offers a shorter recovery time. However, it is limited to smaller gland sizes and may not provide as effective long-term relief in larger prostates. Potential side effects include retrograde ejaculation, erectile dysfunction, urinary incontinence, and temporary urinary retention (Mayo Clinic, 2025; Cleveland Clinic, 2025).

2.5.3 Open Prostatectomy: Open prostatectomy is indicated for very large prostates (>80–100 mL) and when other complications like bladder stones or diverticula coexist. This procedure involves making an abdominal incision to access and remove the inner portion of the prostate. There are three main approaches**:**

a. **Suprapubic (trans vesical) prostatectomy**: This approach involves making an incision in the lower abdomen and entering the bladder through its dome. The prostate is accessed via the bladder neck, and the adenoma is removed directly through the bladder cavity. It is effective for large prostates with coexisting bladder pathology and for patients who have undergone prior transurethral resection of the prostate. Potential side effects include persistent bladder dysfunction, retrograde ejaculation, erectile dysfunction, and ileus. (Mayo Clinic, 2024)

b. **Retro pubic prostatectomy**: An incision is made in the lower abdomen, just above the pelvic bone, accessing the prostate in front of the seminal vesicles without entering the bladder. The inner part of the prostate is enucleated from its capsule and removed through the incision. It is effective for very large glands and ensures thorough tissue removal. Side effects may include erectile dysfunction, wound infection, retrograde ejaculation, and urinary leakage (Mayo Clinic, 2024)

c. **Perineal (transperineal) Prostatectomy**: This approach involves an incision between the scrotum and anus to access and remove the prostate through the pelvic floor muscles. This technique is used for small prostates where exposure is adequate, for patients with previous abdominal surgeries, and for obese patients where abdominal access is challenging. Side effects include erectile dysfunction, rectal injury during dissection, incontinence or sphincter damage, and difficulty in preserving ejaculatory function (Mayo Clinic, 2024).

2.6 The Role of Medicinal Plants in BPH Treatment

There is growing scientific interest in the use of medicinal plants for the management of benign prostatic hyperplasia (BPH), driven by the limitations of conventional therapies and the demand for natural, safer, and cost-effective alternatives. Standard pharmaceutical agents such as 5α-reductase inhibitors and α1-adrenergic blockers, although effective, are often associated with adverse effects including reduced libido, erectile dysfunction, hypotension, and gynecomastia (Obi-Abang *et al.,* 2022). In contrast, plant-based therapies offer multifaceted mechanisms, typically exhibiting anti-inflammatory, antioxidant, anti-proliferative, and hormonal-modulatory activities, which are highly relevant in addressing the multifactorial pathophysiology of BPH (Ogunmodede *et al.,* 2023).

2.6.1 Serenoa repens (Saw Palmetto): *Serenoa repens,* commonly known as Saw Palmetto, is a small palm native to the southeastern United States. Its berries have been traditionally used to treat urinary symptoms associated with BPH. Saw palmetto is believed to exert its effects by inhibiting 5α-reductase, the enzyme responsible for converting testosterone to dihydrotestosterone (DHT), a potent androgen implicated in prostate growth. A study by Sudeep et al. (2019) investigated the effects of saw palmetto extract on testosterone-induced BPH in rats. Rats were administered lipophilic extracts of *Serenoa repens* at doses ranging from 160–320 mg/kg for 4–8 weeks. It was observed that Saw palmetto decreased prostate oxidative stress and inflammatory cytokines, reduced prostate weight, and improved or preserved RBC/Hb levels (i.e., no anemia, and in disease states partial correction of

inflammation-related anemia). The extract shows a benign hematological safety profile in chronic use

2.6.2 Pygeum africanum (African Plum Tree): *Pygeum africanum*, also known as the African plum tree, is native to central and southern Africa. Its bark has been used in traditional medicine to treat urinary disorders and BPH. The bark contains triterpenes and phytosterols that exhibit anti-inflammatory and anti-edematous effects in the prostate. A study by Lee et al. (2024) administered methanolic bark extract of *Pygeum africanum* to BPH-induced rats at doses of 200–400 mg/kg/day for 30 days. The results showed significant reduction in prostate index, improved urinary flow and bladder weight, and decreased inflammation and oxidative stress markers.

2.6.3 Cucurbita pepo (Pumpkin Seed): *Cucurbita pepo*, commonly known as pumpkin, is widely cultivated for its seeds, which have been used in folk medicine to treat urinary symptoms related to BPH. Pumpkin seed oil is rich in phytosterols and essential fatty acids, exerting anti-proliferative effects on prostate cells and potentially acting as a mild alpha-blocker. In a testosterone-induced benign prostatic hyperplasia (BPH) rat model, administration of seed oil derived from Cucurbita pepo (pumpkin) led to a significant reduction in prostate weight, attenuation of inflammation (reduced IL-1β and IL-6), and improvement in antioxidant enzyme activities such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx), without detectable adverse hematological effects (stable RBCs and Hb). **(**Omotosho et al., 2025).

2.6.4 Zanthoxylum zanthoxyloides (Fagara): *Zanthoxylum zanthoxyloides*, commonly known as Fagara, is a plant whose root bark has been used in traditional medicine for

its antimicrobial, anti-inflammatory, and antispasmodic properties. The root bark contains saponins and alkaloids that suppress prostatic smooth muscle tension and modulate endocrine activity. A study by Nwachukwu et al. (2023) administered methanolic root extract of *Zanthoxylum zanthoxyloides* to BPH-induced rats at doses of 100–300 mg/kg for 30 days. The results showed prostate shrinkage, decreased cellular hyperplasia, downregulated DHT levels and α-adrenergic receptor expression, and normalization of urinary frequency.

2.6.5 Alstonia boonei: *Alstonia boonei*, known as the stool wood, is a tree native to tropical Africa. Its stem bark has been traditionally used for pain and inflammation relief. The stem bark contains polyphenols and flavonoids that exert antioxidative and antiproliferative effects. A study by Akinyemi et al. (2023) administered stem bark extracts of *Alstonia boonei* to BPH rat models at doses of 250–500 mg/kg. The study observed inhibition of testosterone-induced prostate enlargement, significant reduction in inflammatory cytokines, and restoration of antioxidant defense markers.

Urtica dioica (Nettle Root):

Urtica dioica, commonly known as nettle, is a plant whose roots have been used in traditional medicine for the treatment of BPH due to their anti-inflammatory, antioxidant, and androgen-modulating properties. Nettle root extract has been shown to reduce prostate weight, lower serum DHT levels, and improve antioxidant enzyme activity. A study by Ghorbanibirgani et al. (2023) administered nettle root extract to BPH-induced male rats at doses ranging from 50 to 200 mg/kg for 28 days. The treatment significantly reduced prostate weight and index, lowered serum DHT levels, improved antioxidant enzyme **activity (SOD and CAT),** decreased glandular hyperplasia, and reduced inflammatory cytokines (IL-6 and TNF-α). Hematological parameters were largely unchanged and stable.

2.6.6 Ageratum conyzoides (Goatweed): *Ageratum conyzoides*, commonly known as goat weed, is a plant used in traditional medicine for its anti-inflammatory and antimicrobial properties. The plant's extract has been shown to inhibit prostate growth, reduce androgen receptor signaling, and increase apoptosis in prostate cells. A study by Boye et al. (2024) administered ethanoic extract of *Ageratum conyzoides* to male rats at doses of 20, 50, and 100 mg/kg for 42 days. The study observed a dose-dependent decrease in prostate weight/index and epithelial thickness, alongside reduced androgen receptor signaling and increased apoptosis, with effects comparable to finasteride**.** It appears neutral in rat hematology.

*Picralima nitida***: Botanical and Ethno pharmacological Background**

Picralima nitida belonging to the family of Apocynaceae, commonly referred to as akuamma, is a small evergreen tree indigenous to West and Central Africa. The plant grows up to 15meters in height and produces yellowish fruits containing several seeds. It thrives in rainforest and moist savanna regions and has been widely studied for its medicinal properties. It is widely used in traditional medicine in Nigeria, Ghana, and Cameroon for treating ailments such as fever, dysentery, pain, and malaria. In Ghana, standardized capsules containing dried and powdered seeds are commercially available as "Picap" for pain relief. The stem bark and seeds are particularly valued for their antipyretic, antidiabetic, and analgesic activities. Despite its historical use, the plant’s potential in managing urologic disorders, including BPH, remains under-investigated. (Inkoto, C. L. 2020).

2.6.7 Phytochemical Composition

Studies have revealed that *Picralima nitida* contains a variety of bioactive compounds, notably

i. **Alkaloids (e.g.,** Akuammicine, Akuammidine): *Picralima nitida* stem bark contains indole alkaloids such as akuammicine and akuammidine, which exhibit receptor-binding affinity to opioid and adrenergic receptors. These compounds act as adrenergic antagonists, potentially relaxing smooth muscle tone in the prostate and bladder neck, thereby improving urinary flow and alleviating symptoms of lower urinary tract obstruction. Additionally, they may influence neurotransmission and pain modulation, which are pertinent in addressing urinary discomfort associated with benign prostatic hyperplasia (BPH) (Menzies et al., 1998).

ii. **Flavonoids (e.g., Quercetin, Rutin):** Flavonoids are polyphenolic compounds with potent antioxidant properties that neutralize reactive oxygen species (ROS), thereby reducing oxidative stress implicated in the development and progression of BPH. They also exhibit anti-inflammatory properties by inhibiting enzymes like cyclooxygenase (COX) and lipoxygenase (LOX) and reducing the levels of inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6). By mitigating inflammation and oxidative damage, flavonoids support the protection and restoration of prostate tissue (Csikós, 2021).

iii. **Tannins:** Tannins are water-soluble polyphenolic compounds known for their astringent, anti-diarrheal, and anti-inflammatory properties. They are found in high concentrations in the stem bark and help strengthen capillary walls, reduce tissue swelling, and inhibit pro-inflammatory mediators, thereby contributing to decreased prostate enlargement and vascular congestion in BPH (Akbari et al., 2022).

iv. **Terpenoids (e.g., Lupeol, β-Sitosterol):** Terpenoids are a large class of organic compounds with several biological activities present in *Picralima nitida*. They possess

anti-proliferative, anti-tumor, and antimalarial effects. These compounds can inhibit abnormal cellular growth in the prostate by interfering with growth signaling pathways and may help in reducing stromal and epithelial hyperplasia in the prostate gland. They also demonstrate anti-cancer, anti-inflammatory effects, and anti-androgenic properties, further enhancing their relevance in BPH management (Mottaghipisheh et al., 2022).

v. **Phenolic Acids:** Phenolic acids are effective scavengers of free radicals and modulators of inflammatory responses. They reduce oxidative damage to DNA and proteins in prostate cells and help maintain cellular homeostasis. Their role in antioxidant defense complements the action of flavonoids in protecting prostate tissue from oxidative damage commonly seen in aging and BPH (Pejčić et al., 2019).

vi. **Saponins:** Saponins are glycosides known for their foaming characteristics and membrane-disrupting properties. They are found in the seeds and leaf extracts of *Picralima nitida* and possess antimicrobial, anti-inflammatory, immunomodulatory, antifungal, and cholesterol-lowering effects. They may help reduce prostatic inflammation and regulate lipid metabolism (Takayama, H. 2004).

vii. **Glycosides (e.g., Strophanthin):** Glycosides are found in the seeds and bark. They possess antihypertensive and cardiotonic effects. Glycosides have shown potential in inhibiting cell proliferation in prostate epithelial cells (Menzies, 1998).

These compounds are known for their ability to modulate immune responses, inhibit oxidative stress, and potentially suppress abnormal cellular growth.

2.7.1 Pharmacological Activities of Pricralima nitida

The pharmacological properties of *Picralima nitida*, particularly its stem bark, seeds, and leaves, have been widely investigated, revealing diverse therapeutic potentials. These activities are attributed to its rich phytochemical profile, including indole alkaloids, flavonoids, tannins, terpenoids, and phenolic acids

i. **Analgesic and Anti-inflammatory Effects:** The alkaloids, particularly akuammine and pseudo-akuammigine, have demonstrated significant analgesic and anti-inflammatory effects. These compounds exert their actions through interactions with opioid receptors, with some alkaloids showing micromolar activity at the mu-opioid receptor and potent activity as kappa-opioid receptor agonists (Duwiejua et al., 2002; Menzies et al., 1998).

ii. **Antioxidant Properties**: *Picralima nitida* exhibits potent antioxidant activity, attributed to its phenolic compounds, flavonoids, and terpenoids. These antioxidants play a crucial role in scavenging free radicals, thereby mitigating oxidative stress and reducing the risk of chronic diseases (Onyekachukwu et al., 2025).

iii. **Antimicrobial Activity**: The plant's extracts have shown antimicrobial effects against various pathogens, including *Escherichia coli* and *Staphylococcus aureus*. These activities are primarily due to the presence of saponins, tannins, and alkaloids, which disrupt microbial cell membranes and inhibit growth (Obasi et al., 2012).

iv. **Antidiabetic Effects**: Studies have indicated that *Picralima nitida* possesses hypoglycemic properties. The seed extract has demonstrated faster hypoglycemic activity than the standard drug tolbutamide, suggesting its potential as an alternative treatment for diabetes (Inya-Agha et al., 2006)

v. **Antimicrobial and Antidiarrheal Activities:** The methanol extract of *Picralima nitida* has been reported to possess antidiarrheal properties, comparable to ciprofloxacin. It significantly reduces the frequency of fecal release and stool density in rats, highlighting its potential as an antimicrobial agent (Kouitcheu et al., 2013).

vi. **Antidepressant-like Effects**: Recent studies have explored the antidepressant-like effects of *Picralima nitida* seed extract. The total crude alkaloidal extract has shown potential in modulating neurotransmitter systems, suggesting its efficacy in managing depressive disorders (Okyere et al., 2025).

Plate 2: *Picralima nitida* Stem bark

Plate 3: *Picralima nitida* Tree

2.7.2 BPH-Induced Animal Models: A Tool for Preclinical Studies

Animal models play a pivotal role in elucidating the pathophysiology of benign prostatic hyperplasia (BPH) and evaluating the efficacy of potential therapies. Male Wistar rats are predominantly utilized due to their manageable size, cost-effectiveness, hormonal responsiveness, and sensitivity to androgen manipulation. BPH induction is typically achieved through the following models:

i. **Testosterone Propionate (TP) Model:** The testosterone propionate-induced model is widely accepted and reproducible for experimental BPH induction. Rats receive daily subcutaneous or intramuscular injections of testosterone propionate at doses ranging from low to high over a period of 28 days. Testosterone propionate elevates circulating

testosterone levels, which is locally converted to dihydrotestosterone (DHT) by 5α-reductase in the prostate. This leads to epithelial and stromal hyperplasia, mimicking histological and biochemical features of human BPH. The model facilitates the study of oxidative stress, inflammation, and androgen receptor signaling in prostatic enlargement (Tang et al., 2025).

ii. **Dihydrotestosterone (DHT) Model:** This model employs exogenous DHT, bypassing the need for endogenous testosterone conversion. DHT is administered via subcutaneous injection or slow-release pellets for several weeks. DHT binds with higher affinity to androgen receptors than testosterone, resulting in increased transcriptional activity of genes that promote cell proliferation and hypertrophy in the prostate. This model provides consistent and predictable prostate enlargement, eliminating variability seen in TP conversion models (Tang et al., 2025).

iii. **Estrogen/DHT Combination Model:** This model mimics the age-related hormonal imbalance in men where the testosterone-to-estrogen ratio declines. Rats are administered a combination of estradiol valerate and DHT subcutaneously, usually in a 10:1 ratio, for 4–6 weeks. Estrogen promotes stromal proliferation and inflammatory infiltration, while DHT induces glandular hyperplasia, producing a model that replicates both stromal and epithelial features of human BPH. It is particularly useful in evaluating anti-inflammatory agents and therapies targeting stromal-epithelial interactions (Tang et al., 2025).

iv. **Finasteride-Treated Model (Positive Control):** Finasteride is a selective 5α-reductase inhibitor used to validate the androgen-dependence of induced BPH and to serve as a benchmark therapy. Finasteride is administered orally or intraperitoneally, often alongside TP or DHT for 2–4 weeks. It blocks the conversion of testosterone to DHT, resulting in

shrinkage of prostatic tissue, reduction in inflammatory cytokines, and suppression of oxidative stress markers. Commonly applied as a positive control to compare the therapeutic efficacy of novel anti-BPH agents (Tang et al., 2025).

2.7.3 Parameters Used to Evaluate BPH in Animal Models

To validate the success of BPH induction and therapeutic response, researchers assess:

a) Prostate weight and index (weight relative to body weight)
b) Histopathological examination of prostatic tissues (glandular hyperplasia, stromal thickening)
c) Serum PSA levels (in some advanced models)
d) Oxidative stress markers (e.g., MDA, SOD)
e) Inflammatory markers (e.g., TNF-α, IL-6)
f) Hormone levels (e.g., testosterone, DHT, estradiol)

In addition to these, hematological indices such as RBC, WBC, hemoglobin, and platelet counts are often measured to determine systemic effects of both disease and treatment.

2.7.4 Hematological Parameters in Toxicological and Efficacy Studies

Hematological assessments are critical in evaluating the systemic safety and efficacy of pharmacological agents. BPH and its treatment may alter:

a. Red Blood Cell (RBC) count
b. Hemoglobin (Hb) concentration
c. Packed Cell Volume (PCV)

d. White Blood Cell (WBC) count and differentials

Such alterations provide insights into drug-induced hematotoxicity or immunomodulation. For herbal agents like *Picralima nitida*, improvements in these parameters may reflect anti-inflammatory and hematopoietic activities.

2.7.5 Importance of Animal Models in BPH Research

Animal models are valuable tools for simulating the hormonal, cellular, and morphological changes that characterize BPH in humans. These models allow researchers to:

a. Mimic disease pathogenesis and progression
b. Investigate the molecular mechanisms involved
c. Assess biochemical and histological alterations
d. Evaluate therapeutic interventions before clinical trials.

By providing reliable and reproducible systems, animal models help bridge the gap between in vitro studies and human clinical applications.

CHAPTER THREE

3.0.0 MATERIALS AND METHODS

3.1 MATERIALS

3.1.1. Plant Collection and Identification

The stem bark of *Picralima nitida* was harvested from a tree located in Ugbowo, Ovia North-East Local Government Area of Edo State. The plant was identified and authenticated in the Department of Plant Biology and Biotechnology at the University of Benin, Benin City, Edo State, with the voucher number UBH-P424.

3.1.2 Preparation of the sample

Fresh stem barks of the plant sample were cleaned to remove dirt and insects. The cleaned stem barks were then dried at room temperature before being pulverized into a powder using a clean mechanical and electronic blender.

3.1.3 Chemicals and Reagents

The reagents employed for the qualitative and quantitative tests of the phytochemicals included ethyl acetate, Wagner reagent, Mayer reagent, lead acetate, Tollens reagent, ammonia, sodium hydroxide, gelation solution, chloroform, sulphuric acid, ferric chloride, Sodfolindenis reagent, sodium trioxocarbonate (IV), isobutyl alcohol, magnesium carbonate, ethanol, concentrated aqueous ammonium hydroxide, hydrochloric acid, MacFarland solution, 200-400 mesh silica gel, barium sulfate, 1,1-Diphenyl-2-picrylhydrazyl (DPPH), and ascorbic acid. For the synthesis of Cu-Fe bimetallic nanoparticles, copper (II) tetraoxosulphate (VI) pentahydrate and iron(II) chloride hexahydrate were used as precursor salts. Absolute ethanol, normal saline, formal saline (10 %), chloroform, distilled water, antioxidant reagents (MDA, SOD, catalase), Monobind Accu Elisa testosterone kit (Product code: 3725-300), PSA kit (Product code: 3725-300), cadmium chloride,

lead acetate, zinc sulphate, selenium. Distilled water was used as the extraction solvent, and throughout the study, whenever needed.

3.1.4 Apparatus and equipment used.

Various laboratory equipment and tools were used throughout the study, including beakers, conical flasks, crucibles, measuring cylinders, volumetric flasks, glass rods, dropping pipettes, wash bottles, vials, Whatmann No. 1 filter paper, sieving cloth, Petri dishes, Bunsen burners, inoculating loops, funnels, stirring bars, spatulas, a mechanical grinder, an electric blender, magnetic stirrers and hot plates, autoclaves, incubators, a hot air oven, a handheld pH meter, a muffle furnace, an analytical weighing balance, a centrifuge, and a UV-Visible spectrophotometer, Plain bottles, cotton wool, centrifuge, analytical weighing balance, Hand gloves, Soxhlet extractor apparatus, Whatmann paper, filter cloth, oral gastric tube, Syringes, Spatula, Beakers, Measuring cylinders, foil paper, Dissecting kits, Surgical blades, UV Spectrophotometer, Microscope, slides and cover slips, Microscopic slide rack, Microplate reader, among others.

3.1.5 Method of extraction

To extract the phytochemicals from the stem bark of *Picralima nitida*, the procedure described by Ifijen *et al.* (2024) was followed. Fifty grams of the powdered stem bark were weighed and transferred into a 1000 mL Erlenmeyer flask containing 500 mL of distilled water. The flask was placed on a magnetic stirrer hot plate and heated at 60°c for 1 hour, with constant stirring at 1000 rpm. After cooling, the solution was filtered through two layers of cheesecloth, followed by filtration through Whatman No. 1 filter paper to remove any residues. The filtrate was collected and stored at 4°c for use in the synthesis process of BNPs. The *Picralima nitida* stem bark extract was then concentrated using a rotary evaporator and further dried using a freeze dryer.

3.1.6 Determination of Percentage Yield of Extract.

The percentage yields were estimated using equation (3.1).

$$\boldsymbol{Yield\ of\ extract} = \frac{\boldsymbol{Amount\ of\ extract\ recovered\ from\ solvent}}{\boldsymbol{Total\ amount\ of\ plant\ materia}}\ \boldsymbol{x\ 100} \qquad \text{Eqn (3.1)}$$

3.2 QUALITATIVE PHYTOCHEMICAL SCREENING

3.2.1 Test for Alkaloids

The procedure for detecting alkaloids in the methanol extract of *Picralima nitida* stem bark was conducted according to the methodology described by Zhang *et al.* (2020). The process involved the use of three specific reagents: Dragendorff's solution, Wagner's reagent, and picric acid, each known for its efficacy in alkaloid detection through distinct chemical reactions. First, the methanol extract was distributed into three separate test tubes, labelled A, B, and C, each containing approximately 1 mL of the extract.

Test Tube A: Dragendorff's Reagent

For the first test, 2mL of Dragendorff's reagent, a solution of potassium bismuth iodide, was added to test tube A. Dragendorff's reagent is a widely used qualitative test for alkaloids due to its sensitivity. The presence of alkaloids in the extract would react with the reagent to form a reddish-brown precipitate. The appearance of this characteristic precipitate indicated a positive result, confirming the presence of alkaloids in the sample.

Test Tube B: Wagner's Reagent

In the second test, 2mL of Wagner's reagent, which consists of iodine in potassium iodide, was added to test tube B. Wagner's reagent is another commonly used reagent for alkaloid detection. Similar to Dragendorff's reagent, it reacts with alkaloids to form a reddish-brown precipitate. The formation of this precipitate indicated a positive test for alkaloids in the methanol extract of *Picralima nitida* stem bark.

Test Tube C: Picric Acid

The final test involved adding 2mL of picric acid to test tube C. Picric acid, a chemical compound known for its ability to detect alkaloids, reacts to form a yellowish precipitate in the presence of these compounds. The appearance of this yellowish precipitate confirmed the presence of alkaloids in the sample.

Overall, the use of these three reagents: Dragendorff's solution, Wagner's reagent, and picric acid provided a comprehensive analysis for the presence of alkaloids in the methanol extract of *Picralima nitida* stem bark, each reagent confirming the presence through distinct colorimetric changes.

3.2.2 Test for Saponins

The procedure for detecting saponins in the methanol extract of *Picralima nitida* stem bark followed the methodology described by Kancherla *et al.* (2019). Water was added to a portion of the sample extract, which was then boiled for approximately 3 minutes and subsequently filtered. To the filtrate, 5mL of distilled water was added, and the mixture was shaken vigorously. Persistent frothing indicated the presence of Saponins.

3.2.3 Test for Tannins

The method employed to detect tannins in the methanol extract of *Picralima nitida* stem bark closely adhered to the procedures detailed by Auwal *et al.* (2014). Initially, a solution was prepared by mixing 10mL of distilled water with 2mL of the extract. This mixture underwent heating for 5 minutes and was subsequently divided into two equal parts through filtration.

In the first part of the filtrate, a few drops of Ferric chloride solution were added. The appearance of a blush precipitate upon addition indicated the presence of hydrolysable tannins. This qualitative test serves as a reliable indicator for these types of compounds, crucial for identifying certain chemical characteristics of the extract.

For the second part of the filtrate, approximately 5 drops of dilute hydrochloric acid (HCl) were introduced, followed by boiling for 5 minutes. The development of a red precipitate during this process was indicative of condensed tannins. This reaction provides complementary information about the presence of different tannin types within the extract, aiding in a comprehensive chemical profile assessment.

3.2.4 Test for Flavonoids

The detection of flavonoids in the methanol extract of *Picralima nitida* stem bark followed closely the method outlined by Wallace *et al.* (2024). Initially, the extract was subjected to boiling in 10 mL of distilled water and subsequently filtered to obtain a clear filtrate. This filtrate was then divided into two equal portions, labeled A and B, each containing 5mL.

In portion A of the extract, a few drops of 10% lead acetate solution were introduced. The appearance of a yellowish precipitate upon addition indicated a positive test result for the presence of alkaloids, aligning with established protocols for alkaloid detection.

For portion B, 5 mL of 20% NaOH solution was added, followed by the incremental addition of dilute HCl drops. The formation of a colorless solution in portion B was observed, which is indicative of the presence of flavonoids. This step confirmed the absence of alkaloids in portion B and provided additional insight into the phytochemical composition of the extract.

3.2.5 Test for Phenolic compound

The analysis for phenolic compounds in the methanol extract of *Picralima nitida* stem bark was conducted in accordance with the methodology described by Wallace *et al.* (2024), as outlined by Godlewska *et al.* (2023). Initially, 1mL of the extract was mixed with 5mL of 99% ethanol. Subsequently, a single drop of 10% ferric chloride (FeCl3) solution was added to the mixture.

A positive test result was indicated by the formation of a pale-yellow solution. This colour change serves as a visual marker for the presence of phenolic compounds in the extract. Such compounds are known for their antioxidant properties and are crucial in various biological and pharmacological studies to assess the potential health benefits of natural products.

3.2.6 Test for Cardiac Glycosides

The method used to detect cardiac glycosides in the methanol extract of *Picralima nitida* stem bark followed the protocol outlined by Auwal *et al.* (2014). Specifically, 1mL of the extract was mixed with 1mL of glacial acetic acid and a drop of ferric chloride solution. This mixture was then layered with 1mL of concentrated H2SO4. The presence of glycosides was indicated by the formation of a brown ring in the solution, confirming the presence of these compounds.

3.3 Phytochemical Quantification of *Picralima nitida EXTRACT*

3.3.1 Alkaloids

The quantification of alkaloids in *Picralima nitida* extract was conducted following the method outlined by Kancherla *et al.* (2019). Initially, 5 grams of the plant material were weighed and placed into a 250-milliliter beaker. To this, 200 milliliters of a 20% acetic acid solution in ethanol were added. The mixture was covered and left to stand for 2-4 hours to allow for the thorough extraction of alkaloids. After this period, the mixture was filtered to obtain the extract, which was then concentrated by evaporating the solvent.

Following the concentration process, ammonium hydroxide was added to the extract to precipitate the alkaloids. This resulted in the formation of a precipitate, which was separated by filtration using a pre-weighed filter paper. The precipitate was then dried in an oven at 60°c for 30 minutes. Once dried, the filter paper with the precipitate was reweighed.

The content of alkaloids in the samples was determined by the weight difference method, which involves calculating the difference in weight before and after drying the precipitate. This process ensures an accurate quantification of the alkaloid content present in the *Picralima nitida* extract.

$$Weight\ of\ alkaloid = \frac{\mathrm{Wr} - \mathrm{Wf} \times 100}{\mathrm{Ws}}\ x\ 100 \qquad \text{Eqn (2.2)}$$

Where, Wr = Weight of filter paper with residue (g)

Wf = Weight of filter paper (g)

Ws = Weight of sample analyzed (g)

3.3.2 Flavonoids

The quantification of flavonoids in *Picralima nitida* extract was performed using the method described by Ortega-Medrano *et al.* (2023). Initially, 1 gram of the plant sample was subjected to repeated extraction using 100 milliliters of 80% aqueous methanol at room temperature. This process ensured thorough extraction of the flavonoids. The resulting mixture was then filtered through a Whatman No. 1 filter paper into a pre-weighed 250-milliliter beaker to remove any solid residues.

The filtrate was subsequently placed in a water bath and allowed to evaporate to dryness. This step was crucial for concentrating the flavonoid content by removing the solvent. After complete evaporation, the beaker containing the dried extract was weighed again. The weight difference before and after evaporation provided the mass of the flavonoid content.

To determine the percentage of flavonoids, the mass of the dried extract was used in conjunction with equation (3.3). This method ensures accurate quantification of flavonoids in the plant extract by accounting for both the extraction efficiency and the concentration process.

$$\%Weight\ of\ \text{flavonoid} = \frac{\text{Wr} - \text{Wf} \times 100}{\text{Ws}}\ x\ 100 \qquad \text{Eqn (2.3)}$$

Where W1 = Weight of filter paper (g)

W2 = Weight of filter paper + dried residue (g)

Ws = Weight of sample (g)

3.3.3 Saponins

The quantification of Saponins in *Picralima nitida* extract was performed using the method described by Senguttuvan *et al.* (2014). Five grams of the sample were added to a solution of 20% acetic acid in ethanol and allowed to stand in a water bath at 50°c for 24 hours. The mixture was then filtered, and the filtrate was concentrated to one-quarter of its original volume using a water bath. Concentrated ammonium hydroxide was added dropwise to the extract until a precipitate formed. The solution was allowed to settle, and the precipitate was collected by filtration and weighed. The saponin content was then calculated as a percentage, following Eqn (2.4).

$$\%Weight\ of\ Saponins\ = \frac{\mathrm{Wr - Wf \times 100}}{\mathrm{Ws}}\ x\ 100 \qquad \text{Eqn (2.4)}$$

Where W1 = Weight of filter paper (g)

W2 = Weight of filter paper + dried residue (g)

Ws = Weight of sample (g)

3.3.4 Phenols

The quantification of phenols in *Picralima nitida* extract was conducted using the method described by Wado *et al.* (2022). The procedure began with 10 grams of the plant sample being subjected to defatting using petroleum ether. This defatting process lasted for four hours, ensuring that non-polar compounds were removed, which could otherwise interfere with the subsequent extraction of phenolic compounds.

After the defatting step, the residue was extracted with 80% methanol, a solvent chosen for its effectiveness in solubilizing phenolic compounds. This extraction step also included a

saponification process that lasted for two hours. Saponification involves breaking down complex molecules such as esters into simpler molecules, which helps in releasing bound phenolic compounds, making them more accessible for extraction.

Following the saponification and extraction, the crude extract was obtained by simple filtration. This filtration step is critical for separating the liquid extract from the solid plant residues. The filtrate, which contains the extracted phenols, was then subjected to evaporation to remove the solvent, leaving behind the crude extract. The residue from the evaporated filtrate was further purified by re-extracting it with chloroform and water. Chloroform is a non-polar solvent that helps in separating phenolic compounds from other non-phenolic constituents, enhancing the purity of the phenolic extract. After this re-extraction, the mixture was filtered again to obtain the phenolic extract.

The final step involved evaporating the filtered residue to dryness using an oven set at 60°C for two hours. This drying process ensured that all remaining solvents were removed, leaving behind a dry residue containing the phenolic compounds. The residue was then weighed to a constant weight, which is crucial for quantifying the phenols accurately. This method ensures that the phenols extracted from *Picralima nitida* are free from non-phenolic contaminants, allowing for precise quantification. The use of multiple extraction and purification steps, along with controlled drying, contributes to the reliability and accuracy of the phenolic content determination in the plant extract. The percentage phenol content was estimated using Eqn 2.5.

$$\% \text{ Phenol} = \frac{\text{Weight of residue(g)}}{\text{Weight of sample taken(g)}} \; x \; 100 \qquad \text{Eqn (2.5)}$$

3.3.5 Tannin

The quantification of tannin in *Picralima nitida* extract was conducted using the method described by Achikanu *et al. (*2020). In this procedure, 1 gram of the plant sample was first macerated with 50 milliliters of distilled water. Maceration helps in breaking down the plant material and releasing the tannins into the water, ensuring an effective extraction.

After maceration, the mixture was filtered to separate the liquid extract from the solid residues. From this filtered extract, 1 milliliter of the filtrate was carefully pipetted into test tubes. To this aliquot, 2 milliliters of saturated picric acid were added. Picric acid reacts with tannins, forming a complex that can be measured spectrophotometrically. The absorbance of the resulting solution was then measured at 530 nm using a spectrophotometer. This wavelength is chosen because it corresponds to the maximum absorbance of the tannin-picric acid complex, allowing for accurate quantification.

A standard curve was prepared using different concentrations of tannic acid, which served as the reference for determining the tannin content in the *Picrlima nitida* extract. The absorbance readings of the tannin extracts were compared against this standard curve to calculate the tannin concentration. Finally, the tannin content was expressed as grams of tannin equivalent (TAE) per 100 grams of dry weight. This expression standardizes the results, making them comparable across different studies and samples.

3.4 Examination of the potential therapeutic effects of the extract on testosterone-induced benign prostatic hyperplasia (BPH) using the Wistar rat model.

3.4.1 Preparation of stock solution

To prepare the stock solution, the dose was calculated using the body weight of each animal to be administered. The stock solution was made with 1 gram of extract, which was weighed in 20ml of distilled water, and allowed to dissolve properly

3.4.2 Animal management

A total of 30 adult albino Wistar rats were used for this experiment, comprising all males, each with an average weight ranging from 120 to 210 grams. The animals were purchased from Ambrose Ali University animal house. The rats were housed in wooden cages in the anatomy department animal house at the University of Benin. The animals were placed in clean plastic cages under laboratory settings at a temperature of 22^{o}c to 24^{o}c for 12-hour light and 12-hour darkness. The animals were fed with a constant supply of water and commercial pellet rat feed (Standard Grower's mash, Top feed grower Nig. Ltd, Edo state, Nigeria) and clean water for 14 days as a standard procedure for acclimatization before the experiment was carried out. The institution and national committee guidelines for the care and use of animals were strictly followed in this study.

3.5 BPH induction

BPH was induced in rats through daily intraperitoneal (IP) injections of testosterone propionate (TP) (3 mg/kg, dissolved in corn oil) for 21 days.

3.5.1 Experimental Design

The rats were divided into six (6) groups of five (5) rats each. Group 1 was not induced nor treated (normal control), group 2 was induced with testosterone propionate (TP) (3mg/kg b.w) but not treated (Untreated control), group 3 was given TP along with 1 mg/kg b.w of finasteride (standard control). In contrast, group 4 was given standard drugs only, group 5 was given a low dose of *Picralima nitida* stem bark extract (100mg/kg b.w), and group 6 was given a high dose of *Picralima nitida* stem bark (500mg/kg b.w), respectively. Groups 1 and 2 received the vehicle throughout the duration of the study. An experimentally developed BPH model was created in the male rats by hypodermic injection of testosterone (3 mg/kg body weight (b.w)) for three (3) weeks, as reported by Al-Trad *et al*. (2019), with little adjustment. The extract was given orally. The PSA levels of the rats were determined to confirm that the induction was successful. The animals were treated with finasteride (group 3) and graded doses *of Picralima nitida* stem bark extract for 21 days. We carried out a pilot LD50 study, which showed that the stem bark extract was safe up to 5000 mg/kg, and this informed the choice of doses (Aghedo and Ogbeide, 2022). The rats used for this study were maintained in accordance with the guidelines of the National Institutes of Health Guide for the Care and Use of Laboratory Animals. Ethical approval for the study was obtained from the Department of Science Laboratory Technology, University of Benin, under the reference number UNIBEN/SLT/00001.

3.5.2 Treatment of BPH

Treatment with standard drug and different doses of extract commenced on the next day, which represents the first day of treatment, and it continued for 21days. The oral administration (treatment) was done once per day by the use of gavages. Carboxymethyl cellulose (CMC) was used as the vehicle. The weight and morphological body appearance of the individual rats were

recorded at the beginning of the experiment and every week for three weeks using an electronic weighing balance. The body weight gain was estimated by the subtraction of the final weight from the initial weight. The percentage prostate index and PSA differences were calculated by the difference in mean prostate index between the induced groups without treatment minus that of the treated group, multiplied by 100. After treatment, the rats were deprived of food and water overnight and sacrificed. Blood samples and tissues (prostate gland, testis, liver, and kidney) were collected for analysis.

3.6.0 ANIMAL SACRIFICE AND RELATED ASSESSMENTS

After the period of administration (21 days), the animals were sedated using chloroform and sacrificed to expose the organs and abdominal aorta.

3.6.1 COLLECTION OF ORGANS AND BLOOD

The animal's blood was collected through the abdominal aorta using a 5ml syringe and placed in a plain bottle. The blood was centrifuged (3000 rpm for 10 min) and the resulting supernatant serum was withdrawn into another plain tube and stored in a refrigerator at − 20 ◦C for biochemical, testosterone, Prostate-specific Antigen (PSA), and antioxidant analysis.

3.6.2 Hematological Analysis

5ml of the blood was put immediately into one tube containing EDTA, and was subjected to blood cell enumeration with an automated hematological analyzer (Dymind 2021 model) (Sysmex XE2100, TOA Medical Electronics, Kobe, Japan), including red blood cell (RBC), white blood cell (WBC), hemoglobin (HGB) and hematocrit (HCT) and others.

3.6.3 Statistical Analysis

Statistical analysis was carried out using SPSS and GraphPad.

CHAPTER 4

4.0 RESULT AND DISCUSSION

4.1 Percentage yield of the extract

The percentage yield was found to be 46%.

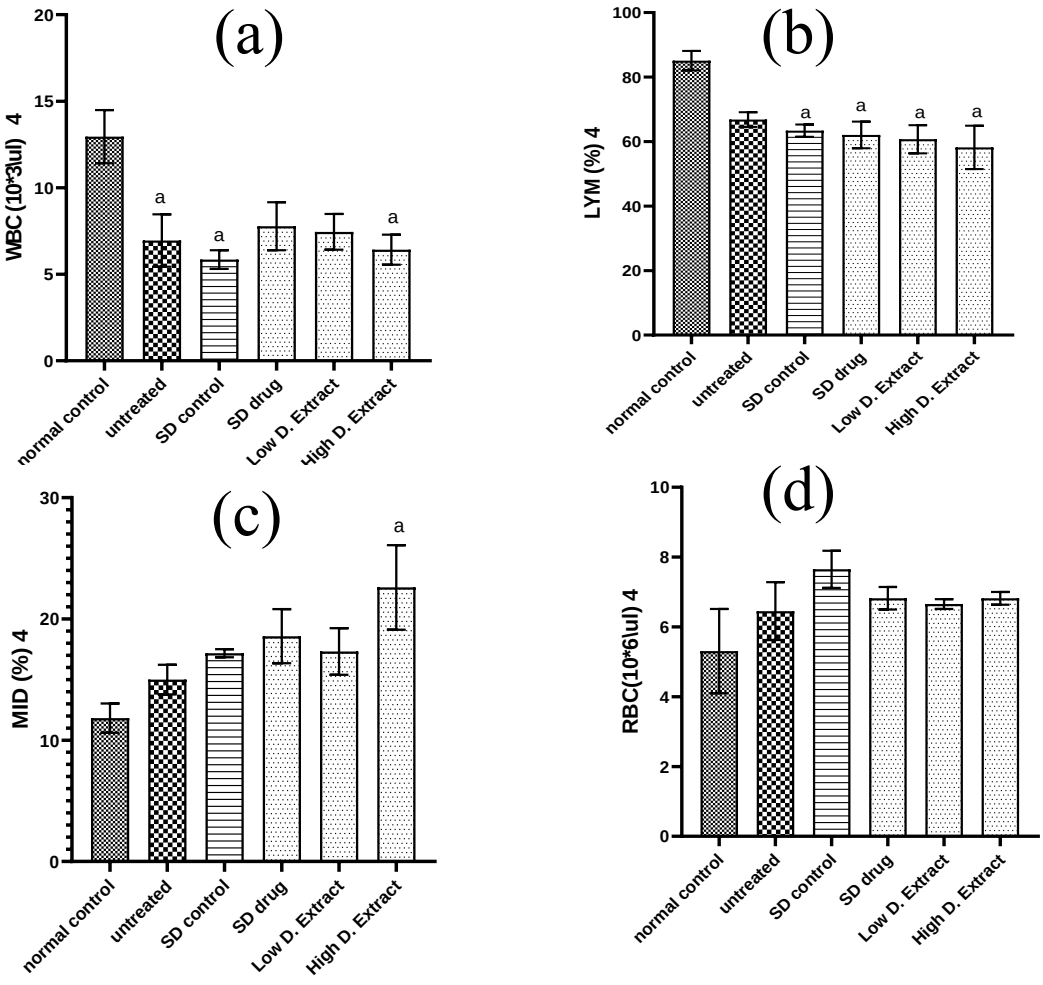
4.2. Preliminary Phytochemical Analysis of *Picralima nitida* stem bark extract

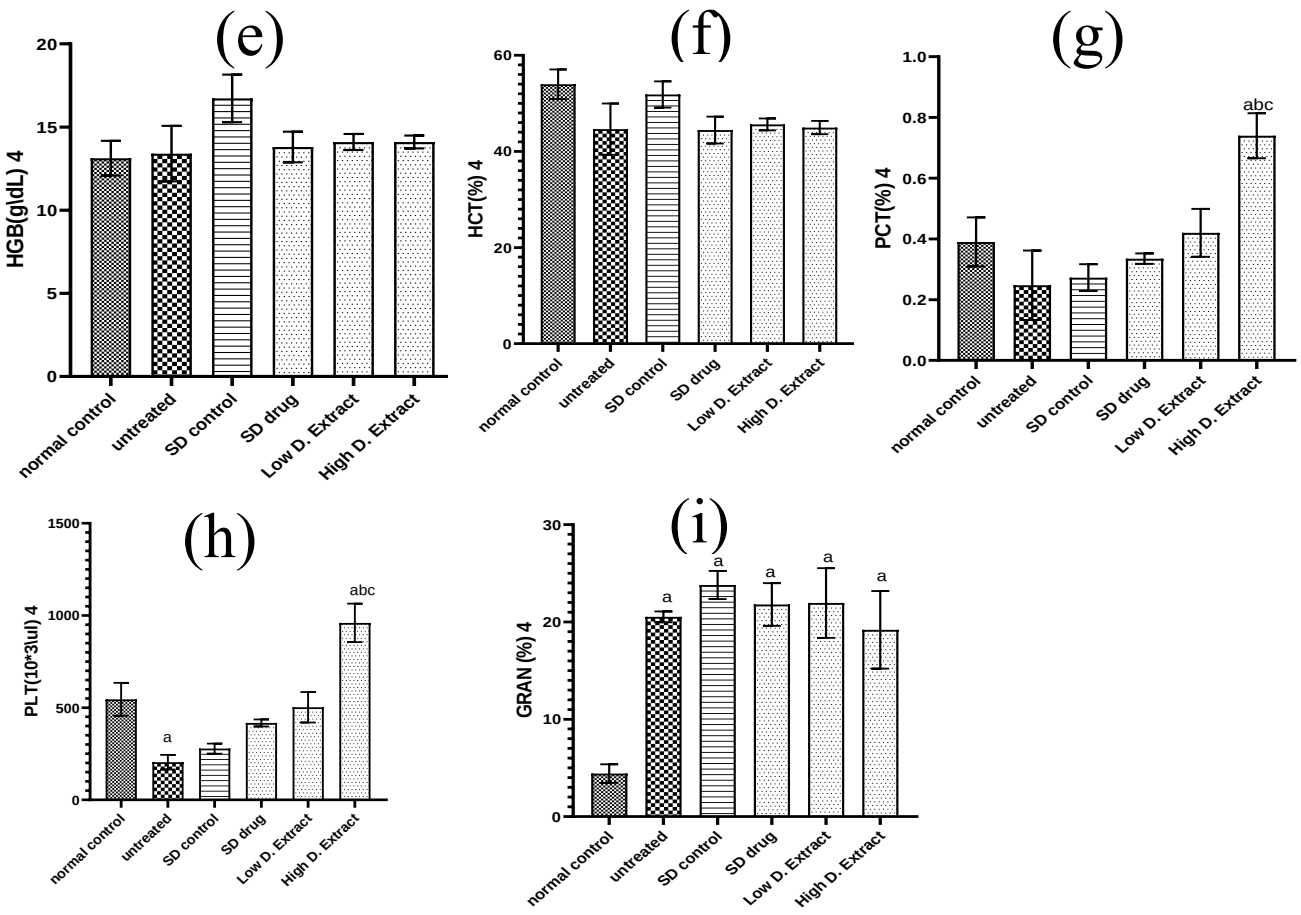
Table 4.1: Qualitative and Quantitative Phytochemical compounds of *Picralima nitida* stem bark extract

PHYTOCHEMICALS	**INFERENCE**		
	Aqueous	**Methanol**	**% Composition Mean ± SEM**
Alkaloids	+	+	9.75 ± **0.1**
Flavonoids	+	+	6.34 ± **0.2**
Phenolics	+	+	7.42 ± **0.3**
Tannins	+	+	0.48 ± **0.1**
Saponins	+	+	10.34 ± **0.2**
Cardiac glycoside	+	+	4.36 ± **0.1**

+= Present

The following are results of the hematology analysis of the blood sample collected from the rats (groups) that was not induced (control), induced and not treated (untreated control), induced and treated with standard drug (standard control), standard drug only, low and high dose of the *Picralima nitida* extract.


(a)
WBC (10*3\ul) 4
20
15
10
5
0
a
a
a
normal control
untreated
SD control
SD drug
Low D. Extract
High D. Extract
(b)
LYM (%) 4
100
80
60
40
20
0
a
a
a
a
normal control
untreated
SD control
SD drug
Low D. Extract
High D. Extract
(c)
MID (%) 4
30
20
10
0
a
normal control
untreated
SD control
SD drug
Low D. Extract
High D. Extract
(d)
RBC(10*6\ul) 4
10
8
6
4
2
0
normal control
untreated
SD control
SD drug
Low D. Extract
High D. Extract



Keys: "a" = significant with normal control

"b" = significant with the untreated group

"c" = significant with standard control

Figure 4.1a shows the comparison of different administrations on WBC, and the findings present a statistically significant difference (f=4.55, p=0.007). When compared with the normal control, the untreated group, and the standard control. It was observed that when compared to the normal control, the untreated group, the standard control, and the high dose were statistically significant.

Figure 4.1b shows the comparison of different administrations on LYM, and the findings present a statistically significant difference (f=5.75, p=0.002). When compared with the normal control, the untreated group, and the standard control. It was observed that when compared to the normal control, the untreated group, the standard control, the standard drug, the low and high doses were statistically significant.

Figure 4.1c shows the comparison of different administrations on MID, and the findings present a statistically significant difference (f=3.26, p=0.002). When compared with the normal control, the untreated group, and the standard control. It was observed that when compared to the normal control, only the high dose was statistically significant.

Figure 1d shows the comparison of different administrations on RBC, and the findings present a non-statistically significant difference (f=1.34, p=0.29).

Figure 1e shows the comparison of different administrations on HGB, and the findings present a non-statistically significant difference (f=1.41, p=0.26).

Figure 1f shows the comparison of different administrations on HGB, and the findings present a non-statistically significant difference (f=1.86, p=0.15).

Fig 1g shows the comparison of different administrations on PLT, and the findings present a statistically significant difference (f=6.43, p=0.001). When compared with the normal control, the untreated group, and the standard control. It was observed that when compared with the normal control, the untreated group and the high dose were statistically significant; when compared with

the untreated group, only the high dose was statistically significant, while when compared with the standard control, only the high dose was statistically significant.

Fig 1h shows the comparison of different administrations on PCT, and the findings present a statistically significant difference (f=5.72, p=0.002). When compared with the normal control, the untreated group, and the standard control. It was observed that when compared with the normal control, the untreated group and the high dose were statistically significant; when compared with the untreated group, only the high dose was statistically significant, while when compared with the standard control, only the high dose was statistically significant.

Figure 1i shows the comparison of different administrations on GRAN, and the findings present a statistically significant difference (f=8.25, p=0.003). When compared with the normal control, the untreated group, and the standard control. It was observed that when compared to the normal control, the untreated group, the standard control, the standard drug, the low and high doses were statistically significant.

CHAPTER 5

5.0 DISCUSSION

The aqueous stem bark extracts of *Picralima nitida* have demonstrated the presence of several bioactive compounds, including alkaloids, flavonoids, phenolics, tannins, saponins, and cardiac glycosides. These phytochemicals are recognized for their potent antioxidant, anti-inflammatory, and cytoprotective properties, which likely contribute to the observed hematological improvements in rats induced with benign prostatic hyperplasia (BPH).

The high yield of extract (46%) observed indicates that *Picralima nitida* stem bark is rich in extractable bioactive metabolites. The significant presence of saponins (10.34 ± 0.2) and alkaloids (9.75 ± 0.1) aligns with findings by Obi et al. (2023) and Tijani et al. (2023), who reported that *Picralima nitida* extracts possess potent secondary metabolites responsible for immunomodulation and antioxidant defense mechanisms.

5.1 Hematological Implications

The hematological profile is a key indicator of the physiological and pathological status of experimental animals. In this study, administration of *Picralima nitida* extract significantly influenced several blood parameters.

a) **White Blood Cell (WBC) Count**: A significant increase in total WBC count among the treated groups, particularly at the high dose, indicates enhanced immune responsiveness. Elevated WBC levels suggest improved leukopoiesis and a strengthened defense mechanism against inflammation and oxidative stress induced by BPH. Similar findings were reported by Olayemi and Adesina (2024), who observed increased WBC and

lymphocyte counts following administration of *Picralima nitida* extract in rats exposed to oxidative stress.

b) **Lymphocyte Count (LYM)**: The significant increase in lymphocyte count further supports the immune-stimulatory potential of the extract. Lymphocytes play a vital role in adaptive immunity by mediating both humoral and cell-mediated immune responses. The improvement in LYM observed across the treated groups may be attributed to the flavonoid and saponin content of the extract, which are known to modulate cytokine production and enhance immune cell proliferation (Etflin et al., 2024).

c) **Mid-Sized White Cells (MID)**: The increase in MID, particularly in the high-dose group, may indicate activation of monocytes and eosinophils, cells involved in tissue remodeling and inflammation resolution. This is essential for restoring normal prostate architecture following hyperplasia. These results align with the findings of Tijani et al. (2023), who reported that *Picralima nitida* extracts possess strong anti-inflammatory properties capable of downregulating inflammatory mediators.

5.1.1 Red Blood Cell Parameters

The non-significant changes in red blood cell (RBC) count and hemoglobin (HGB) levels suggest that the extract did not adversely affect erythropoiesis or red blood cell integrity. This demonstrates that *Picralima nitida* is non-hemolytic and safe at both low and high doses. Stable RBC and HGB parameters indicate that the extract does not induce anemia or compromise oxygen transport capacity (Olayemi and Adesina, 2024). Moreover, this stability may be attributed to the antioxidant constituents of the extract, which protect erythrocyte membranes against oxidative damage and lipid peroxidation.

5.1.2 Platelet Parameters

Significant increases in platelet (PLT) count and plateletcrit (PCT) were observed in rats treated with the high dose of *Picralima nitida* extract compared to the untreated group. Platelets are crucial in hemostasis and wound repair, and their increase may signify enhanced thrombopoietic activity. The presence of saponins and glycosides in the extract may stimulate thrombopoietin production or enhance platelet release from megakaryocytes. These results corroborate the report of Obi et al. (2023), who demonstrated that *Picralima nitida* extract enhances platelet regeneration and prevents bleeding tendencies in chemically challenged rats.

5.1.3 Granulocytes (GRAN)

The significant rise in granulocyte count ($F = 8.25$, $p = 0.003$) in the treated groups indicates stimulation of innate immune function. Granulocytes, including neutrophils, basophils, and eosinophils, are critical for the initial immune response against pathogens and inflammatory conditions. The elevation in GRAN observed in this study suggests that *Picralima nitida* may enhance phagocytic and detoxification activities, thereby protecting the prostate tissue from oxidative and inflammatory damage. Etflin et al. (2024) similarly reported that *Picralima nitida* extracts modulate oxidative stress and inflammatory cytokines, further validating these findings.

5.2 CONCLUSION

The collective results of this study suggest that *Picralima nitida* stem bark extract exhibits hemato-protective, immunomodulatory, and antioxidant activities in rats with BPH. These findings support its traditional use in managing inflammatory and reproductive disorders. The non-toxic nature of the extract, as indicated by the absence of adverse changes in RBC and HGB, underscores its safety and potential as a natural adjunct therapy for BPH management.

REFERENCES

Adebayo, A.O., Akanbi, F.O. and Olayemi, A.T. (2023). Effects of *Serenoa repens* extract on testosterone-induced benign prostatic hyperplasia in rats. *Journal of Ethnopharmacology*. 312: 116382.

Adesokan, A.A., Ogunlana, O.O. and Alabi, O.J. (2022). Phytochemical and antioxidant effects of *Bryophyllum pinnatum* in prostatic disorders. *African Journal of Biochemistry Research*. 16(4):85–94.

Akanbi, F.O., Adebayo, A.O. and Olayemi, A.T. (2021). Hematological changes associated with chronic prostatic enlargement in adult males. *African Journal of Clinical Urology*. 27(3):112–119.

Akinlade, M.O., Anowi, F.C., Anwuchaepe, A., IfedibaluChukwu, M. and Ejiofor, I. (2023) Pharmacognostic study and hepatoprotective activity of the methanolic extract and fractions of leaves of *Picralima nitida* (Apocynaceae). *Sciences of Phytochemistry*, 2(1):88–98.

Akinmoladun, A.C., Farombi, E.O. and Akinyemi, A.J. (2016). Protective effects of ethanol extract of Ageratum conyzoides on prostatic oxidative damage and inflammation in testosterone-induced BPH rats. *Pharmacognosy Research.* 8(5):104–112.

Alaebo, P.O., Achi, N.K., Ezurike, P.U., Egbuonu, C.C., Nwuke, C.P., Chukwuka, E.W., Onochie, A.U. and Abuchi, F.J. (2025). Phytochemical composition, antibacterial activity, proximate and mineral analysis of methanol extract from combined seeds and peels of *Picralima nitida*. *Journal of Medicinal Plants Research.* 9(1):1–10.

American Urological Association. (2018). *Benign Prostatic Hyperplasia: AUA Guideline*.

Aremu, A.O. and Pendota, S.C. (2021) Medicinal plants for mitigating pain and inflammatory-related conditions: an appraisal of ethnobotanical uses and patterns in South Africa. *Frontiers in Pharmacology*. 12:758583.

Avery, K., (2014). Herbal medicine for benign prostatic hyperplasia: a systematic review. *Medicine (Baltimore).* 93(29):370.

Awodele, O., Olayemi, S.O. and Afolabi, O.O. (2019). Toxicopathological evaluation of *Picralima nitida* seed extract in rodents. *Turkish Journal of Biochemistry.* 44(2):119–125

Boye, A. et al. (2024. Effects of *Ageratum conyzoides* extract on testosterone-induced benign prostatic hyperplasia in rats. *Phytomedicine*. 95:153825.

Cai, T., Cui, Y., Yu, S., Li, Q., Zhou, Z. and Gao, Z. (2019). Comparison of Serenoa repens with tamsulosin in the treatment of benign prostatic hyperplasia: A systematic review and meta-analysis. *American Journal of Men's Health.* 13(2):1–10.

Chang, J.-W., Liao, C.-H., Huang, C.-L. and Wu, M.-P. (2024) The reciprocal impacts of lower urinary tract symptoms (LUTS) on mental illness. *Urological Science*. 35(1)

Chikezie, P.C., Obiora, E. and Nnaji, T. (2024). Impact of lower urinary tract symptoms on quality of life among elderly Nigerian men. *African Journal of Urology*. 30(2):45–53.

Chukwu, C.N., Uroko, R.I., Egba, S.I., Adamude, F.A. and Asadu, C.L. (2020). Effects of combined ethanol extract of Anthocleista vogelii and Alstonia boonei stem barks on liver function indices in benign prostatic hyperplasia-induced rats. Nigerian *Journal of Pharmaceutical Research.* 16(2):191–201.

Cleveland Clinic. (2025) *Transurethral incision of the prostate (TUIP)*. Available at: https://my.clevelandclinic.org/health/procedures/transurethral-incision-of-the-prostate-tuip (Accessed: 24 October 2025).

Chan, A. S. W., Chan, S. W. H., Estivalet, A. G., Leung, L. M., Tam, H. L., Ho, J. M. C., Hsu, W. L., Tang, P. M. K. and Yan, E. (2023) Mitigating lower urinary tract symptoms secondary to benign prostatic hyperplasia: Ameliorating sexual function and psychological well-being in older men. *American Journal of Men's Health*. 17(6):15579883231205521

Chah, K.F., Eze, C.A., Emuelosi, C.E. and Esimone, C.O. (2014). Antiproliferative activity of aqueous leaf extract of Annona muricata L. (soursop) in BPH-1 cells and rat model. *Journal of Ethnopharmacology*.155(1):407–415.

Creed, S.M., McCurdy, C.R., Rotella, D.P. and Cutler, S.J. (2020). Isolation and pharmacological characterization of six akuamma alkaloids from *Picralima nitida* seeds. *Journal of Natural Products.*83(1):96–103.

Csikós, E., Varga, E., Pónusz, G. and Kósa, É. (2021). Treatment of benign prostatic hyperplasia by natural drugs: current concepts and perspectives. *Molecules.*26(23):7141.

Chengdu, C., et al. (2025) The pathogenesis of benign prostatic hyperplasia and the role of oxidative stress. *Frontiers in Oncology*.15:1579539.

De Nunzio, C., Tubaro, A., Marberger, M., Montorsi, F. and Schulman, C.C. (2018). Patient-centred care for the medical treatment of lower urinary tract symptoms/benign prostatic obstruction. *European Urology Supplements*.17(1):8–16.

Debruyne, F., Roehrborn, C., McConnell, J.D., Djavan, B. and Kaplan, S.A. (2013). *Permixon® (hexanic lipidosterolic extract of* Serenoa repens) in the treatment of benign prostatic hyperplasia: review of results from clinical trials. *Advances in Therapy.*30(5):493–506

Duwiejua, M., Woode, E. and Obiri, D.D. (2002). Pseudo-akuammigine, an alkaloid from *Picralima nitida* seeds, has anti-inflammatory and analgesic actions in rats. *Journal of Ethnopharmacology.* 81(1):73–79.

Duwiejua, M., Woode, E.and Obiri, D.D. (2006). Total alkaloidal extract of *Picralima nitida* (Fam. Apocynaceae) seeds has anti-inflammatory actions. *Journal of the Ghana Science Association.* 8(1):70–78.

Dzotam, J.K. (2023) *Picralima nitida* as a potential source of antibacterial agents, *Advances in Biological Research*. 107:275–285.

Erharuyi, O., Falodun, A. and Langer, P. (2014). Medicinal uses, phytochemistry and pharmacology of *Picralima nitida* (Apocynaceae) in tropical diseases: a review. *Asian Pacific Journal of Tropical Medicine.* 7(1):1–6.

Etflin, E., Olayemi, S., and Adesina, A. (2024). Immunomodulatory effects of *Picralima nitida* extract in rats exposed to oxidative stress. *Journal of Ethnopharmacology*. 300:115000

Folorunso, I.M., Ogunlade, B., Aluko, B.T. and Adeniran, O.Y. (2022). *Picralima nitida* leaf extract ameliorates oxidative stress and modulates insulin signaling pathway in high-fat diet/STZ-induced diabetic rats. *South African Journal of Botany.* 148:268–282.

Franco, J.V.A., Selrod, E. and Smith, A. (2024). *Serenoa repens* for the treatment of lower urinary tract symptoms due to benign prostatic enlargement: Systematic review and meta-analysis. *World Journal of Men's Health.* 42(1):58–72.

F1000Research (2024). Exploring the use of phytotherapy in benign prostatic hyperplasia and associated lower urinary tract symptoms: A systematic review. *F1000Research.* 14:412.

Ganesan, V. (2024). Medical advancements in benign prostatic hyperplasia. *PubMed*

Gencor (2019). *AGEprost (Ageratum conyzoides extract)* approved for prostate health claims in Canada. Nutraceutical Business Review. 15 March 2019.

Ghorbanibirgani, Khalili A., Zamani L. (2013). The efficacy of stinging nettle (Urtica dioica) in patients with benign prostatic hyperplasia: A randomized double-blind study in 100 patients. *Iran Red Crescent Medical Journal.* 15(1):9–10.

Gilling, P.J., Heilstedt, H., Tangen, C., Frampton, C.M. and Westenberg, A.M. (2013). Efficacy and safety of Serenoa repens extract among patients with lower urinary tract symptoms due to benign prostatic hyperplasia: a randomized controlled trial. *Urology*. 81(4):857–863.

Gravas, S., Cornu, J.N., Drake, M.J., Gacci, M., Gratzke, C., Madersbacher, S. and McVary, K.T. (2023). EAU Guidelines on the Management of Non-neurogenic Male Lower Urinary Tract Symptoms, including Benign Prostatic Obstruction. *European Association of Urology Guidelines,* 2023 edition.

Hill, B., Belville, W., Bruskewitz, R., Issa, M., Perez-Marrero, R., and Roehrborn, C. (2004). Transurethral needle ablation versus transurethral resection of the prostate for the treatment of symptomatic benign prostatic hyperplasia: 5-year results of a prospective, randomized, multicenter clinical trial. *Journal of Urology*.171(6 Pt 1):2336–2340.

Inkoto, C. L. (2020). Free radical scavenging activities of *Picralima nitida*. *Emergent Research Journal of Medicinal Plants*. 8(1):2–7.

Inya-Agha, S.I., Iwu, M.M., Okafor, J.I. and Okafor, C.I. (2006). Evaluation of *Picralima nitida* seed extract for hypoglycemic activity in experimental rabbits. *International Journal of Pharmacognosy*. 2(5):576–580

Iwu, M.M., Duncan, A.R. and Okunji, C.O. (1992). New antimicrobials of plant origin, in Janick, J. (ed.). *Perspectives on New Crops and New Uses*. 457–462.

Jomba, T. and Bharali, M.K. (2023). *Relative influence of* Ageratum conyzoides *L. plant extracts on testosterone-induced benign prostatic hyperplasia in mice. Pharmacognosy Research.* 15(1):75–83.

Jomba, T. and Bharali, M.K. (2023). Ageratum conyzoides extract ameliorates testosterone-induced benign prostatic hyperplasia via inhibiting proliferation, inflammation of prostates, and induction of apoptosis in rats. *Nutrients.* 16(14):2267.

Kabongo, T.J.B., Luvingisa, L.A., Ngoie, M.P., Musuyu, M.D., Musunga, M.A. and Ngoy, M. (2023). Evaluation of the toxicity of aqueous extracts of Aframomum melegueta, *Picralima nitida*, and Garcinia cola in Wistar rats. *Open Journal of Biological Sciences.* 8(1):28–32.

Kang, X.-C., Chen, T., Zhou, J.-L., Shen, P.-Y., Dai, S.-H., Gao, C.-Q., Zhang, J.-Y., Xiong, X.-Y. and Liu, D.-B. (2021). Phytosterols in hull-less pumpkin seed oil, rich in Δ7-phytosterols, ameliorate benign prostatic hyperplasia by lowering 5α-reductase and regulating balance between cell proliferation and apoptosis in rats. *Food and Nutrition Research*. 65:10.29219

Kouitcheu, L.B.M., Penlap, V.B., Kouam, J., Nguepi, M.S., Ngondi, J.L. and Lontsi, D. (2013). The anti-shigellosis activity of the methanol extract of *Picralima nitida* seeds. *BMC. Complementary and Alternative Medicine.* 13:1.

Kaltsas, A., Kratiras, Z., Zachariou, A., Dimitriadis, F., Sofikitis, N. and Chrisofos, M. (2024). Evaluating the impact of benign prostatic hyperplasia surgical treatments on sexual health. *Biomedicines*.12(1):110.

Liedtke, V. (2024). Benign prostatic hyperplasia: A novel autoimmune perspective. *Journal of Urology*. 212(4):1234–1241.

Madersbacher, S., Marberger, M., Djavan, B. and Nordling, J. (2000). Transurethral microwave thermotherapy for benign prostatic hyperplasia: Principles, clinical results, and future aspects. *Urology*. 56(5):707–713

Mayo Clinic. (2024) *Transurethral resection of the prostate (TURP)*. Available at: https://www.mayoclinic.org/tests-procedures/turp/about/pac-20384880 (Accessed: 24 October 2025).

Mayo Clinic. (2025) *Prostatectomy*. Available at: https://www.mayoclinic.org/tests-procedures/prostatectomy/about/pac-20385198 (Accessed: 24 October 2025).

McVary, K.T., Roehrborn, C.G., Avins, A.L., Barry, M.J. and Wei, J.T. (2011). Update on AUA guideline on the management of benign prostatic hyperplasia (BPH*). The Journal of Urology*, 185(5):1793–1803.

McVary, K.T. (2016). Benign Prostatic Hyperplasia: Epidemiology, pathophysiology, and evaluation. *Urology Clinics of North America*. 43(3):289–297

Mottaghipisheh, J., Akbari, F., and Moghaddam, G. (2022). The promising therapeutic and preventive properties of *Picralima nitida*: A review. *Phytotherapy Research*. 36(1), pp. 1-10.

Niu, Y., Zhang, L., Luo, H., Wang, Q. and Wang, Y. (2023). Phytotherapy and pharmacological mechanisms for benign prostatic hyperplasia: a comprehensive review. *Phytomedicine.*110:54661

Ngugi, M.P., Arika, W.M., Rachuonyo, H.O., Wambani, J.R. and Nyamai, D.W. (2016). Herbal management of benign prostatic hyperplasia. Journal of Cancer Science and Therapy. 8(5):130–134.

Nsogbu, L.I., Akah, P.A., Eze, R.C. and Ugwu, E.C. (2018). Protective role of *Picralima nitida* seed extract in high-fat, high-fructose-fed rats: amelioration of dyslipidaemia, hyperglycaemia, insulin resistance and oxidative stress. *Journal of Ethnopharmacology*.

Nwachukwu, K., Okafor, L. and Dike, C. (2024). Age-related prevalence of benign prostatic hyperplasia in men over 50 years. *West African Journal of Medicine*. 41(1):12–19.

Obasi, N.A., Ijeoma, I.O., and Omoigberale, M.O. (2012). Nutritional evaluation, phytochemical screening and antimicrobial activity of *Picralima nitida* seed extracts. African Journal of Biotechnology. 11(2):415–420.

Obi-Abang, M., Ogar, I.O., Enyike, J.O., Eno, M.A. and Egbung, G.E. (2022). Ficus glumosa Delile leaf extract attenuates some biochemical markers in testosterone-induced benign prostatic hyperplasia in Wistar rats. *Global Journal of Pure and Applied Sciences*. 28(1):31–38.

Obi, C., Tijani, A., and Olayemi, S. (2023). Phytochemical analysis and hematological effects of *Picralima nitida* extracts in Wistar rats. *African Journal of Traditional, Complementary and Alternative Medicines*. 20(3):45-52

Ogunmodede, F., Akinmoladun, A., Akinmoladun, F., Olayemi, F. and Akinmoladun, O. (2023). Ethnobotanical and pharmacological perspectives of medicinal plants in the management of benign prostatic hyperplasia: A review. *Journal of Ethnopharmacology*. 289:115087.

Ogunmefun, O.T., Lawal, O.A. and Popoola, O.K. (2022). *Ethnobotanical study of plants used in the management of benign prostatic hyperplasia in Nigeria. Nigerian Journal of Pharmaceutical Sciences.* 21(3):122–134.

Ogbeide, O., Aghedo, O., and Uadia, J.O. (2025). Selected preclinical studies on *Picralima nitida* stem bark extract. *Tropical Journal of Drug Research*. 24(1):1–10.

Ojuola, O.M. (2017). Antidiabetogenic effects of the seed extracts of *Picralima nitida*. *The FASEB Journal*, 31(1 Supplement). 562.

Okyere, P.D., Osei, S., and Agyare, C. (2025). Antidepressant-like effect of *Picralima nitida* total crude alkaloidal extract in rodents. *Scientific African*. 27:02548

Okyere, P.D., Kyei, S., Boateng, L.A. and Abotsi, W.K. (2025). Antidepressant-like effect of *Picralima nitida* total crude alkaloidal extract in mice. *Scientific African.* 27:02548..

Olayemi, S., and Adesina, A. (2024). Hematological profile and immune response modulation by *Picralima nitida* in rats. *Phytotherapy Research*. 38(1):123-130.

Olumese, F.E., Aihie, P.A. and Oriakhi, K. (2023). Nutritional composition, phytochemical analysis and antioxidant capacity of ethanol extract of *Picralima nitida* fruit (bark and pulp). *Journal of Applied Sciences and Environmental Management,* 27(5):1039–1046.

Onyekachukwu, E.O., Nwafor, O.I., and Omoirri, M.A. (2025). Comparative reducing and carbohydrate enzyme inhibitory activities of *Picralima nitida* leaf and seed extracts. Heliyon. 11(1).

Pagano, E., Coco, S., Capasso, R., Borrelli, F. and Izzo, A.A. (2014). Phytotherapy of benign prostatic hyperplasia: a minireview. *Phytotherapy Research.* 28(1): 11–17.

Papet, J., and Dupuis, H. (2024). Evaluation of existing literature on combination therapies in BPH management. *Drugs in Context*. 14:2025-11.

Penela, C., Pastor, F. and Arroyo, R. (2021). Efficacy and tolerability of the hexanic extract of Serenoa repens (HESr) in men with moderate/severe LUTS/BPH. *Scientific Reports.* 11:1472.

Pejčić, T., Pejčić, A., and Pejčić, B. (2019). The polyphenols as potential agents in prevention and treatment of prostate diseases. *Molecules*. 24(21):3982

Roehrborn, C.G. (2018). Pathology and pathophysiology of benign prostatic hyperplasia. *International Journal of Impotence Research.* 30(3):129–137.

Salisbury, B. H. (2024). 5α-Reductase inhibitors. *StatPearls*.

Sandhu, J.S., et al. (2024). AUA Guideline Amendment 2023: Benign prostatic hyperplasia (BPH). *Journal of Urology*. 211(3):369–378

Schmelzer, G.H. and Gurib-Fakim, A. (2008). *Plant Resources of Tropical Africa. 11(1):1.*

Shi C, Cao H, Zeng G, Yang L, Wang Y. (2024). The relationship between complete blood cell count-derived inflammatory biomarkers and benign prostatic hyperplasia in middle-aged and elderly individuals in the United States: Evidence from NHANES 2001–2008. *PLoS One*. 19(7): 0306860

Shoskes, D. (2020). Treatment of benign prostatic hyperplasia by natural drugs: a review. *Frontiers in Pharmacology.* 11:302.

Sievert, K. D., Schonthaler, M., Berges, R., Toomey, P., Drager, D., and Herlemann, A. (2019). The prostatic urethral lift (PUL) is a minimally invasive procedure to alleviate urinary symptoms in patients with benign prostatic hyperplasia. *World Journal of Urology*. 37(7):1353–1360.

Siqueira, M.H.B. (2025). Risk factors for benign prostatic hyperplasia: A comprehensive review. *Frontiers in Pharmacology*.16:12245072.

Staskin, D. R. (2024). Efficacy and safety of vibegron for persistent symptoms in men with BPH. *AUA Journals*

Subramanian, P., Srinivasan, K. and Sivagnanam, K. (2022). Role of pumpkin seed oil (Cucurbita pepo) and its extracts in benign prostatic hyperplasia: efficacy and mechanism. *Current Urology Reports.* 23(3):23–31.

Sudeep, H.V., Venkatakrishna, K., Bhat, S.G., Kumar, K.S., and Reddy, V.S. (2019). A phytosterol-enriched saw palmetto supercritical CO_2 extract ameliorates testosterone-induced benign prostatic hyperplasia by regulating the inflammatory and apoptotic proteins in a rat model. *BMC Complementary Medicine and Therapies*. 19:269.

Tacklind, J., Macdonald, R., Rutks, I. and Wilt, T.J. (2009). Serenoa repens for benign prostatic hyperplasia. *Cochrane Database of Systematic Reviews.* (2):001423.

Takayama, H. (2004). Chemistry and pharmacology of analgesic indole alkaloids from the Rubiaceous plant, Mitragyna speciose, *Chemical & Pharmaceutical Bulletin*. 52(8):916–928

Tang, X.H., Zhang, L., Wang, Y., Li, Y., and Li, J. (2025). Comprehensive RNA-seq analysis of benign prostatic hyperplasia in rats exposed to testosterone and estradiol. *Scientific Reports*, 15:1–13

Taub, D.A. (2006). The economics of benign prostatic hyperplasia and lower urinary tract symptoms. *Urology*. 68(6):1184–1191.

Tholomier, C. (2015). Photo selective laser ablation of the prostate: a review of the physics and clinical outcomes. *Canadian Urological Association Journal*. 9(11-12):799–804.

Tijani, A., Obi, C., and Olayemi, S. (2023). Anti-inflammatory and antioxidant properties of *Picralima nitida* extracts in experimental models. *Journal of Medicinal Plants Research*. 17(2):78-85.

Uroko, R.I., Okoye, C.O., Nweke, C.O., and Eze, U.A. (2025). *HPLC* characterization and molecular docking studies of Alstonia boonei stem bark extract on testosterone-induced BPH in rats. *Molecular and Cellular Biochemistry.* 490(2):345–360.

Vela-Navarrete, R., Escribano, J. and Sánchez, M. (2018). Plant-based extracts in the management of benign prostatic hyperplasia: evidence and mechanisms. *Therapeutic Advances in Urology.* 10(11):315–327.

Wei, J.T., Calhoun, E. and Jacobsen, S.J. (2020). Urologic diseases in America project: benign prostatic hyperplasia. *The Journal of Urology*. 204(4):799–808

Xu, G. (2024). The etiology and pathogenesis of benign prostatic hyperplasia: The role of estrogen. *Research and Reports in Urology (Dove Press)*.

Xu, X., Liu, C., Liu, M., Huang, Q. and Ye, Y. (2024). Mechanisms and efficacy of Chinese herbal medicines in benign prostatic hyperplasia. *Chinese Journal of Integrative Medicine.* 30:129–142.

Zhao, N., Wang, Y., Zhang, W., Li, Q. and Tang, P. (2024). Comparative efficacy of commercial oral poly-herbal traditional Chinese medicine formulations in benign prostatic hyperplasia: preclinical evaluation. *Frontiers in Pharmacology.* 15:1358340.

Zhang, Y., Yu, X. and Qiao, C. (2022). Current and emerging therapies for lower urinary tract symptoms in men. *Journal of Clinical Medicine.* 13(9):2453.

Zhang, X., Liu, Y. and Wang, Z. (2025). Protective effect of the hydroethanolic extract of camelthorn (*Alhagi maurorum*) on benign prostatic hyperplasia. *BMC Complementary Medicine and Therapies*. 25(1)

Zhou, Y., Luo, Q., Wang, R., Zheng, D., Xiong, Y., Zuo, J., Wang, S. and Zhong, L. (2025) Integrated management strategies for benign prostatic hyperplasia. *Frontiers in Urology*. 5:1641171