SYSTEMATIC REVIEW

REVISED Exploring the use of phytotherapy in benign prostatic hyperplasia [BPH]: a systematic review

[version 2; peer review: 1 approved, 1 approved with reservations]

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Abstract

Background

Benign prostatic hyperplasia [BPH] is a prevalent condition among aging men, characterized by prostate gland enlargement leading to lower urinary tract symptoms [LUTS]. Conventional treatments like alpha-blockers and 5-alpha-reductase inhibitors, though effective, often result in adverse effects. This has spurred interest in phytotherapy, leveraging plant-derived compounds to mitigate BPH symptoms due to their safety, cost-effectiveness, and patient

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preference.

Method

A literature search was conducted across PubMed, Scopus, and Google Scholar for articles published up to June 2024 using PRISMA 2020 guidelines. Eligible studies involve preclinical models of BPH, interventions specifically targeting plant or plant-based therapy, quantitative outcomes related to BPH treatment and ameliorations, and studies with clear methodology and reporting of the administration and plant-based products.

Results

The review highlighted 84 studies involving diverse plants and bioactive compounds. Prominent examples include Serenoa repens [saw palmetto], Urtica dioica [nettle root], Cucurbita pepo [pumpkin seed], and Pygeum africanum [African cherry]. These plants exhibit mechanisms such as 5α-reductase inhibition, anti-inflammatory effects, and modulation of oxidative stress. Clinical and preclinical findings demonstrate improved urinary flow, reduced prostate volume, and alleviated LUTS. However, variability in methodologies, extract preparations, and dosages poses challenges to standardization.

Conclusion

Phytotherapy holds significant potential in BPH management, offering symptom relief with minimal side effects. While promising, further robust clinical trials are essential to validate efficacy, establish standardized protocols, and ensure integration into mainstream therapeutic frameworks.

Keywords
Benign Prostatic Hyperplasia [BPH], Phytotherapy, 5α-Reductase Inhibition, Anti-inflammatory Effects, Lower Urinary Tract Symptoms [LUTS]

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REVISED **Amendments from Version 1**

The revised manuscript titled *"Exploring the Use of Phytotherapy in Benign Prostatic Hyperplasia (BPH): A Systematic Review"* has undergone thorough improvements following the reviewers' feedback. The abstract was rewritten to clearly describe the research methods, including databases used, selection criteria, and how studies were identified, while removing repeated content between methods and results. All botanical names were italicized for consistency, and numerous citation and punctuation errors were corrected throughout the text. The introduction was refined for better clarity and logical flow, ensuring factual accuracy and proper citation alignment, with the study's rationale and objectives clearly stated. In the methods section, sentences were restructured for clarity and consistency in style and referencing. The results and discussion were significantly strengthened by adding quantitative data to support findings, including a new table summarizing changes in BPH biomarkers across various plants. The discussion was reorganized to reduce repetition, highlight the key bioactive compounds responsible for therapeutic effects, and identify the plant families showing the highest efficacy in managing BPH. Figure quality and paragraph formatting were also improved for readability. The conclusion was rewritten into a single coherent paragraph. Overall, the revised version now presents a more polished, logical, and academically sound paper that fully addresses the reviewers' comments and enhances the quality and impact of the work.

Any further responses from the reviewers can be found at the end of the article

Introduction

Reproduction in humans involves internal organs that are not visible and external organs that are visible for copulation. The movement of sperm cells during copulation is enhanced by a fluid medium produced by accessory genital glands.[1] The prostate is a special genital gland that constitutes the invisible part of the male reproductive system.[2] The primary purpose of the prostate is to produce fluid called semen, which is combined with testicular sperm cells and other glandular secretions.[3] Disturbances associated with prostate dysfunction are the primary cause of infertility in males. These disturbances include prostate cancer, prostatitis, and prostatic hyperplasia.

Benign prostatic hyperplasia [BPH] also known as enlarged prostate is a common male reproductive disorder associated with age.[4] While the exact aetiology of BPH remains unidentified, it has been proposed that roughly 90% of testosterone may be transformed by 5α-reductase in prostate cells to dihydrotestosterone (DHT).[5] DHT promotes protein synthesis, growth and differentiation of prostate cells due to high affinity to androgen.[6] Symptoms of BPH include obstruction of the urinary bladder due to enlarged tissues and increased neck muscle tone of the bladder, which result in the inability to empty the bladder, urgent need to urinate, and weak urine output.[7] Studies have shown that BPH affects 30% of men above 65 years and account for 26.6 % of urinary disturbances in men.[8] It has been reported that 80% of men over 80 years have BPH.[9] In the United States of America (USA), 30% to 50% of infertility cases are attributed to males.[10] Additionally, statistics revealed that in the United Kingdom BPH occurs in 20 out of 100 males of reproductive age.[11] In developing countries in sub-Sahara Africa such as Nigeria and Kenya, the burdens of this disease have increased markedly in the last decade due to poor medical care and the economic reality facing these countries.[12] In Africa, about 40% of men aged 50 to 70 years are under medication for the treatment and management of BPH.[13]

Phytotherapy, surgery, and lifestyle modification are among the therapeutic options for treating BPH from European and non-European guidelines.[14] Phytotherapy is the use of medications made from plants or herbs to cure or prevent illnesses. In recent years the use of phytotherapy to mitigate reproductive impairments such as BPH has attracted global attention.[15,16] Scientists have reported that certain plant-derived phytochemicals could mitigate the adverse effects of BPH, and that polyphenols could improve male reproductive function.[17] Additionally, Ref. 18, suggested that the efficacy of this phytotherapy in the treatment and management of BPH is dose-dependent.

Benign Prostatic Hyperplasia [BPH] is a frequent prostate gland enlargement in older men. This might cause lower urinary tract issues, including frequent urination, poor urine flow, and an inability to empty the bladder. Many seek treatment for these symptoms because they affect their quality of life. Alpha-blockers and 5-alpha-reductase inhibitors are among the main classes of drugs used in the treatment of BPH. However, herbal treatments for BPH and LUTs are becoming more popular because they are safe, cheap, and simple to get. *Serenoa repens* [saw palmetto] is one of the most researched BPH herbs. People have used saw palmetto from *S. repens* berries to treat urinary problems caused by an enlarged prostate. Saw palmetto may inhibit 5-alpha-reductase, which converts testosterone into prostate-growing dihydrotestosterone [DHT]. By blocking inflammatory enzymes and lowering pro-inflammatory cytokines, saw palmetto has anti-inflammatory properties that may help ease the symptoms of conditions like BPH. Traditional medicine uses Pygeum, a bioactive compound from Prunus Africana [African cherry tree], to treat urinary and prostate health. Pygeum may help BPH and LUTs by reducing urinary frequency, enhancing urine flow, and reducing bladder residual urine. Phytosterols, ferulic acid, and other bioactive substances possess anti-inflammatory properties and hence can reduce swelling and inflammation. A thorough review indicated that pygeum reduced symptoms in men more than a

placebo.[19] Beta-sitosterol, as a DHT inhibitor, can reduce prostate inflammation, thereby relieving urine symptoms. Beta-sitosterol improves urine flow, reduces residual urine volume, and relieves urinary symptoms in clinical trials.[20] The meta-analysis of various research found that beta-sitosterol improved symptoms more than placebo in men.[21] BPH patients frequently use saw palmetto in combination with *Urtica dioica* [nettle root] nettle root extract.[14] The mixture also reduces sex hormone binding to prostate receptors, limiting their growth-promoting effects. Research has shown that nettle roots improve urinary symptoms and life quality.[22] The essential fatty acids, phytosterols, and other nutrients in pumpkin seed [*Cucurbita pepo*] extract may enhance prostate health.[23] It may reduce inflammation, strengthen bladder function, and limit prostate cell growth. According to Ref. 24, pumpkin seed extract can improve BPH symptoms such as frequent and midnight urination. Rye grass pollen extract [Secale cereale] is another natural BPH treatment. Its water-soluble and fat-soluble components may be anti-inflammatory, muscle-relaxing, and hormone-modulating. Rye grass pollen extract may relieve BPH urinary symptoms, according to several studies.[14] Some herbal medicines may help manage BPH and LUT symptoms. Their efficacy is variable, with some studies showing benefits and others showing none. Herbal products are less regulated than conventional drugs; therefore, quality and strength can vary. Herbal products are typically harmless, although they may interact with other drugs or create negative effects. The efficacy, safety, and optimal use of these herbal remedies for BPH and LUTs require further research. Even though herbal medicines may help some people, BPH and LUT management should include lifestyle changes, regular monitoring, and conventional medical treatments if needed.

However, the mechanism by which these phytotherapies regulate body functions and mitigate the adverse effects of BPH is still under scientific investigation.[25] reported that active ingredients present in plants for the treatment of BPH include lectins β-sitosterol and phytosterols. Based on different therapeutic measures employed for the treatment and management of BPH, we conducted a systematic review to explore the use of phototherapy in BPH. Therefore, this review will evaluate the effectiveness and safety of plant-based treatments known as phytotherapy for managing benign prostatic hyperplasia (BPH), a common condition in aging men that causes lower urinary tract symptoms.

2. Method

2.1 Search strategies

A comprehensive literature search of published works on phytotherapy for the management of BPH was systematically undertaken on the PubMed, Web of Science (WoS), and Scopus databases up to June 20, 2024. The following search terms were used: “natural product”, plants, foods, supplements, nutraceuticals, “benign prostatic hyperplasia”, management, amelioration, treatment, therapy, and remedy. Boolean operators; AND/OR/NOT, were used to develop search strategies according to the specifications of each of the databases according to the search strategy formulation methods reported by Refs. 26–28. The search was restricted to peer-reviewed literature published in English. The paper selection process was conducted in conformity with the Preferred Reporting Items for Systematic Reviews and Meta-analyses [PRISMA] 2020 guideline,[29] in accordance with previous studies.[30]

2.2 Selection criteria, and data extraction

The following inclusion criteria were applied for articles to be selected for the study: studies involving preclinical models of BPH, interventions specifically targeting plant or plant-based therapy, studies reporting quantitative outcomes related to BPH treatment and ameliorations, peer-reviewed articles published in English, studies with clear methodology and reporting of the administration and plant-based products. The exclusion criteria set for the screening and selection included: studies not focusing on BPH, and studies lacking preclinical models of BPH. Human studies were to be excluded, non-English publications, studies lacking clear reporting of outcomes or methodology, review articles, editorials, commentaries, and conference abstracts.

The data extracted from each of the included studies are: name of the plant or plant-based product, plant part [for plant extract], method of extraction [for plant extract], category [supplement, capsule, plant-extract, etc.], year of publication, method of induction, BPH model [e.g. rat, droso, mice, rabbit, etc], duration of treatment, nature of the study [protective or therapeutic]. A broad spectrum of plants was investigated for BPH management, reflecting their pharmacological diversity and ethnopharmacological relevance. Additionally, key details about each plant, including their scientific names, English names, botanical families, parts used, and countries of origin were highlighted in this review. The diversity of these plants reflects the global interest in phytotherapy for BPH and its integration into traditional and modern medicinal practices.

3. Results

3.1 Search results

The search identified a total of 694 articles: comprising 201 articles from WoS, 334 from Scopus and 159 articles from PubMed. The articles were transferred to Rayyan digital platform for assessment and selection for the systematic review

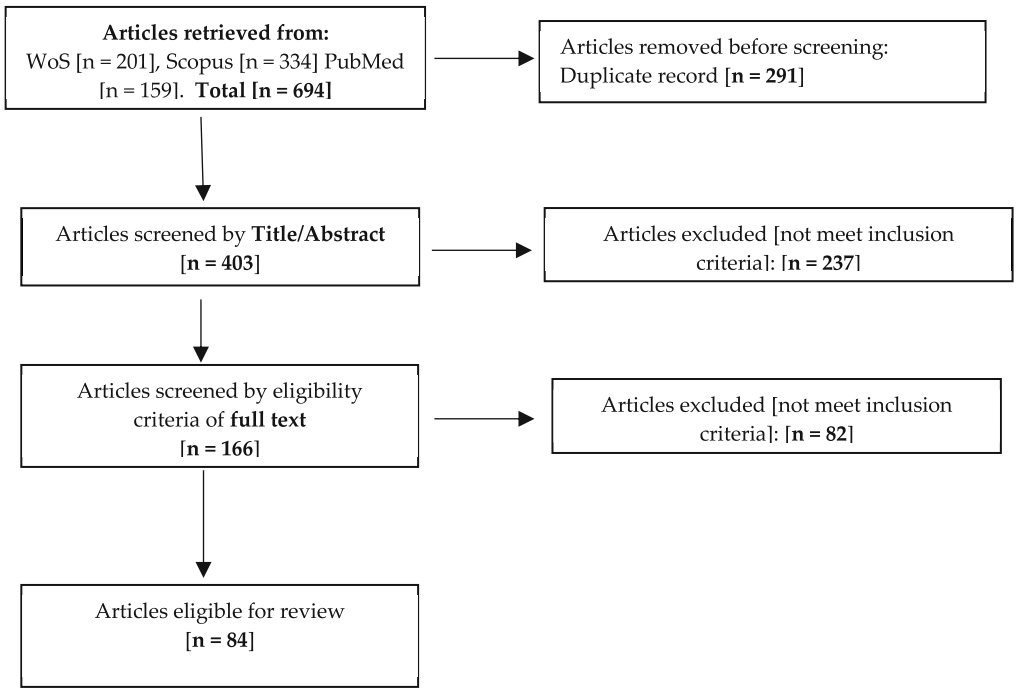

Figure 1. PRISMA flow chart for study selection.

methodology.[31] Using the platform, 494 duplicate were detected from the entries, leading to the deletion of 291 articles, whereas 163 articles were resolved. With other articles that have only single entries, a total of 403 articles were screened via title/abstract consideration, and full text screening sequentially, in accordance with the eligibility criteria. Ultimately, only 84 publications were examined in the study, having met the eligibility requirements [Figure 1].

3.2 Study characteristics

Several natural products and plant extracts were studied for their potential role in managing benign prostatic hyperplasia [BPH]. These included purple rice,[32] and *Couroupita guianensis Aubl.,*[33] *Epilobium angustifolium,*[34,35] green tea, soybean, and camellia oil,[36] *Panax ginseng* and bee-pollen,[37] and saw palmetto[38,39] (Table 1 and refer extended data Table 2).[140] Other notable plants included *Brassica campestris L.* pollen,[40] *Melandrii Herba,*[37] *Croton membranaceus,*[41] and *Caesalpinia bonduc.*[42] Additionally, plants such as *Cistanches salsa,*[43] *Withania coagulans,*[44] *Cucurbitacin E glucoside,*[45] *Moringa peregrina,*[46] and Antrodan[47] were also analyzed for their therapeutic properties in treating BPH [Table 1 and extended data Table 2]. Other samples included Lycopene and Curcumin,[40] funtumia Africana and *Abutilon Mauritianium* leaves[48] *Spermacoce radiata* and *Hypselodelphys poggeana,*[48] and *Pygeum africanum*[14] [Table 1 and extended data Table 2].

Table 1. Search strategies.

Database	Search strategy
Scopus	**TITLE-ABS-KEY** [“natural product” OR plant* OR food* OR supplement* OR nutraceutical*] AND [“benign prostatic hyperplasia”] AND [manag* OR ameliorat* OR treat* OR therap* OR remed* OR protect*]
WoS	[“natural product” OR plant* OR food* OR supplement* OR nutraceutical*] AND [“benign prostatic hyperplasia”] AND [manag* OR ameliorat* OR treat* OR therap* OR remed* OR protect*] **Title**
PubMed	[[[“natural product”**[Title/Abstract]** OR [plant***[Title/Abstract]** OR [food***[Title/Abstract]** OR [supplement***[Title/Abstract]** OR [nutraceutical***[Title/Abstract]**]] AND [“benign prostatic hyperplasia” **[Title/Abstract]**] AND [[manag***[Title/Abstract]** OR [ameliorat***[Title/Abstract]** OR [treat***[Title/Abstract]** OR [therap***[Title/Abstract]** OR [remed***[Title/Abstract]** OR [protect* **[Title/Abstract]**]] NOT [review **[Publication Type]**]

The types of extracts used varied widely depending on the plant. For instance, fractionation was used for purple rice[32] while in many studies the ethanolic extracts were applied [Table 1]. Studies using ethanolic extract include those of *Brassica campestris* L. pollen,[40] *Melandrii herba*,[37] *Cistanches salsa*,[49] and *Moringa peregrina*[50] Aqueous extracts were also common, as seen with Panax ginseng,[37] *Pygeum africanum,*[51] and Alginate Oligosaccharide[52] [Table 1]. Some studies used more specific combinations like Lycopene and Curcumin,[40] while others used supercritical fluid extraction, such as in the study of Saw palmetto oil.[53] Unique extracts like *cucurbitacin* E glucoside,[45] Curcuma oil,[54] and phenolic extracts from date seeds[55] were also explored [Table 1 and extended data Table 2].

3.3 Evaluation methods and mechanisms of action reported in the included studies

Various evaluation methods were used in these studies, reflecting a diversity of approaches to studying bioactive compounds. Western blot analysis was employed in studies of *Couroupita guianensis Aubl.,*[33] Saw palmetto,[53] and *Cinnamomum cassia* and *Rosa laevigata.*[33] Biochemical analysis was utilized in studies of *Epilobium angustifolium L*[56] and *Panax ginseng.*[37] Additionally, histopathological examination was frequently performed, as seen in studies with *Croton membranaceus,*[57] Caesalpinia bonduc,[42] *Brassica napus L,*[58] and *Pao Pereira* Extract.[59] Moreover, LC/MS-QTOF and ELISA tests were used to analyze compounds in some studies, such as with *Juglans regia,*[60] while immunohistochemistry was utilized in the study of *Panax ginseng* and bee-pollen.[37]

The mechanisms of action reported in the included studies have been presented in Table 1. Purple rice[32] exhibited protective effects against testosterone-induced BPH in rats, while *Couroupita guianensis Aubl.*[33] suppressed BPH-related biomarkers and improved the prostate index. *Epilobium angustifolium L*[56] extracts demonstrated an inhibitory effect on prostate enlargement, although the specific mechanisms were not elaborated. The combination of green tea, soybean, and camellia oil[36] inhibited the Dihydrotestosterone (DHT) and the Androgen Receptor (AR) complex and macrophage inflammation, showcasing their anti-inflammatory potential.

In the case of *Panax ginseng* and bee-pollen,[37] the aqueous extract was found to reduce prostate weights and DHT levels while decreasing prostatic epithelial hyperplasia. Similarly, saw palmetto oil[53] regulated inflammatory and apoptotic proteins in BPH rats. Another example was *Croton membranaceus*, where extracts acted as alpha-1 blockers and 5α-reductase inhibitors,[61] while *Caesalpinia bonduc*[42] inhibited DHT formation via 5α-reductase, leading to reduced BPH symptoms. Furthermore, curcumin and lycopene[40] were shown to inhibit inflammatory factors and regulate hormone levels associated with BPH. Similarly, *Pygeum africanum*[14] exhibited anti-androgenic effects by inhibiting fibroblast proliferation. Lastly, the study of *Phellodendri chinensis* cortex and *Anemarrhenae rhizoma*[14] showed these compounds' ability to reverse metabolite imbalances associated with BPH, while *Moringa peregrina*[50] exerted anti-inflammatory, anti-proliferative, and anti-angiogenic effects on BPH tissues.

3.4 Oxidative, Apoptotic, and Prostate Biomarkers

1. **Oxidative Stress Indicators**: The prominent elevated oxidative stress markers such as malondialdehyde, in BPH models, reflect increased lipid peroxidation and cellular damage. Again, the enhanced production of reactive oxygen species could lead to oxidative stress when the intracellular antioxidant defense system is overwhelmed. Antioxidant treatments, such as plant-derived polyphenols [*e.g., Lycopene and Curcumin*], have shown reductions in MDA levels, demonstrating their capacity to restore oxidative balance.[40]

2. **Apoptotic Biomarkers**: The pro-apoptotic markers [e.g., Bax, caspase-3] and anti-apoptotic markers [e.g., Bcl-2] are displayed in the Figure 2. Their concentrations are usually assayed during BPH investigation. Effective phytotherapy enhances apoptotic pathways in BPH tissues, as seen in studies of *Juglans regia* and *Annona muricata*, promoting programmed cell death to reduce hyperplasia.[62,63]

3. **Prostate-Specific Biomarkers**: Prostate-specific antigen [PSA] levels are elevated in untreated BPH but reduced following phytotherapeutic interventions like *Saw palmetto* and *Pygeum africanum*.[64] Alpha-blockers and 5-alpha-reductase inhibitors are among the main drugs employed in BPH treatment. *Saw palmetto* inhibits 5-alpha-reductase, which converts testosterone into prostate-growing dihydrotestosterone [DHT]. In animal model, *Croton membranaceus* extracts acted as alpha-1 blockers and 5α-reductase inhibitors,[65] while *Caesalpinia bonduc*[42] inhibited DHT formation via 5α-reductase, leading to reduced BPH symptoms.

3.5 Inflammatory biomarkers associated with BPH

Figure 3 shows the association of inflammatory markers with BPH. Elevated levels of TNF-α, IL-1β, IL-6, IL-8, COX-2, iNOS, in untreated BPH models and poorly managed clinical trials highlight the role of inflammation in the disease progression. Treatment with anti-inflammatory phytochemicals [e.g., phytosterols from *Urtica dioica* or essential oils from *Artemisia judaica*] reduces these cytokine levels, relieving BPH symptoms.[22,66] Similarly, NF-κB activation, a

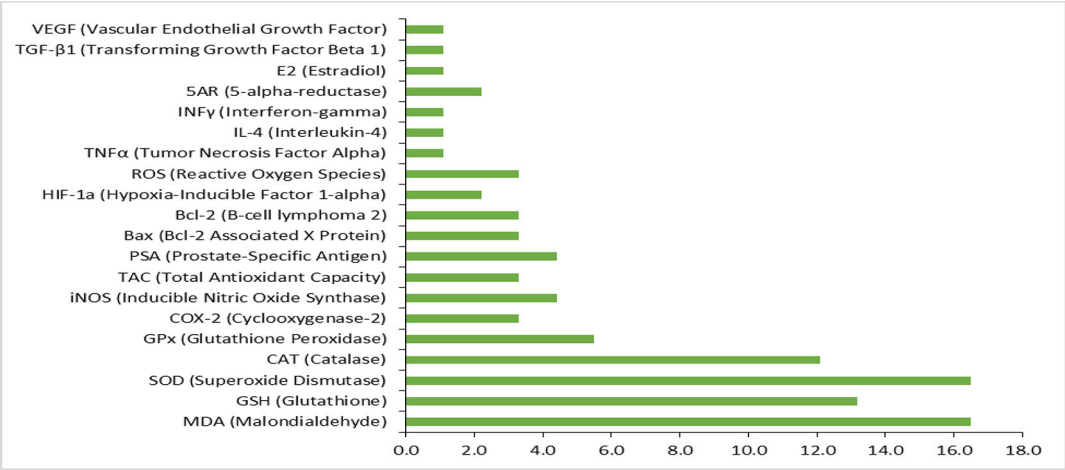

Figure 2. Oxidative, Apoptotic, and Prostrate Biomarkers.

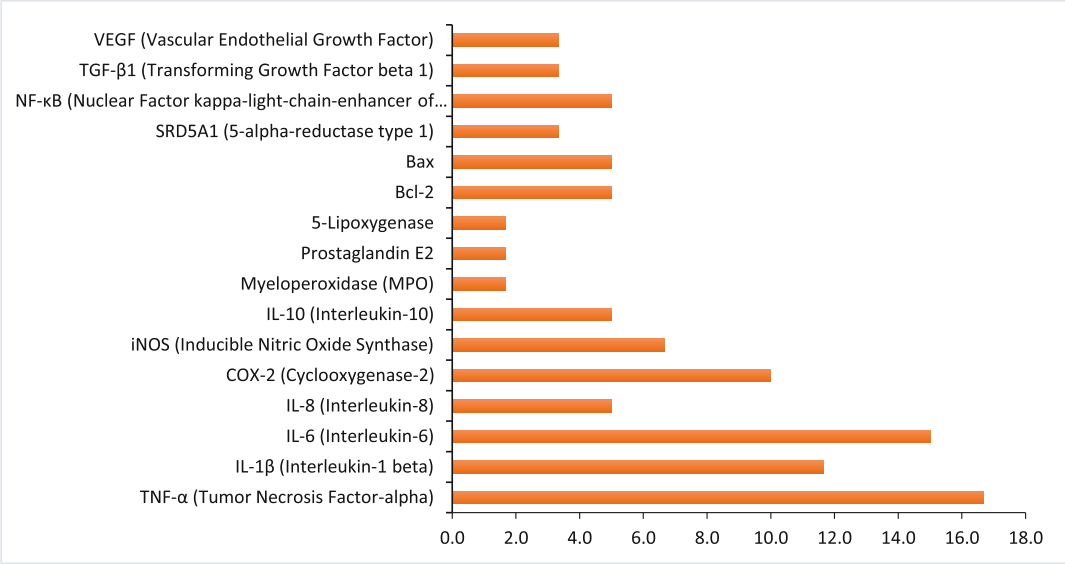

Figure 3. Inflammatory biomarkers associated with BPH.

hallmark of chronic inflammation, is suppressed by bioactive compounds in plants like *Curcuma longa* and *Epilobium angustifolium.*[67,68] This inhibition reduces inflammatory signaling and limits tissue proliferation in the prostate. Lower inflammatory markers after phytotherapy correlate with symptom improvement, such as reduced prostate volume and enhanced urinary flow. Studies on *Cucurbita pepo* and *Panax ginseng* support these outcomes.[24,37]

3.6 List of plants investigated

Extended data Table 3[140] shows plants studied for their therapeutic roles to manage Benign Prostatic Hyperplasia [BPH]. Table 3 lists the plants used according to their scientific names, English names, families, parts used, and country of origin.

Plant families and species diversity

All the listed plants are of different botanical families: Moringaceae, Brassicaceae, Araceae, Annonaceae, Cucurbitaceae, Fabaceae, and Urticaceae. Notably, the most predominant family was the Moringaceae family, for example, Moringa peregrina, which reduces inflammation, cell growth, and angiogenesis in BPH tissues.[50] Another is Annona muricata from the Annonaceae family, which stops 5α-reductase and lowers PSA levels and prostatic hyperplasia.[63] Again, Lepidium meyenii [Red Maca] and *Cucurbita pepo* [pumpkin] from the Brassicaceae family are known to have hormonal and prostate health effects,[24,69] while *Urtica dioica* from the Urticaceae family also stops 5α-reductase activity and has a

strong anti-androgen effect.[22] The variety of plants used in phytotherapy shows the different ways they can target pathways related to BPH, such as androgen signaling, inflammation, and oxidative stress.

Plant parts utilized

The parts used in research reflect the concentration of bioactive compounds. Researchers have studied a variety of plant parts, including leaves, seeds, fruits, tubers, whole plants, and even the stem itself. This variation is due to the different phytochemical profiles in different plant tissues.

Leaves: For instance, *Urtica dioica* [stinging nettle] leaves are rich in phytosterols and essential fatty acids, which exhibit anti-inflammatory effects,[70] while purple rice leaves have protective effects against testosterone-induced BPH in rats.[71]

Seeds: *Cucurbita pepo* [pumpkin] seeds are a traditional remedy for urinary issues, containing phytosterols and tocopherols that reduce prostate growth,[72] while *Glycine max* [soybean] inhibits the DHT-AR complex and macrophage inflammation, showcasing their anti-inflammatory potential.[73]

Roots and Tubers: Plants like *Colocasia esculenta* [Cocoyam] offer high antioxidant potential, making them useful for reducing oxidative stress associated with BPH.[74]

Fruits: *Kigelia africana* prevents and reverses testosterone-induced prostatic hyperplasia,[75] while *Xylopia aethiopica* [spice tree] possesses a protective effect against BPH in rats.[76]

Whole plant: *Lepidium meyenii* [red maca] modulates inflammatory pathways in BPH,[69] while *Croton membranaceus* [croton plant] extracts act as alpha-1 blockers and 5α-reductase inhibitors.[65]

Geographical Relevance

The plants listed originate from various geographical locations. The geographical spread of plants emphasizes their accessibility and ethnopharmacological importance. This also indicates a global interest in utilizing phytotherapy for BPH management. Notable examples include:

Africa: *Colocasia esculenta* [cocoyam, from Nigeria] and *Annona muricata* [Soursop, from Nigeria] are widely used in traditional African medicine for urinary and prostate health.[77]

Asia: Plants such as *Lepidium meyenii* [Red Maca, from Peru] and *Panax ginseng* [from Korea] highlight phytotherapy practices in traditional Peru and Korean medicine.[37]

Europe: *Epilobium angustifolium* [Rosebay Willowherb, from Poland] and *Epilobium angustifolium* [Rosebay Willowherb, from Italy] are known anti-inflammatory agents used in European herbal medicine.[78,79]

3.7 Families of plants investigated

Distribution across botanical families

Figure 4 showcases the diversity of plant families contributing to BPH treatment research, with notable representation from:

Urticaceae: for instance, *Urtica dioica*, which is known for inhibiting 5α-reductase and reducing DHT levels.[80]

Brassicaceae: example *Lepidium meyenii* [Red Maca], which modulates hormonal balance and inflammation.[69]

Asteraceae: for instance, *Taraxaci herba* [Dandelion], reduces prostate weights and lowers serum testosterone and DHT levels.[81]

Moringaceae: example, *Moringa peregrine* which exerts anti-inflammatory, anti-proliferative, and anti-angiogenic effects on BPH tissues.[82]

Annonaceae: notably, *Annona muricata* which inhibits 5α-reductase, reducing PSA levels and prostatic hyperplasia.[77]

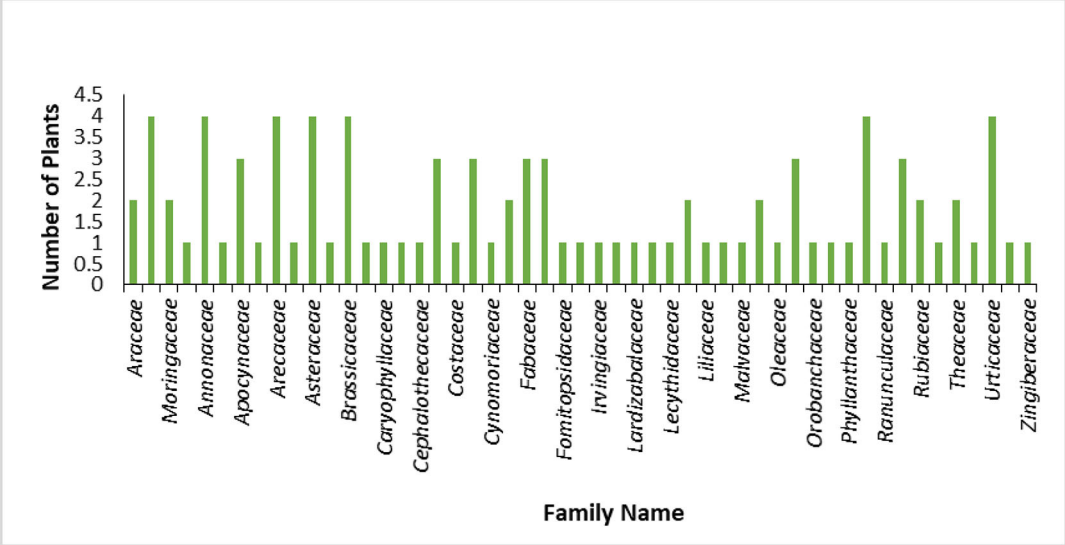

Figure 4. Families of plants investigated.

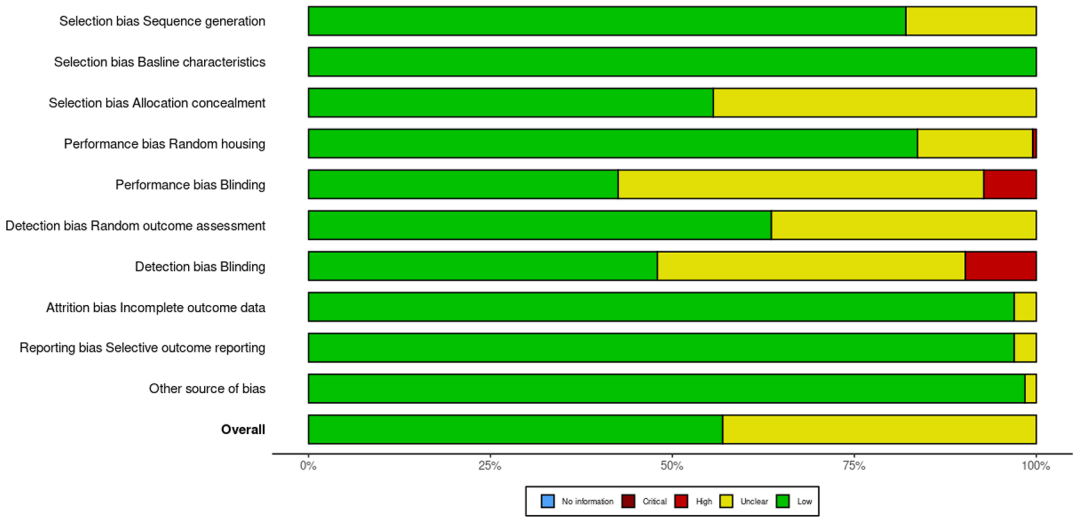

Figure 5. Risk of bias analysis of the included articles.

3.8 Risk of bias analysis

The Risk of Bias Visualization [robvis] tool was used in this systematic review to methodically assess and display any potential biases in the included papers. As shown in Figure 5.

4. Discussion

Benign prostatic hyperplasia [BPH] is a prevalent urological condition among aging men, significantly impacting their quality of life.[83] BPH is characterized by the benign enlargement of the prostate gland and frequently results in lower urinary tract symptoms [LUTS], such as nocturia, inadequate bladder emptying, and frequent urination.[83] Although traditional treatments like alpha-blockers and 5-alpha-reductase inhibitors are effective, they frequently cause side effects like dizziness, sexual dysfunction, and hypotension. This has led to interest in alternative treatments, especially phytotherapy, which uses substances derived from plants to reduce symptoms and slow the progression of the disease. These symptoms are caused by mechanical obstruction and secondary changes in bladder function.

This systematic review highlights the growing interest in phytotherapy as a viable approach to managing benign prostatic hyperplasia [BPH]. A wide range of plants and plant-based products were evaluated, showcasing their potential in

mitigating the symptoms and underlying causes of BPH. The most common sign of BPH is an enlarged prostate, which can also result from other conditions such as prostatitis, prostate cancer, or age-related hormonal changes.[84] The findings provide insight into the potential therapeutic uses of plant-based therapies, which are being explored in increasing numbers due to their accessibility, low risk of adverse effects, and patient preference for natural therapies.

This review highlights several known plants that showed efficacy in reducing symptoms of BPH, thy include: purple rice,[32] saw palmetto,[64] *Eulobium angustifolium*,[59] green tea, soybean, and camellia oil,[36] Panax ginseng and bee-pollen,[37] Croton membranous,[85] Brassica campestris L. pollen,[86] and Caesalpinia bonduc.[42] These plants possess anti-inflammatory qualities, suppress hormones that promote prostate growth, and enhance urine flow measurements. The review also underscores the role of bioactive compounds such as phytosterols, polyphenols, and essential fatty acids. For instance, beta-sitosterol has shown promising results in reducing prostate inflammation and enhancing urinary flow, as demonstrated in both clinical and preclinical studies.[20]

These phytotherapies primarily act by inhibiting 5α-reductase, reducing inflammatory markers, and regulating hormone levels, thus improving urinary symptoms and quality of life for patients.[22,87,88] Furthermore, antioxidants like lycopene and curcumin have been effective in reducing oxidative stress, a key contributor to BPH progression.[89] These findings align with global trends favoring safer, cost-effective, and accessible treatments, particularly in regions with limited access to advanced medical care, such as sub-Saharan Africa.[12]

4.1 Diversity of species and plant families

The plants reviewed in this work belong to a wide range of botanical families, underscoring the pharmacological diversity being explored for managing BPH. Notable examples include the Arecaceae (*Serenoa repens*), Brassicaceae (*Lepidium meyenii*, *Cucurbita pepo*), Urticaceae (*Urtica dioica*), Moringaceae (*Moringa peregrina*), and Annonaceae (*Annona muricata*).[69,90] This taxonomic variety highlights the different phytochemical pathways such as 5α-reductase inhibition, androgen modulation, anti-inflammatory activity, and oxidative stress reduction, through which these species exert therapeutic effects.[82,91] The broad distribution across plant families also reflects ethnopharmacological knowledge, where different cultural practices have converged on botanicals with demonstrable benefits for prostate health.[92,93]

Comparative data across studies further illustrate differences in efficacy among these plant families. For instance, *Serenoa repens* (Arecaceae) has been shown to reduce serum PSA levels by about 30% and improve IPSS scores by 25–35%, offering outcomes comparable to finasteride but with fewer adverse effects.[92,93] *Moringa peregrina* (Moringaceae) extracts have demonstrated a 20–25% reduction in prostate volume and significant suppression of inflammatory cytokines in animal models; however, large-scale clinical validation remains limited. Soybean isoflavones (Fabaceae) have been reported to have more modest effects, with 10–15% reductions in PSA and 15–20% improvements in urinary flow in controlled trials. Similarly, *Cucurbita pepo* (Brassicaceae) seed oil reduced IPSS by over 40% in a 12-week trial involving 2,000 men. These findings suggest that while Arecaceae (particularly saw palmetto) remains the most consistently effective family in reducing BPH biomarkers and symptoms, other families such as *Moringaceae*, *Brassicaceae*, and *Fabaceae* provide complementary benefits through distinct mechanisms. This diversity across plant families not only reinforces the therapeutic potential of phytotherapy but also underscores the opportunity for combination or standardized multi-target therapies that harness the strengths of different phytochemical classes.

4.2 Geographical distribution

The plants reviewed in this study, originate from diverse geographical regions, underscoring the accessibility and ethnopharmacological significance of BPH treatments across cultures. This also indicates a global interest in utilizing phytotherapy for BPH management. Notable examples include; Africa, where plants like *Annona muricata* [Soursop], *Xylopia aethiopica* [Spice Tree], and *Colocasia esculenta* [cocoyam, from Nigeria],[77] are commonly used in traditional African medicine for urinary and prostate health.[77,94] Other areas include Asia**,** which features plants like *Panax ginseng* [Korean Ginseng] and *Epilobium angustifolium* [Rosebay Willowherb],[33,78,95] reflecting the integration of traditional Chinese and Korean medicine into BPH management and Europe with Plants like *Epilobium angustifolium* from Poland and Italy indicates the role of herbal medicine in European traditions.[78,79] Another location and culture where these herbs are used is America**,** having plants such as *Cucurbita pepo* [Pumpkin Seed] and *Lycopene* from tomatoes,[72] showcasing the focus on nutraceuticals in North and South America. The wide geographical representation indicates the universal burden of BPH and the global interest in accessible and sustainable phytotherapeutic solutions.

4.3 Parts of plants utilized

The parts used in the research reflect the concentration of bioactive compounds. Researchers have studied a variety of plant parts, including leaves, seeds, fruits, tubers, whole plants, and even the stem itself. This variation is due to the different phytochemical profiles in various plant tissues. The Leaves of *Urtica dioica* [stinging nettle] have rich concentrations of phytosterols and essential fatty acids, which exhibit anti-inflammatory effects,[80] while purple rice

leaves have protective effects against testosterone-induced BPH in rats.[96] The Seeds of *Cucurbita pepo* [pumpkin] is a traditional remedy for urinary issues, containing phytosterols and tocopherols that reduce prostate growth,[72] while *Glycine max* [soybean] inhibits the DHT-AR complex and macrophage inflammation, showcasing their anti-inflammatory potential.[73] The roots and tubers of plants like *Colocasia esculenta* [Cocoyam] offer high antioxidant potential, making them useful for reducing oxidative stress associated with BPH,[97] while the fruits of *Kigelia africana* prevent and reverses testosterone-induced prostatic hyperplasia.[75] *Xylopia aethiopica* [spice tree] possesses a protective effect against BPH in rats.[76] Notably, the whole plant parts have been used for some studies. The whole plant parts of plants like *Lepidium meyenii* [red maca] modulate inflammatory pathways in BPH 170[69] while *Croton membranaceus* [croton plant] extracts act as alpha-1 blockers and 5α-reductase inhibitors.[65] *Cistanches salsa* has been recorded to have a combined anti-inflammatory and anti-proliferative effects.[98]

4.4 Mechanisms of action

The plant investigated, characteristics, and mechanism of action of the plants for BPH treatment are shown in Table 1 and extended data Table 2. The studies reviewed revealed multiple mechanisms through which these phytochemicals exert their therapeutic effects. These include hormonal Modulation, Anti-Inflammatory capacity, antioxidative mechanism, and apoptotic regulation. Many compounds inhibit 5α-reductase, reducing dihydrotestosterone [DHT] levels, a key factor in BPH pathogenesis. Phytotherapeutic agents such as those found in saw palmetto and Pygeum africanum, operate through diverse mechanisms that directly target the pathophysiological aspects of BPH.[58,99]

Several clinical trials have evaluated the efficacy of phytotherapy in managing BPH symptoms. Saw palmetto, for instance, has been widely studied, with findings indicating its ability to improve urinary flow rates and reduce LUTS. A meta-analysis comparing saw palmetto with placebo found significant symptom improvement with fewer side effects than conventional medications.[100] Extracts such as saw palmetto [*Serenoa repens*] are rich in fatty acids and phytosterols, which inhibit the enzyme 5-alpha-reductase, reducing dihydrotestosterone [DHT] levels. DHT plays a pivotal role in prostate growth, and its inhibition can significantly curb prostate enlargement.[64] Additionally, these agents exhibit anti-inflammatory effects by downregulating pro-inflammatory cytokines and reducing oxidative stress, both of which are implicated in prostate tissue hyperplasia.

Despite these findings, variability in study design and outcomes presents challenges. Some studies demonstrate negligible differences between phytotherapeutic agents and placebos, underscoring the need for robust and standardized research. Differences in extraction methods, dosages, and patient populations contribute to the heterogeneity of results. Other agents, like pygeum [*Prunus africana*], [*Cinnamomum cassia and Rosa laevigata*] act as anti-androgens and reduce cholesterol accumulation in the prostate, which is linked to glandular hyperplasia. The obstructive symptoms of BPH are lessened by the anti-inflammatory properties of pygeum bark [*Prunus africana*]. Rats' prostate stromal cells' basal growth is inhibited by the bark when it is stimulated by TPA [tissue plasminogen activator], bFGF, EGF, IGF-I, and PDBu [phorbol 12,13-butyrate].[14] Stinging nettle [*Urtica dioica*] demonstrates estrogen-modulating properties and also inhibits sodium-potassium ATPase activity in the prostate cells, helping to regulate cellular activity.[80] The multi-faceted actions of these compounds make them particularly appealing as therapeutic agents. According to studies on animals, U. dioica's flavonoid concentration significantly reduces platelet aggregation and enhances the lipid profile.[101,102] Additionally, it was discovered that the stinging nettle methanol extract dramatically reduced the experimentally induced prostate development.[14]

Cucurbita pepo [*pumpkin*]: Pumpkin seed extract's therapeutic benefits include alleviating the symptoms of lower urinary tract ailments, prostate abnormalities, and urinary tract disorders.[103] Pumpkin seed extracts may mitigate testosterone-induced hypertrophy by blocking the rise in prostate weight and protein synthesis brought on by testosterone and prazosin Furthermore, 10 g of pumpkin extract per day has tonic effects on the bladder and urethra.[104,105] The effects of pumpkin seed oil were assessed in a clinical investigation including more than 2000 males with BPH. For 12 weeks, the patients took 500–1000 mg of the oil daily. Consequently, the medication reduced the IPSS by 41.4%, and over 96% of patients experienced no negative side effects, suggesting that pumpkin seed oil greatly reduced patients' urinary dysfunction.[106] Pumpkin seed oil enhances the antioxidative defense system, reducing oxidative stress markers, while compounds such as Juglans regulate hyperplastic prostate tissues, aiding in volume reduction. Purple rice[32] exhibited protective effects against testosterone-induced BPH in rats, while *Couroupita guianensis Aubl.*[107] suppressed BPH-related biomarkers and improved the prostate index. *Epilobium angustifolium L*[108] extracts demonstrated an inhibitory effect on prostate enlargement, although the specific mechanisms were not elaborated. In the case of *Panax ginseng* and bee-pollen,[37] the aqueous extract was found to reduce prostate weights and DHT levels while decreasing prostatic epithelial hyperplasia. Similarly, Saw palmetto oil[87] regulated inflammatory and apoptotic proteins in BPH rats. Another example was *Croton membranaceus*, where extracts acted as alpha-1 blockers and 5α-reductase inhibitors,[65] while *Caesalpinia bonduc*[42] inhibited DHT formation via 5α-reductase, leading to reduced BPH symptoms. Furthermore, curcumin and lycopene[89] were shown to

inhibit inflammatory factors and regulate hormone levels associated with BPH. Lastly, the study of *Phellodendri chinensis* cortex and *Anemarrhenae rhizoma*[109] showed these compounds' ability to reverse metabolite imbalances associated with BPH, while *Moringa peregrina*[82] exerted anti-inflammatory, anti-proliferative, and anti-angiogenic effects on BPH tissues. *Pygeum africanum*[88] exhibited anti-androgenic effects by inhibiting fibroblast proliferation.

4.5 Plants targeting androgen signaling and 5α-reductase activity

Several plants exert their therapeutic effects by targeting androgen signaling, particularly by inhibiting 5α-reductase, a key factor in BPH progression. *Serenoa repens* [Saw Palmetto] has been widely studied for its ability to inhibit 5α-reductase, reduce DHT levels, and alleviate urinary symptoms.[110] Its anti-inflammatory properties further enhance its therapeutic profile.[64,87] These findings suggest that *Serenoa repens* could be a primary candidate for phytotherapy in BPH, especially for patients seeking non-invasive treatments. Pygeum africanum [African Cherry] is known for reducing urinary frequency and residual urine, this plant demonstrates anti-androgenic effects through the inhibition of fibroblast proliferation and DHT production.[88] These properties make *Pygeum africanum* suitable for managing both symptoms and underlying causes of BPH. *Urtica dioica* [Nettle Root] plant complements *Serenoa repens* in combination therapies by inhibiting sex hormone binding to prostate receptors, thereby limiting prostate growth.[22] Such synergies highlight the potential for combination therapies to enhance efficacy.

4.6 Plants with anti-inflammatory properties

Elevated levels of TNF-α, IL-1β, IL-6, IL-8, COX-2, iNOS, in untreated BPH models and poorly managed clinical trials highlight the role of inflammation in the disease progression. Chronic inflammation is a critical factor in BPH progression. Treatment with anti-inflammatory phytochemicals [e.g., phytosterols from *Urtica dioica* or essential oils from *Artemisia judaica*] reduces these cytokine levels, relieving BPH symptoms.[22,111] Similarly, NF-κB activation, a hallmark of chronic inflammation, is suppressed by bioactive compounds in plants like *Curcuma longa* and *Epilobium angustifolium.*[33,112] This inhibition reduces inflammatory signaling and limits tissue proliferation in the prostate. Lower inflammatory markers after phytotherapy correlate with symptom improvement, such as reduced prostate volume and enhanced urinary flow. Plants with anti-inflammatory properties offer an alternative or complementary approach to conventional treatments. Studies on *Cucurbita pepo* and *Panax ginseng* support these outcomes.[24,37] Curcuma longa [Turmeric] and Cucurbita pepo [Pumpkin Seed] are both very common plants that contain bioactive compounds like curcumin and phytosterols, which reduce pro-inflammatory cytokines and inhibit macrophage-driven inflammation.[72,89] These effects correlate with improved urinary symptoms and reduced prostate size, suggesting their potential as adjunctive treatments in BPH management. Epilobium angustifolium [Rosebay Willowherb] plant inhibits DHT-induced androgen receptor translocation and decreases prostate-specific antigen [PSA] levels, emphasizing its dual anti-inflammatory and androgen-regulating effects.[112] Similarly, *Pygeum africanum*[88] exhibited anti-androgenic effects by inhibiting fibroblast proliferation. The combination of green tea, soybean, and camellia oil[36] inhibited the DHT-AR complex and macrophage inflammation, showcasing their anti-inflammatory potential.

4.7 Plants with antioxidant properties

Oxidative stress contributes to the pathogenesis of BPH by inducing cellular damage and inflammation. Several plants reviewed show promise in counteracting oxidative stress. Lycopene [Tomato Extract] and Curcumin, both restore oxidative balance by reducing malondialdehyde [MDA] levels, a marker of lipid peroxidation. This protective effect mitigates BPH symptoms and slows disease progression. *Annona muricata* [Soursop] plant's antioxidant activity, mediated by its ability to inhibit 5α-reductase, positions it as a promising candidate for managing BPH.[77,89]

4.8 Phytotherapy with multi-modal effects

Several plants demonstrate a combination of anti-androgenic, anti-inflammatory, and antioxidant activities, making them highly versatile. Croton membranaceus act as an alpha-1 blocker and 5α-reductase inhibitor. This plant addresses multiple pathways involved in BPH pathogenesis. Clinical studies show significant symptom improvement, supporting its potential for broader clinical applications.[14,65,85] Cistanches salsa and Moringa peregrina plants exhibit anti-inflammatory, anti-proliferative, and anti-angiogenic effects on prostate tissues, emphasizing their role in both symptom management and disease modification.[82,98] *Serenoa repens* [Saw Palmetto] derived from the saw palmetto fruit, is one of the most widely used phytotherapeutic agents for BPH. Its lipid extracts inhibit 5α-reductase, reducing DHT levels and mitigating prostate enlargement. Numerous clinical trials have shown significant improvements in IPSS and peak urinary flow rates.[113–115] Despite its popularity, recent studies suggest its effects may be equivalent to placebo in certain settings, underscoring the need for more rigorous investigations.

Saw Palmetto [*Serenoa repens*] - Saw palmetto remains a common therapy for BPH. Extracts derived through supercritical fluid extraction regulated inflammatory and apoptotic proteins in BPH models, reducing PSA and prostate volume 29.[116] The dual mechanism of 5α-reductase inhibition and androgen receptor antagonism underscores its role as a natural alternative to conventional medications.[117]

Pygeum africanum [African Plum] - *Pygeum africanum* has been extensively studied for its role in BPH management.[88,118,119] Extracts from its bark exhibit multiple mechanisms of action, including inhibition of oxidative stress, inhibition of fibroblast proliferation, modulation of androgen receptor activity, and reduction of prostatic inflammation.[119] Pygeum inhibits the activity of growth factors and reduces androgen receptor binding, resulting in prostate size reduction and improved urinary symptoms.[118] Meta-analyses have demonstrated moderate improvements in urinary flow and nocturia reduction.[14,120] However, variations in study designs and treatment durations warrant further research to validate its therapeutic potential.

Purple Rice [*Oryza sativa*] - Purple rice has demonstrated protective effects against testosterone-induced benign prostatic hyperplasia [BPH] in animal models.[32] The crude ethanolic extract of purple rice modulated oxidative stress and reduced inflammation in the prostate tissue. These effects are attributed to the bioactive anthocyanins present in purple rice, which act as potent antioxidants. Key findings included the reduction of prostate size and the suppression of pro-inflammatory cytokines such as TNF-α and IL-6.

Couroupita guianensis Aubl., has shown promising results in regulating BPH biomarkers.[107] Using western blot analysis, studies revealed that extracts from this plant improved the prostate index and reduced the levels of prostate-specific antigen [PSA] and androgen receptor expression.[107] These effects highlight its potential as an anti-inflammatory and anti-proliferative agent in managing BPH.

Cucurbita pepo [Pumpkin] - *Cucurbita pepo*, commonly known as pumpkin, is extensively used in managing BPH symptoms.[121] The seeds contain bioactive compounds such as phytosterols, which exert antiandrogenic effects by inhibiting 5α-reductase and preventing the conversion of testosterone to dihydrotestosterone [DHT].[72] Clinical trials have demonstrated significant improvements in urinary flow rates and reductions in prostate volume following pumpkin seed extract administration.[122,123] However, the variability in extraction methods and dosages across studies highlights the need for standardized formulations to optimize its therapeutic potential.

Cucurbitacin E Glucoside - Cucurbitacin E glucoside, a triterpenoid compound, exhibits potent anti-inflammatory and antiproliferative effects, making it a promising agent for BPH management.[45] Studies have demonstrated its ability to inhibit the NF-κB signaling pathway, which reduces the production of pro-inflammatory cytokines like TNF-α and IL-6.[45,124] Additionally, its role in oxidative stress regulation is evident through its capacity to enhance superoxide dismutase [SOD] activity and decrease malondialdehyde [MDA] levels, key oxidative biomarkers associated with BPH progression.[45]

Epilobium ang [Fireweed] - Fireweed extracts have been traditionally used in European medicine for prostate health. The ethyl acetate and n-butanol extracts were found to inhibit DHT-induced androgen receptor translocation, reducing PSA levels.[108] The bioactive polyphenols and flavonoids in Epilobium angustifolium contribute to its anti-inflammatory and anti-androgenic effects, making it a viable candidate for phytotherapy in BPH management.

Green Tea, Soybean, and a combination of green tea extract, soybean, and camellia japonica oil demonstrated synergistic effects in inhibiting the DHT-androgen receptor complex and suppressing macrophage-mediated inflammation.[125,126] This blend reduced oxidative stress markers, including MDA and SOD levels, while improving apoptotic regulation via caspase activation.[126] This combination therapy highlights the potential benefits of integrating multiple plant compounds for comprehensive BPH management.

Panax Ginseng and Bee Pollen - Panax ginseng and bee pollen, have shown significant efficacy in reducing prostate weights and DHT levels while ameliorating prostatic epithelial hyperplasia.[14] Immunohistochemistry and biochemical analyses revealed the anti-inflammatory and anti-androgenic properties of these extracts, mediated through the down-regulation of androgen receptor pathways and pro-inflammatory cytokines.[127]

Urtica dioica [Stinging Nettle] - Urtor its anti-inflammatory properties and ability to inhibit SHBG binding, thereby reducing the proliferation of prostate cells.[80] While randomized controlled trials demonstrate significant symptom relief and reductions in IPSS scores,[128] its weak inhibition of 5α-reductase and limited influence on prostate size suggest it may be more effective in combination therapies.

Brassica campestris L. Pollen - Ethanol-refined extracts of Brassica camplen have demonstrated improvements in BPH symptoms. This extract has been reported to act as an antioxidant, reducing ROS levels and enhancing apoptotic markers such as Bax and caspase-3.[40] Additionally, it modulates androgen receptor pathways, contributing to the reduction of prostatic hyperplasia.

Caesalpinia bonduc - Seed extracts of Caesalpinia bonduc exhibit significant anti-androgenic effect by inhibiting 5α-reductase.[42] This action reduces DHT formation, leading to a decrease in prostate volume and inflammation. LC/MS-QTOF analyses confirmed the presence of bioactive compounds responsible for these therapeutic effects.[129] Cistanches salsa—Ethanol extracts of Cistanches salsa were shown to improve BPH symptoms by regulating stress and enhancing apoptotic markers. The pro-apoptotic effects are mediated through caspase-3 activation and down-regulation of Bcl-2, reducing prostate size and improving urinary symptoms.[98] *Withania coagulans* - Withania coagulans, also known as vegetable rennet, has potent anti-inflammatory and apopin BPH management. Studies have revealed its ability to inhibit pro-inflammatory cytokines such as IL-6 and TNF-α while enhancing apoptotic pathways, thereby mitigating prostatic hyperplasia.[130]

Moringa peregrina, also known as Moringa peregrine, is recognized for its rich antioxidant profile, which contains bioactive compounds such as quercetin and kaempferol. These compounds reduce oxidative stress by scavenging free radicals and upregulating endogenous antioxidant enzymes.[82] The plant also exhibits significant anti-inflammatory properties by modulating the expression of cyclooxygenase [COX] enzymes and reducing the levels of prostaglandins, which are elevated in BPH. Clinical and preclinical evaluations indicate its potential in decreasing prostate volume and alleviating LUTS symptoms.

Antrodan - Antrodan, a polysaccharide derived from the Antrodia cinnamomea mushroom, has been studied for its anti-inflammatory and apoptotic properties in BPH treatment.[50] It inhibits inflammatory mediators, such as interleukins [IL-1β, IL-6] and TNF-α, by downregulating the MAPK pathway. Furthermore, Antrodan induces apoptosis in hyperplastic prostate cells by activating caspases and modulating the Bcl-2/Bax ratio, crucial apoptotic biomarkers.[131]

Lycopene and Curcumin - Lycopene, a carotenoid found in tomatoes, and curcumin, a polyphenol derived from turmeric, have synergistic effects in managing BPH.[89] Lycopene reduces oxidative stress by neutralizing reactive oxygen species [ROS], while curcumin inhibits inflammation by suppressing the NF-κB pathway.[49,132] Both compounds have been shown to downregulate prostate-specific antigen [PSA] levels and reduce prostate volume.[89] Their antioxidant properties also contribute to decreased levels of MDA and increased activity of SOD and catalase.

Funtumia africana and *Abutilon mauritianium* Leaves - These plants are traditionally used for their anti-inflammatory and antioxidant properties. Bioactive compounds in *Funtumia africana*, such as alkaloids and flavonoids, inhibit pro-inflammatory cytokines and reduce oxidative damage in prostate tissue.[48] Similarly, *Abutilon mauritianium* leaves contain phenolic compounds that enhance antioxidant defenses and modulate apoptotic pathways, aiding in prostate health restoration.[48]

Spermacoce radiata and Hypselodelphys poggeana - The combined use of Spermacoce radiata and Hypselodelphys poggeana has shown potential in reducing BPH symptoms.[48] These plants possess bioactive compounds that inhibit 5α-reductase activity, thereby reducing DHT levels. Additionally, their anti-inflammatory effects are mediated through the suppression of COX-2 expression and the reduction of inflammatory biomarkers like TNF-α.

Other Phytotherapeutics - Several other plants, including *Urtica dioica* [stinging nettle] and Secale cereale [rye grass pollen], have shown promise in managing BPH symptoms.[14,133] *Urtica dioica* exerts its effects by inhibiting inflammatory pathways and androgen receptors,[134] while Secale cereale enhances urinary flow and reduces residual volume through anti-inflammatory and anti-androgenic mechanisms.[135,136] While these agents are supported by clinical evidence, their inclusion in combination therapies warrants further exploration to optimize efficacy. Additional plants such as *Secan* and *Serenoa repens* [saw palmetto] have been investigated for BPH management. Rye grass pollen demonstrates anti-inflammatory and antiandrogenic activities, while saw palmetto inhibits 5α-reductase. Although these agents show promise, most studies emphasize the need for larger, long-term trials to validate their efficacy.

4.9 Limitations and controversies

While the promise of phytotherapy is clear, several limitations in the reviewed studies warrant discussion

1. Lack of consistency and Standardization in methodologies: the lack of consistency in methodologies, such as variations in plant extraction techniques and dosages, poses a challenge to reproducibility and comparability. The amounts of active chemicals in the extracts produced by different studies vary, which causes conflicting findings in different research.

2. Insufficient Long-term Data: The majority of studies focus on immediate results, which leaves gaps in our knowledge of the longevity and effectiveness of these therapies.

3. Individual Variability: Therapies may become more complex as a result of patient reactions to phytotherapy that differ depending on genetics, the severity of the condition, and concurrent drugs.

4. The regulatory landscape for phytotherapy is less stringent than that for conventional drugs, leading to variability in product quality and potency.

Controversies also exist regarding the efficacy of certain phytotherapies. While some studies report significant improvements in urinary symptoms and prostate size reduction, others find no better outcomes than placebo.[21] For example, although *Saw palmetto* has been extensively studied, its efficacy remains debated, highlighting the need for more rigorous research to resolve these inconsistencies.[64]

4.10 Integration into clinical practice

The conventional care of BPH is supplemented by phytotherapy. Phytotherapeutic substances provide a feasible and less harmful option for patients with mild to moderate symptoms who prefer natural treatments. The absence of standardized products, however, forces practitioners to rely on higher-ups, validated supplements. Phytotherapy may also be helpful when combined with traditional therapies, especially for patients who want to reduce their symptoms without experiencing worsening adverse effects.

4.11 Implications for future research

Phytotherapy offers a viable alternative to conventional treatments, particularly in regions with limited access to healthcare resources. However, the lack of standardization in extraction processes and dosages, coupled with a paucity of high-quality clinical trials, limits its integration into evidence-based practice.[137,138] Future research should prioritize harmonizing methodologies and exploring combination therapies to maximize efficacy.

The diverse mechanisms and bioactive compounds of these plants highlight their potential for tailored therapies in BPH management. Plants like *Serenoa repens* and *Pygeum africanum* could serve as front-line treatments, especially for mild to moderate cases.[64,88,139] Anti-inflammatory and antioxidant-rich plants, such as *Curcuma longa* and *Lycopene*, may act as supportive therapies, reducing reliance on conventional drugs and mitigating side effects. Moreover, emerging therapies like *Croton membranaceus* suggest opportunities for integrative approaches that combine multiple therapeutic pathways.

However, standardization in extraction methods, dosages, and clinical protocols remains essential to harness these plants' full potential. This synthesis underscores the need for large-scale clinical trials to validate these findings and establish phytotherapy as a cornerstone in the holistic management of BPH.

4.12 Knowledge gaps and research opportunities

Despite the promising potential of phytotherapy, significant gaps remain in our understanding of its mechanisms, efficacy, and long-term safety. Many studies reviewed were preclinical, relying on animal models, with limited human clinical trials to validate their findings.[32,107] The variability in extraction methods and dosages further complicates the standardization of these treatments, making it difficult to draw firm conclusions or develop universal guidelines for their use.

Future research should prioritize:

1. Conducting large-scale, multicenter clinical trials to evaluate the efficacy and safety of promising phytotherapies such as *Croton membranaceus* and *Cucurbita pepo* in diverse populations.[65,72]

2. Exploring underutilized plants with ethnopharmacological relevance, particularly in regions like Africa and Asia, where traditional medicine plays a vital role.[13]

Investigating the synergistic effects of combining phytotherapy with conventional treatments, which may offer enhanced outcomes while minimizing side effects.

5. Conclusion

In conclusion, this systematic review underscores the potential of phytotherapeutic agents in managing benign prostatic hyperplasia [BPH] through their anti-inflammatory, antioxidant, and hormone-modulating properties. Promising agents such as saw palmetto, *Pygeum africanum*, *Urtica dioica*, and *Moringa peregrina* have shown efficacy in reducing prostate enlargement, alleviating inflammation, and improving urinary symptoms.

Despite these encouraging findings, various inconsistencies in study designs, sample sizes, and treatment protocols pose challenges to drawing definitive conclusions about their therapeutic benefits. This review emphasizes both the promise of phytotherapy and the need for further research to facilitate its integration into mainstream medical practice.

Phytotherapy presents a cost-effective alternative for managing BPH, particularly in low-income settings. To fully realize its potential, it is essential to address existing knowledge gaps, standardize methodologies, and conduct robust clinical trials. By doing so, plant-based therapies could play a pivotal role in a holistic approach to BPH management that harmonizes traditional remedies with modern medical practices.

Author roles

Mbyemeire H: Conceptualization, Investigation, Methodology, Project Administration, Software; Fasogbon IV: Data Curation, Formal Analysis, Resources, Software, Supervision; **Musyoka AM:** Conceptualization, Data Curation, Formal Analysis, Methodology, Validation; **Oviosun A:** Formal Analysis, Project Administration, Resources, Visualization; **Ojiakor VO:** Data Curation, Formal Analysis, Investigation, Resources, Software; **Agunloye MO:** Formal Analysis, Software, Visualization, Writing – Original Draft Preparation; **Wusa M:** Investigation, Methodology, Resources, Software; **Okon MB:** Data Curation, Investigation, Methodology, Software; **Ikuomola EO:** Conceptualization, Investigation, Methodology; **Dangana RS:** Formal Analysis, Methodology, Software; **Usman IM:** Formal Analysis, Funding Acquisition, Writing – Original Draft Preparation; **Etukudo EM:** Data Curation, Methodology, Validation; **Terkimbi SD:** Investigation, Software, Validation, Visualization; **Danchal CV:** Investigation, Resources, Software, Visualization; **Mujinya R:** Investigation, Methodology, Software; **Mbina SA:** Conceptualization, Validation, Visualization; **Okon IA:** Investigation, Resources, Software, Visualization; **Alum EU:** Formal Analysis, Investigation, Validation; **Abubakar IB:** Software, Supervision, Validation, Visualization; **Mitaki NB:** Conceptualization, Investigation, Resources, Software; **Anyanwu GE:** Resources, Supervision, Validation, Writing – Review & Editing; **Ugwu OPC:** Methodology, Software, Validation, Visualization; **Jega SA:** Investigation, Resources, Software, Supervision; **Uti DE:** Investigation, Software, Validation, Visualization; **Aja L:** Data Curation, Formal Analysis, Visualization; **Owembabazi E:** Resources, Supervision, Validation, Visualization; **Kembabazi S:** Investigation, Resources, Software, Validation; **Chinedu AP:** Resources, Software, Visualization, Writing – Original Draft Preparation; **Olorunnisola OS:** Investigation, Supervision, Validation, Writing – Review & Editing; **Aja PM:** Formal Analysis, Resources, Supervision, Writing – Review & Editing.

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Data availability

No data are associated with this article.

Extended data

Open Science Frameork: Exploring the use of phytotherapy in benign prostatic hyperplasia [BPH]: a systematic review. (https://doi.org/10.17605/OSF.IO/7NZ39)[140]

This project contains the following extended data:

- Tables.rar
- manuscript.rar

Reporting guidelines

Open Science Frameork: PRISMA checklist and flowchart for "Exploring the use of phytotherapy in benign prostatic hyperplasia [BPH]: a systematic review" https://doi.org/10.17605/OSF.IO/7NZ39.[140]

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Publisher Full Text

Open Peer Review

Current Peer Review Status: ✔ ?

Version 2

Reviewer Report 26 February 2026

https://doi.org/10.5256/f1000research.190686.r460754

✔ **Gift Crucifix Pender**
Pharmacology and Toxicology, University of Rwanda College of Medicine and Health Sciences Huye, Butare, Southern Province, Rwanda

The authors have addressed all concerns earlier raised. I therefore recommend that this study be considered for indexing.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Pharmacology &Toxicology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 28 May 2025

https://doi.org/10.5256/f1000research.178170.r380126

? **Paul Ndubuisi Anyiam**
[1] Department of Biochemistry, College of Natural Sciences, Michael Okpara University of Agriculture Umudike, Umuahia, Abia State, Nigeria
[2] Department of Biochemistry, College of Natural Sciences, Michael Okpara University of

Agriculture Umudike, Umuahia, Abia State, Nigeria

Thank you for the opportunity to review this manuscript. Find my comments and suggestions below;

General comment: The review manuscript by Mbyemeire et al. on the use of phytotherapy for the treatment and/or management of BPH is interesting and addresses a relevant topic. The paper is generally well-structured, and the English language is acceptable. However, mainly problem with the manuscript is incorrect reference citations, and the discussion of the findings is weak. Also, the findings are presented in a qualitative manner without sufficient quantitative evidence from the literature to support the conclusions. Other comments and suggestions are provided below;

1. The absence of line numbers in the manuscript makes the review process very difficult. Please include line numbers for review.

Abstract:

1. The report from the methodology section was incorrectly repeated in the results section, which needs to be corrected.
2. The abstract should briefly mention the methodology, including the search engines consulted and the keywords used during the literature search under the methodology section.
3. All botanical names should be italicized throughout the manuscript.

Introduction:

1. Second paragraph, line 7. Please correct the citation error; it is currently written as 'Ref.9,' which does not follow standard referencing format. Correct this throughout the manuscript.
2. In paragraph 3, Line 5, '..*[17] reported that*....' This should be corrected as well. The correct format should be '*Stewart et al.[17] reported that*.. Correct similar error throughout the paper.
3. In paragraph 3, line 6; '*Additionally Ref.18 suggested that*..., Please correct this citation to ' *Additionally, Katsimperis et al.[18] suggested that*..' correct similar citation throughout the manuscript.
4. Paragraph 4, in line 1. Since the abbreviation for Benign Prostate Hyperplasia has been introduced, use only the abbreviation (BPH) thereafter. Please apply this consistently throughout the paper.
5. At the end of the introduction, after the objective, please add a sentence stating the rationale or purpose of the review study.
6. The sentence, '*the most common sign of BPH is an enlarged prostate,*' should be revised to acknowledge that prostate enlargement can also result from other conditions such as prostatitis, prostate cancer, or age-related hormonal changes.

Results:

1. The manuscript lacks quantitative data to support the efficacy of the reviewed plants, relying solely on qualitative discussion. For example, comparing the extent to which saw palmetto reduces elevated BPH biomarkers (such as PSA levels) compared to Moringa or soybean across studies would better illustrate their potential in BPH management and improve the paper's overall quality.
2. Consider including a table summarizing the findings on the percentage increase or reduction of BPH biomarkers for each plant. This would provide a clear overview of each plant's potential in BPH management and also support the purpose of the review.
3. In section 3.3, second paragraph. What is the full meaning of DHT-AR?
4. Section 3.4 appears disconnected from the rest of the discussion. Please add a connecting sentence to improve the logical flow.
5. Figure 5: Please improve the quality and readability of the text in Figure 5.

Discussion:

1. Section 4.1 of the discussion appears to repeat the results and should be either rephrased or removed.
2. Paragraph 5 in the discussion section; '*A broad spectrum of plant*...' would be more appropriately placed in the introduction or methodology section.
3. Which plant family among those mentioned demonstrates the highest efficacy in managing and/or treating BPH?
4. A brief discussion of the key bioactive components in each plant that may drive the observed effects would be valuable
5. Also, the discussion throughout the paper is mainly qualitative. Incorporating more quantitative data from the literature (as suggested in result section) would strengthen the discussion.
6. In Section 4.4, line 2, the phrase '...*the studies reviewed revealed..*' should be checked for grammar and corrected
7. Line 6, Section 4.4, contains the phrase '*Example include saw palmetto and Pygeum africanum*,' which appears as an incomplete sentence Please revise for clarity.
8. Section 4.4, line 6 contains the term "*AntiInflammchemicals*," which is unclear. Please rephrase this term for better understanding.
9. The statement, "Extracts such as saw palmetto are rich in fatty acids and phytosterols," requires a supporting reference citation.
10. The entire manuscript requires proper paragraph formatting for consistency.

Conclusion.

1. Please remove the paragraph breaks in the conclusion and rewrite it as a single block of text.
2. From your analysis, include information identifying the plant or plant family with the highest efficacy against BPH.

Best regards

Are the rationale for, and objectives of, the Systematic Review clearly stated?

Partly

Are sufficient details of the methods and analysis provided to allow replication by others?

Yes

Is the statistical analysis and its interpretation appropriate?

Partly

Are the conclusions drawn adequately supported by the results presented in the review?

Partly

If this is a Living Systematic Review, is the 'living' method appropriate and is the search schedule clearly defined and justified? ('Living Systematic Review' or a variation of this term should be included in the title.)

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Biochemical pharmacology, functional ingredients, nutraceuticals and Chemistry of food proteins

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 31 Oct 2025

Angela Mumbua Musyoka

1
General comment: The review manuscript by Mbyemeire et al. on the use of phytotherapy for the treatment and/or management of BPH is interesting and addresses a relevant topic. The paper is generally well-structured, and the English language is acceptable. However, mainly problem with the manuscript is incorrect reference citations, and the discussion of the findings is weak. Also, the findings are presented in a qualitative manner without sufficient quantitative evidence from the literature to support the conclusions. Other comments and suggestions are provided below;

Done

2
The absence of line numbers in the manuscript makes the review process very difficult. Please include line numbers for review.

That is being done.
Done

3

Abstract:
The report from the methodology section was incorrectly repeated in the results section, which needs to be corrected.

That was noted and corrected
Done

4
The abstract should briefly mention the methodology, including the search engines consulted and the keywords used during the literature search under the methodology section.

That has been corrected

5
All botanical names should be italicized throughout the manuscript.

That is noted and corrected

6
Introduction:
Second paragraph, line 7. Please correct the citation error; it is currently written as 'Ref.9,' which does not follow standard referencing format. Correct this throughout the manuscript.

That is corrected

7
In paragraph 3, Line 5,.17 reported that....' This should be corrected as well. The correct format should be 'Stewart et al.17 reported that. Correct similar error throughout the paper.

That is being corrected

8
In paragraph 3, line 6; 'Additionally Ref.18 suggested that..., Please correct this citation to 'Additionally, Katsimperis et al.18 suggested that..' correct similar citation throughout the manuscript.

That is being corrected

9
Paragraph 4, in line 1. Since the abbreviation for Benign Prostate Hyperplasia has been introduced, use only the abbreviation (BPH) thereafter. Please apply this consistently throughout the paper.

That has been corrected. See page 4

10
At the end of the introduction, after the objective, please add a sentence stating the rationale or purpose of the review study.

The correction is made. See page 5

11
The sentence, 'the most common sign of BPH is an enlarged prostate,' should be revised to acknowledge that prostate enlargement can also result from other conditions such as

prostatitis, prostate cancer, or age-related hormonal changes.

The observation has been corrected. See page 10

12
Results:
The manuscript lacks quantitative data to support the efficacy of the reviewed plants, relying solely on qualitative discussion. For example, comparing the extent to which saw palmetto reduces elevated BPH biomarkers (such as PSA levels) compared to Moringa or soybean across studies would better illustrate their potential in BPH management and improve the paper's overall quality.

The correction is made. See page 19

13
Consider including a table summarizing the findings on the percentage increase or reduction of BPH biomarkers for each plant. This would provide a clear overview of each plant's potential in BPH management and also support the purpose of the review.

The table has been made. See Table 2

14
In section 3.3, second paragraph. What is the full meaning of DHT-AR?

That is corrected. See page 6.

15
Section 3.4 appears disconnected from the rest of the discussion. Please add a connecting sentence to improve the logical flow.

That is corrected

16
Figure 5: Please improve the quality and readability of the text in Figure 5.

That is corrected

17
Discussion:
Section 4.1 of the discussion appears to repeat the results and should be either rephrased or removed.

The correction is made by rephrasing as opined. See page 19

18
Paragraph 5 in the discussion section; 'A broad spectrum of plant…' would be more appropriately placed in the introduction or methodology section.

The correction is made by shifting it to the methodology section.

19
Which plant family among those mentioned demonstrates the highest efficacy in managing and/or treating BPH?

The correction is made. See page 19

20
A brief discussion of the key bioactive components in each plant that may drive the observed effects would be valuable

The correction is made. See page 19

21
Also, the discussion throughout the paper is mainly qualitative. Incorporating more quantitative data from the literature (as suggested in result section) would strengthen the discussion.

The correction is made. See page 19

22
In Section 4.4, line 2, the phrase '…the studies reviewed revealed..' should be checked for grammar and corrected
The correction is made. See page 20

23
Line 6, Section 4.4, contains the phrase 'Example include saw palmetto and Pygeum africanum,' which appears as an incomplete sentence Please revise for clarity.
The correction is made. See page 20

24
Section 4.4, line 6 contains the term "AntiInflammchemicals," which is unclear. Please

rephrase this term for better understanding.
The correction is made. See page 20

25
The statement, "Extracts such as saw palmetto are rich in fatty acids and phytosterols," requires a supporting reference citation.
The correction is made. See page 20

26
The entire manuscript requires proper paragraph formatting for consistency.
That has been done properly

27
Conclusion.
Please remove the paragraph breaks in the conclusion and rewrite it as a single block of text.

The observation is well addressed.

28
From your analysis, include information identifying the plant or plant family with the highest efficacy against BPH.
Thanks for the suggestion. See page 19. It has been corrected.

Competing Interests: No competing interests

Reviewer Report 08 May 2025

https://doi.org/10.5256/f1000research.178170.r377452

?

Gift Crucifix Pender
[1] Pharmacology and Toxicology, University of Rwanda College of Medicine and Health Sciences Huye, Butare, Southern Province, Rwanda
[2] Pharmacology and Toxicology, University of Rwanda College of Medicine and Health Sciences Huye, Butare, Southern Province, Rwanda

Review comments for manuscript titled, "**Exploring the use of phytotherapy in benign prostatic**

hyperplasia [BPH]: a systematic review"

1. In the abstract, the authors have not included the method used in the systematic review. The databases/search engines used, how they arrived at the 84 studies selected, and the criteria of selection have not been stated in their method within the abstract. Rather, what is contained in the part of the method is the same as the results, which I have seen as an oversight and should be corrected.
2. In the abstract (line 3 of the method), "Urtica dioica" should be italicized as "*Urtica dioica*", and authors should italicize scientific names of plants within the document, for those that are yet to be italicized.
3. In the introduction (paragraph 2, line 6), full stop is missing just after the end of the statement ending with ".....and weak urine output". (That is, just at the point of citation number 7).
4. In the introduction (paragraph 2, line 7), authors should paraphrase the statement, "In a study by Ref. 9, 80% of men over 80 years have BPH", so that it reads, "It has been reported that 80% of men over 80 years have BPH. [9] This will allow for consistency in the citation/reference style used.
5. In the introduction (paragraph 2, line 8), authors should paraphrase the statement, "In the United States of America [USA], males contribute about 30 to 50% of infertility", so that it reads, "In the United States of America [USA], 30% to 50% of infertility cases are attributed to males". [10]
6. In the introduction (paragraph 3, lines 4-6), authors should paraphrase the statement, "Scientists have examined the possibility that certain plant compounds, known as phytochemicals, could mitigate the adverse effects of BPH.[17] reported that polyphenols present in plant extract can improve male reproductive function", so that it reads, "Scientists have reported that certain plant-derived phytochemicals could mitigate the adverse effects of BPH, and that polyphenols could improve male reproductive function."[17]
7. In the introduction (paragraph 3, lines 6&7), authors should rephrase the statement so that "Ref. 18" does not appear, to maintain scholarly writing format and for consistency of citation style, as mentioned earlier in my previous comment in number 4 above.
8. In the introduction (paragraph 4, lines 3&4), authors should remove "ingredients" from the statement, "Alpha-blockers and 5-alpha-reductase inhibitors are the main ingredients in drugs that treat BPH", so that it reads, "Alpha-blockers and 5-alpha-reductase inhibitors are among the main classes of drugs used in treatment of BPH". This is because, these are actually classes of drugs and not ingredients.
9. In the introduction, (paragraph 3, line 5), "Serenoa repens", should be italicized and authors should check through the manuscript to ensure all scientific names of plants are italicized.
10. The use of Ref. 24, in line 21 (paragraph 4) of the introduction should be reviewed to align with citation style as earlier mentioned in previous comments, and authors should check through the document for such corrections.
11. In line 29, (paragraph 4) of the introduction, authors should add "s" to "LUT", in the statement, "BPH and LUT management should include lifestyle changes....."
12. In the last part of introduction (lines 30-32), authors should rephrase the statement, "However, the mechanism by which these phytotherapies regulate body functions and mitigate the adverse effects of BPH is still under scientific investigation.[25] reported that active ingredients present in plants for the treatment of BPH include lectins β-sitosterol and phytosterols", in such a way that the information comes out clearly and citation number 25 appears at the end of the statement, just as earlier suggested in a previous comment (number 6) above.

13. In the last line of the introduction (paragraph 4), authors mistakenly wrote “phototherapy”, instead of “phytotherapy”, and needs to be corrected.
14. In the method, the statement with the use of “Ref. 26-28”, should be rephrased so that the citations appear just at the end, without using “reported by Ref. 26-28.” That is, “Boolean operators; AND/OR/NOT, were used to develop search strategies according to the specifications of each of the databases in line with the search strategy formulation methods. [26, 27, 28]
15. In the last line of the method, “...as reportedby.[30]”, should be replaced with “.....in accordance with previous studies.[30]
16. In the selection criteria and data collection, the statement, “Human studies were to be excluded,...” should be rephrased as, “Human studies were excluded,.....” since such studies were actually excluded.
17. In the selection criteria and data collection (second paragraph), the statement, “The data extraction extracted from each of the included studies is:” should be re-written as, “The data extracted from each of the included studies are:.....”
18. In the results (3.1 Search results, line 5), the statement, “.....in accordance to the eligibility criteria”, should be written as, “in accordance with the eligibility criteria”. This is because, you either use “according to” or “in accordance with”.
19. In the results (3.2 Study characteristics), the statement, “.....Additionally, plants like....”, should be written as, “Additionally, plants such as.....”. This is because, the use of “like” does not convey the intended message.
20. In the results (3.2, paragraph 2, line 3), full stop is missing at the end of the statement, “....and Moringa peregrine.[51]”
21. In the results (3.4 Oxidative, Apoptotic, and Prostate Biomarkers, number 3 line 3), the use of the statement, “Alpha-blockers and 5-alpha-reductase inhibitors are the main agents in drugs that treat BPH”, should be rephrased to read, “Alpha-blockers and 5-alpha-reductase inhibitors are among the main drugs employed in BPH treatment”. This is because they are actually classes of drugs used in BPH and not agents in drugs, as earlier mentioned in my earlier comment.
22. In the discussion (first line of paragraph 3), authors mistakenly wrote “thy” instead of “they” in the statement, “This review highlights several known plants that showed efficacy in reducing symptoms of BPH, thy include:”, which should be corrected.
23. In the discussion (4.3 Parts of plants utilized, line 12), authors mistakenly wrote BPH170, in the statement, “...modulate inflammatory pathways in BPH 170[70]”, hence should be checked and corrected.
24. In the discussion, (4.4 Mechanisms of action, lines 4&5), there should be a full stop at the end of the statement, “Many compounds inhibit 5α-reductase, reducing dihydrotestosterone [DHT] levels, a key factor in BPH pathogenesis.”
25. In line 6 of the discussion (4.4 Mechanisms of action), the use of “Anti-Inflammchemicals....”, should be “Anti-inflammatory chemicals.....”
26. In line 10 of the discussion (4.4 Mechanisms of action, paragraph 2), the use of “phototherapy” should be corrected to “phytotherapy”, in the statement, “Several clinical trials have evaluated the efficacy of phototherapy in managing BPH symptoms”.
27. In the discussion (4.4 Mechanisms of action, fourth line of paragraph 4), there should be a full stop after the statement ending with “.....and prazosin.”
28. In the discussion, (4.7 Plants with antioxidant properties), the use of “While” in the beginning of the statement in lines 4/5 should be removed, since there is no additional statement to justify its use at the beginning, so that it reads, “*Annona muricata* [Soursop]

plant's antioxidant activity, mediated by its ability to inhibit 5α-reductase, positions it as a promising candidate for managing BPH. [78]. Same comment applies to the statement in line 6 of 4.8 of the discussion.

29. In the discussion (4.8, paragraph 2, lines 3/4), "29" should be deleted from the statement in lines 3/4, ".....and prostate volume 29.[120]"
30. In the discussion (4.8, paragraph 4, line 5), "anensis" should be deleted from the statement ending with "....such as TNF-α and IL-6anensis."
31. In the discussion (4.8, paragraph 10, first line), "has" should be replaced with "have" in the statement, "Panax ginseng and bee pollen has shown...."
32. In the discussion (4.8, paragraph 13, first line), "anti-andrities" should be written as "anti-androgenic effect", in the statement, "Seed extracts of Caesalpinia bonduc exhibit significant anti-andrities by inhibiting 5α-reductase".
33. In the discussion, (4.8 paragraph 14, second line), there is "[m" which should be replaced with a full stop. Authors should please check and correct accordingly.
34. In the last paragraph (4.9 of discussion, on page 15 of the manuscript), authors used APA citation style, "Controversies also exist regarding the efficacy of certain phytotherapies. While some studies report significant improvements in urinary symptoms and prostate size reduction, others find no better outcomes than placebo [Ulbricht, 2016]. For example, although Saw palmetto has been extensively studied, its efficacy remains debated, highlighting the need for more rigorous research to resolve these inconsistencies [Yamada et al., 2022]". This should be corrected to be in harmony with the original citation style used in the manuscript.
35. Generally, it was a good presentation by the authors, and exploring the use of phytotherapeutic approaches in the management of BPH is worthwhile, given its prevalence and disturbing symptoms in patients, which affects quality of life.

Are the rationale for, and objectives of, the Systematic Review clearly stated?

Yes

Are sufficient details of the methods and analysis provided to allow replication by others?

Yes

Is the statistical analysis and its interpretation appropriate?

Yes

Are the conclusions drawn adequately supported by the results presented in the review?

Yes

If this is a Living Systematic Review, is the 'living' method appropriate and is the search schedule clearly defined and justified? ('Living Systematic Review' or a variation of this term should be included in the title.)

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Pharmacology and Toxicology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 31 Oct 2025

Angela Mumbua Musyoka

In the abstract, the authors have not included the method used in the systematic review. The databases/search engines used, how they arrived at the 84 studies selected, and the criteria of selection have not been stated in their method within the abstract. Rather, what is contained in the part of the method is the same as the results, which I have seen as an oversight and should be corrected.
The corrections in the methodological aspect of the abstract are properly addressed. *See page 2 marked with a red indicator.*
Done

In the abstract (line 3 of the method), "Urtica dioica" should be italicized as "Urtica dioica", and authors should italicize scientific names of plants within the document, for those that are yet to be italicized.
All botanical plants reported in all sections of the work have been italicized. See page 2
Done

In the introduction (paragraph 2, line 6), full stop is missing just after the end of the statement ending with ".....and weak urine output". (That is, just at the point of citation number 7).

Corrections made. See page 4
Done

In the introduction (paragraph 2, line 7), authors should paraphrase the statement, "In a study by Ref. 9, 80% of men over 80 years have BPH", so that it reads, "It has been reported that 80% of men over 80 years have BPH. 9 This will allow for consistency in the citation/reference style used.

Corrections made. See page 4
Done

In the introduction (paragraph 2, line 8), authors should paraphrase the statement, "In the United States of America [USA], males contribute about 30 to 50% of infertility", so that it reads, "In the United States of America [USA], 30% to 50% of infertility cases are attributed to males". 10

Corrections made. See page 4
Done

In the introduction (paragraph 3, lines 4-6), authors should paraphrase the statement,

"Scientists have examined the possibility that certain plant compounds, known as phytochemicals, could mitigate the adverse effects of BPH.17 reported that polyphenols present in plant extract can improve male reproductive function", so that it reads, "Scientists have reported that certain plant-derived phytochemicals could mitigate the adverse effects of BPH, and that polyphenols could improve male reproductive function."17

The changes have been made. See page 4
Done

In the introduction (paragraph 3, lines 6&7), authors should rephrase the statement so that "Ref. 18" does not appear, to maintain scholarly writing format and for consistency of citation style, as mentioned earlier in my previous comment in number 4 above.

The changes have been made. See page 4
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In the introduction (paragraph 4, lines 3&4), authors should remove "ingredients" from the statement, "Alpha-blockers and 5-alpha-reductase inhibitors are the main ingredients in drugs that treat BPH", so that it reads, "Alpha-blockers and 5-alpha-reductase inhibitors are among the main classes of drugs used in treatment of BPH". This is because, these are actually classes of drugs and not ingredients.

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In the introduction, (paragraph 3, line 5), "Serenoa repens", should be italicized and authors should check through the manuscript to ensure all scientific names of plants are italicized.

The changes have been made. See page 4
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The changes have been made. See page 4
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In line 29, (paragraph 4) of the introduction, authors should add "s" to "LUT", in the statement, "BPH and LUT management should include lifestyle changes....."

The changes have been made. See page 4
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In the last part of introduction (lines 30-32), authors should rephrase the statement, "However, the mechanism by which these phytotherapies regulate body functions and mitigate the adverse effects of BPH is still under scientific investigation.25 reported that

active ingredients present in plants for the treatment of BPH include lectins β-sitosterol and phytosterols", in such a way that the information comes out clearly and citation number 25 appears at the end of the statement, just as earlier suggested in a previous comment (number 6) above.

The corrections have been made by rephrasing the section appropriately. See page 4
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In the last line of the introduction (paragraph 4), authors mistakenly wrote "phototherapy", instead of "phytotherapy", and needs to be corrected.

That has been corrected.
Done

In the method, the statement with the use of "Ref. 26-28", should be rephrased so that the citations appear just at the end, without using "reported by Ref. 26-28." That is, "Boolean operators; AND/OR/NOT, were used to develop search strategies according to the specifications of each of the databases in line with the search strategy formulation methods. 26, 27, 28

That has been corrected.
Done

In the last line of the method, "...as reportedby.30", should be replaced with ".....in accordance with previous studies.30

That has been corrected. See page 5
Done

In the selection criteria and data collection, the statement, "Human studies were to be excluded,..." should be rephrased as, "Human studies were excluded,....." since such studies were actually excluded.

That has been corrected. See page 5
Done

In the selection criteria and data collection (second paragraph), the statement, "The data extraction extracted from each of the included studies is:" should be re-written as, "The data extracted from each of the included studies are:....."

That has been corrected. See page 5
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In the results (3.1 Search results, line 5), the statement, "......in accordance to the eligibility criteria", should be written as, "in accordance with the eligibility criteria". This is because, you either use "according to" or "in accordance with".

That has been corrected. See page 5
Done

In the results (3.2 Study characteristics), the statement, "…..Additionally, plants like….", should be written as, "Additionally, plants such as……". This is because, the use of "like" does not convey the intended message.

That has been corrected. See page 5
Done

In the results (3.2, paragraph 2, line 3), full stop is missing at the end of the statement, "….and Moringa peregrine.51"

That has been corrected. See page 5
Done

In the results (3.4 Oxidative, Apoptotic, and Prostate Biomarkers, number 3 line 3), the use of the statement, "Alpha-blockers and 5-alpha-reductase inhibitors are the main agents in drugs that treat BPH", should be rephrased to read, "Alpha-blockers and 5-alpha-reductase inhibitors are among the main drugs employed in BPH treatment". This is because they are actually classes of drugs used in BPH and not agents in drugs, as earlier mentioned in my earlier comment.

That has been corrected. See page 7
Done

In the discussion (first line of paragraph 3), authors mistakenly wrote "thy" instead of "they" in the statement, "This review highlights several known plants that showed efficacy in reducing symptoms of BPH, thy include:", which should be corrected.

That has been corrected. See page 10
Done

In the discussion (4.3 Parts of plants utilized, line 12), authors mistakenly wrote BPH170, in the statement, "…modulate inflammatory pathways in BPH 17070", hence should be checked and corrected.

That has been corrected. See page 11
Done

In the discussion, (4.4 Mechanisms of action, lines 4&5), there should be a full stop at the end of the statement, "Many compounds inhibit 5α-reductase, reducing dihydrotestosterone [DHT] levels, a key factor in BPH pathogenesis."

That has been corrected. See page 11
Done

In line 6 of the discussion (4.4 Mechanisms of action), the use of “Anti-Inflammchemicals….”, should be “Anti-inflammatory chemicals……”

That has been corrected. See page 11
Done

In line 10 of the discussion (4.4 Mechanisms of action, paragraph 2), the use of “phototherapy” should be corrected to “phytotherapy”, in the statement, “Several clinical trials have evaluated the efficacy of phototherapy in managing BPH symptoms”.

That has been corrected. See page 12
Done

In the discussion (4.4 Mechanisms of action, fourth line of paragraph 4), there should be a full stop after the statement ending with “……..and prazosin.”

That has been corrected. See page 12
Done

In the discussion, (4.7 Plants with antioxidant properties), the use of “While” in the beginning of the statement in lines 4/5 should be removed, since there is no additional statement to justify its use at the beginning, so that it reads, “Annona muricata [Soursop] plant’s antioxidant activity, mediated by its ability to inhibit 5α-reductase, positions it as a promising candidate for managing BPH. 78. Same comment applies to the statement in line 6 of 4.8 of the discussion.

That has been corrected. See page 13
Done

In the discussion (4.8, paragraph 2, lines 3/4), “29” should be deleted from the statement in lines 3/4, “…..and prostate volume 29.120”

That has been corrected. See page 12
Done

In the discussion (4.8, paragraph 4, line 5), “anensis” should be deleted from the statement ending with “….such as TNF-α and IL-6anensis.”

That has been corrected. See page 14
Done

In the discussion (4.8, paragraph 10, first line), “has” should be replaced with “have” in the statement, “Panax ginseng and bee pollen has shown….”

That has been corrected. See page 14
Done

In the discussion (4.8, paragraph 13, first line), “anti-andrities” should be written as “anti-androgenic effect”, in the statement, “Seed extracts of Caesalpinia bonduc exhibit significant anti-andrities by inhibiting 5α-reductase”.

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That has been corrected. See page 15
Done
Examiner's remarks (Reviewer one)
Response
Status

In the abstract, the authors have not included the method used in the systematic review. The databases/search engines used, how they arrived at the 84 studies selected, and the criteria of selection have not been stated in their method within the abstract. Rather, what is contained in the part of the method is the same as the results, which I have seen as an oversight and should be corrected.
The corrections in the methodological aspect of the abstract are properly addressed. *See page 2 marked with a red indicator.*
Done

In the abstract (line 3 of the method), “Urtica dioica” should be italicized as “Urtica dioica”, and authors should italicize scientific names of plants within the document, for those that are yet to be italicized.
All botanical plants reported in all sections of the work have been italicized. See page 2
Done

In the introduction (paragraph 2, line 6), full stop is missing just after the end of the statement ending with “……and weak urine output”. (That is, just at the point of citation number 7).

Corrections made. See page 4
Done

In the introduction (paragraph 2, line 7), authors should paraphrase the statement, "In a study by Ref. 9, 80% of men over 80 years have BPH", so that it reads, "It has been reported that 80% of men over 80 years have BPH. 9 This will allow for consistency in the citation/reference style used.

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Competing Interests: No competing interests