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Review

A Systematic Review on Herbal Interventions in Prostate Cancer Treatment: Efficacy, Safety, and Implications for African Healthcare

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Abstract

Prostate cancer remains one of the most prevalent malignancies and a major cause of mortality among men globally, with disproportionate impact in low-resource settings such as Africa. Conventional therapies, though effective, are costly and often associated with adverse effects and limited accessibility. This systematic review aimed to identify, synthesise, and critically analyse evidence on the efficacy and safety of herbal interventions for prostate cancer management. Searches were conducted across PubMed Central, ScienceDirect, Cochrane, AJOL, and Google Scholar (2005-2025), yielding 27 eligible studies after screening 23,907 records. Data extraction and quality appraisal were performed using Preferred reporting items for systematic reviews and meta-analyses guidelines and validated bias-assessment tools. Results indicated that several herbal preparations, including *Curcuma longa, Camellia sinensis, Glycine max, Brassica oleracea, and Punica granatum*, produced statistically significant reductions in prostate-specific antigen (PSA) levels (pooled mean difference: (-1.678±0.0774 ng/mL; $p<0.0001$), suggesting potential efficacy in slowing disease progression. Adverse effects were generally mild (Grade 1-2), primarily gastrointestinal. However, only 11% of included studies originated from Africa, highlighting a critical regional research gap. Findings suggest that herbal therapies offer promising, low-cost adjuncts or alternatives to conventional treatments but require further validation through high-quality clinical trials within African contexts. Strengthening local research capacity is essential to integrate evidence-based phytotherapies into prostate cancer management and improve health outcomes across underserved populations.

Keywords

Prostate cancer, Herbal medicine, Safety and efficacy, Low-income population, Phytotherapy, Complementary and alternative medicine, African healthcare

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1. Introduction

Prostate cancer is one of the most prevalent malignancies among men globally, particularly in developed countries, and recently in developing countries. Its pathophysiology is complex and multifactorial, involving genetic, hormonal, and environmental factors [1,2]. Prostate cancer arises from the prostate gland with key genetic mutations, including those in specific tumour suppressor genes like BRCA1, BRCA2, PTEN, and TP53, contributing to tumorigenesis by promoting uncontrolled cell proliferation [2,3]. Hormonal influences, particularly androgens like testosterone, play a crucial role in the growth and maintenance of prostate tissue. Many prostate cancers exhibit overexpression or mutations in androgen receptors, leading to enhanced tumour growth [4,5]. The tumour microenvironment, including interactions with stromal and immune cells, encourages cancer progression and metastasis. This leads to the spread to bones, lymph nodes, and other organs, with the bone microenvironment being particularly conducive to metastatic growth [6]. Understanding these mechanisms is essential for developing targeted therapies, such as androgen deprivation therapy, herbal therapies, and emerging immunotherapies, aimed at improving treatment outcomes for patients with prostate cancer [6,7].

Prostate cancer is one of the leading causes of mortality, according to various reports. Globally, it is ranked second in prevalence, while also ranked as the sixth highest source of cancer mortality [8]. Overall, its prevalence has increased over the years, especially among men of Black descent. Research evidence also supports a strong correlation between the genetic predispositions of these men, their lifestyle, and the increase in prevalence among them [8,9]. Nevertheless, while data reports suggest increased prevalence among this population group, little evidence emanates from Africa, the continent with the largest amount of black people [10]. This indicates a need for enhanced research and data procurement processes in Africa. Out of the forty-seven (47) African countries that are members of the World Health Organisation (WHO), only Egypt, Cape Verde, South Africa, Réunion, Seychelles, São Tomé and Principe, Mayotte, and Mauritius are recorded as having reliable and ongoing data on prostate cancer [11]. Perhaps this may explain why [8] indicated that the incidence is underestimated and underreported in Africa.

Similarly, research evidence has shown that African men with prostate cancer are more likely not to recover from the condition, when compared to their Asian, European and American counterparts [8,12]. Although [12] argued that there is no relationship between race and the probability of recovery from prostate cancer. Regardless, more research evidence is needed to substantiate these points. The prevalence may be due to a combination of reasons, including a low-quality healthcare system, a lack of availability of a skilled healthcare workforce, a lack of education and awareness, socioeconomic status, and other factors [13,14]. While some policymakers have argued from different perspectives, there is no doubt that the economic and financial capabilities of an individual or a population group influence their health choices greatly [13-15]. This lack of financial power, in combination with other determinants of health, has been shown through research as a contributing factor to why African men are at an all-time high in cancer epidemiology [14,15]. Furthermore, evidence from research suggests that oftentimes, diagnosis of cancer does not necessarily translate to management, treatment or recovery [8,16]. This is because most of the affected adults find it difficult to meet the financial demands of orthodox management of prostate cancer. For example, while the cost of managing prostate cancer depends on several factors like stage, insurance coverage, and duration of treatment, the average cost ranges from $28000 to $35,000 in America [8,16,17].

Consequently, with the average yearly wage of the most developed countries in Africa not making up to 20% of this cost [3], there is a need for policymakers and healthcare professionals to turn their focus on the use of complementary and alternative medicines (CAM) that are evidence-based and effective against prostate cancer cells. The use of CAM is one that is ancient; however, most of these practices lack scientific backing, with evidence of adverse effects lingering [18]. However, research projects have been undertaken on a large scale, especially since the dawn of the 21st century. There have been significant breakthroughs in the areas of Ayurverdia, Chinese acupuncture, the use of artificial intelligence and herbal medications in managing various diseases [18,19]. Consequently, it is important to identify and synthesise this evidence regarding their effectiveness in managing prostate cancer. Among the various available CAM, herbal medication should be of particular interest to Africa. This is because Africa is blessed with a rich propagation of millions of medicinal plants with a vast range of health benefits [20]. Therefore, they are readily available, reproducible, and cheaper for the management of disease conditions.

Moreover, a preclinical experimental study by [21], involving *in vitro* prostate cancer cell lines (PC-3, has shown a strong cytotoxic effect by flavonoids extracted from *Fridericia platyphylla* (little beer of the field). Other *in vitro* studies with positive outcomes include [22] on *Panax notoginseng* (Chinese ginseng); [23] on *Cuscuta chinensis* (Chinese dodder); [24] on *Senecio asperulus DC;* [25] on *Moringa peregrina* (wild drumstick tree); [26] on Orobance crenata (Bean broomrape); [27] on *Prunus Africana* (African cherry); [28] on *Alchemilla vulgaris* (Lady's mantle) with high selective index on PC-3 cell-lines; [29] on *Erythrina excelsa* (Mubajangabo/Mulungulu); [30] on *Prunus africana* (African cherry), *Pausinystalia yohimbe,* and *Momordica charantia* (Bitter melon). It is important to point out that various other medicinal plants are potent against PC-3 cell lines, with different parts of the plants and extract methods used. On the other hand, the use of orthodox

therapies like radiotherapy, conventional chemotherapies, radical prostatectomy, and androgen deprivation has been associated with side effects, and resistance in advanced stages of the cancer [31].

This systematic literature review will therefore focus on the identification of different plant-based alternative medicines that are used in managing prostate cancer. This will involve the identification of plant parts and specific phytochemicals implicated in the management of prostate cancer.Their efficacy will be analysed based on two key criteria. For clinical studies, the primary criterion involves overall survival (OS) or prostate-specific antigen progression-free survival (PSA-PFS)/biochemical progression [32]. This particularly means that from the moment the herbal therapy commences, the value of the PSA is monitored and calibrated against the progression of the cancer. If progression is not recorded for localised cancer, or progression is reversed for advanced prostate cancer, through PSA levels, the therapy shall be said to be effective [32,33]. The Secondary criterion for determining efficacy involves progression-free survival (PFS), symptom scores, and adverse events (graded) [34]. This involves analysing the rate of reporting of adverse effects, recurrence of symptoms and overall quality of life using calibrated tools, after therapy. These findings will be triangulated using qualitative studies on the overall quality of life of patients after therapy, which used validated instruments [35]. Consequently, this systematic review aims to identify, synthesise, and critically appraise existing evidence on the use of herbal medicines in the management of prostate cancer, with emphasis on their efficacy, safety, and potential applicability in African contexts where access to orthodox treatments is limited.

2. Methods

2.1 Database Search

Several biomedical and multidisciplinary databases were searched to obtain comprehensive literature on the use of herbal medicine for the management of prostate cancer. This includes PubMed Central, ScienceDirect, Cochrane, Google Scholar, and AJOL. The choice of these databases lies in the availability of articles and the relatedness of the journals to the aim and objectives of this review.

2.2 Search Strategy

For an article to be selected for the first stage of literature search and selection, the following preselected and validated criteria must be met before in-text screening is commenced. The eligibility criteria described in Table 1 highlight key qualities that the methodology and publication of articles must possess before being included or excluded from the review process. Furthermore, the population, intervention, comparison, outcome (PICO) framework shown in Table 2 identifies the population, intervention, comparator and outcome measures that were required for the selection of a quantitative article, while the population, exposure, outcome (PEO) framework provides the basis for the final selection of a qualitative article upon in-text screening.

Table 1. Eligibility criteria.

Inclusion Criteria	Exclusion Criteria
Randomised controlled trials (RCTs), qualitative studies, quasi-experimental studies, and observational studies (cohort, case-control, cross-sectional)	Opinion pieces, case reports, editorials, reviews and meta-analyses
Studies on adults with prostate cancer	Animal or *in vitro* studies; Studies without a specific focus on prostate cancer
Studies published in the English Language or translated into the English language	Studies in any other language
Free-full text	Abstract-only
Studies published between 2005 and 2025	Studies older than 2005

Table 2. PICO framework for quantitative articles.

Category	Description
Population	Adults (≥18 years) diagnosed with prostate cancer (any stage).
Intervention	Herbal medicines (single herbs, extracts, formulations, or combinations used as alternative or complementary treatment).
Comparator	Placebo, conventional therapy, no intervention, or other complementary therapies.
Outcomes	Primary: Clinical outcomes (tumour progression, PSA levels, OS, PFS). Secondary: Quality of life, symptom improvement, biochemical markers, adverse effects, safety.

Table 3. PEO framework for qualitative studies.

Category	Description
Population	Adults (≥18 years) diagnosed with prostate cancer (any stage).
Exposure	Use of herbal medicines (single herbs, extracts, formulations, or combinations used as alternative or complementary treatment).
Outcome	Efficacy and safety of herbal medicines in managing prostate cancer, including OS, PSA-PFS, symptom improvement, and reported adverse effects.

2.3 Search Term Combination

2.3.1 Keywords/MeSH Terms

“Prostate cancer” OR “prostatic neoplasms” AND “herbal medicine” OR “phytotherapy” OR “medicinal plants” OR “alternative medicine” OR specific herbs (e.g., *Curcuma longa, Serenoa repens, Panax ginseng, Prunus africana*).

2.3.2 Comprehensive Search Strategy

("Prostatic Neoplasms" OR "prostate cancer")

("Prostatic Neoplasms" OR "prostate cancer") NOT (BPH OR Benign Prostatic Hyperplasia) AND ("Phytotherapy" OR "Herbal Medicine" OR "Plants, Medicinal" OR "medicinal plants" OR "alternative medicine" OR "*Curcuma longa"* OR "*Serenoa repens*" OR "*Panax ginseng*" OR *"Prunus africana*" OR "*Moringa oleifera*" OR "*Erythrina excelsa*" OR "*Cuscuta chinensis*" OR *"Fridericia platyphylla"*)

2.4 Study Selection and Risk of Bias Assessment

The selection of relevant studies for this review was conducted by three independent reviewers (C.N. Ezinwa, D.O. Ekpo, and S.M. Chime), involving the screening of titles and abstracts before full-text screening. The POCO and PEO framework as described in Tables 2 and 3 guided the intext screening for quantitative and qualitativel studies respectivey. Disagreements were resolved by a discussion session and consensus, with progress recorded using a preferred reporting items for systematic reviews and meta-analyses (PRISMA) flowchart. These articles were assigned numbers and assessed for risk of bias using several critical appraisal tools. The critical appraisal skills programme (CASP) checklists for qualitative studies, and randomised control trials were used in the respective studies, while the Joanna briggs institute (JBI) checklist and risk of bias in non-randomised studies of interventions (ROBINS-I) risk of bias assessment tools were used for observational studies (cohort study, and case-controlled trials), and non-randomised controlled trials, respectively.

2.5 Data Extraction and Analysis

Two of the authors (D.O. Ekpo and S.M. Chime) independently extracted relevant data from the included studies, using consensus to settle discrepancies. Information on study characteristics (author and year of publication, and research design); participant details, including sample size, age, and cancer stage; intervention details, including herb preparation, dose and duration, specific phytochemical agent, and availability in Africa; comparator used, outcomes including adverse effects, PSA value before and after intervention. These data were analysed in accordance with the objectives of the study, with descriptive analysis used for the study characteristics expressed as frequencies and means. The adverse effects were described using the common terminology criteria for adverse events (CTCAE), developed by the United States of America Cancer Institute. Grade 1-3 represents mild to moderate effects, grade 4 represents severe or life-threatening effects, while grade 5 is recorded as death [36]. The statistical significance of the mean of the PSA pre and post-intervention was analysed using a pooled descriptive T-test, with the combined value recorded as the standard error of mean (SEM).

2.6 Review Registration and Review Guideline

The protocol for this review was registered in PROSPERO with the registration code: CRD420251159969. The study followed the revised guidelines proposed by PRISMA [37].

3. Result

3.1 Search Outcomes

The literature search yielded a total of 23,907 articles, with Google Scholar yielding the most at 15,384, followed by PubMed Central at 7,950 articles, ScienceDirect at 512 articles, AJOL and Cochrane Centre for Clinical Trials yielded the

least at 51 and 10 articles, respectively as indicated in Figure 1. Preliminary screening using the titles and abstracts led to the removal of 13,406 duplicate articles. This was achieved with the aid of Ryyan software. Full-text screening led to the removal of 3,180 articles. Ultimately, 27 articles were selected for the review upon critical assessment for risk of bias. A complete representation of the selection process is depicted in Figure 1 [36].

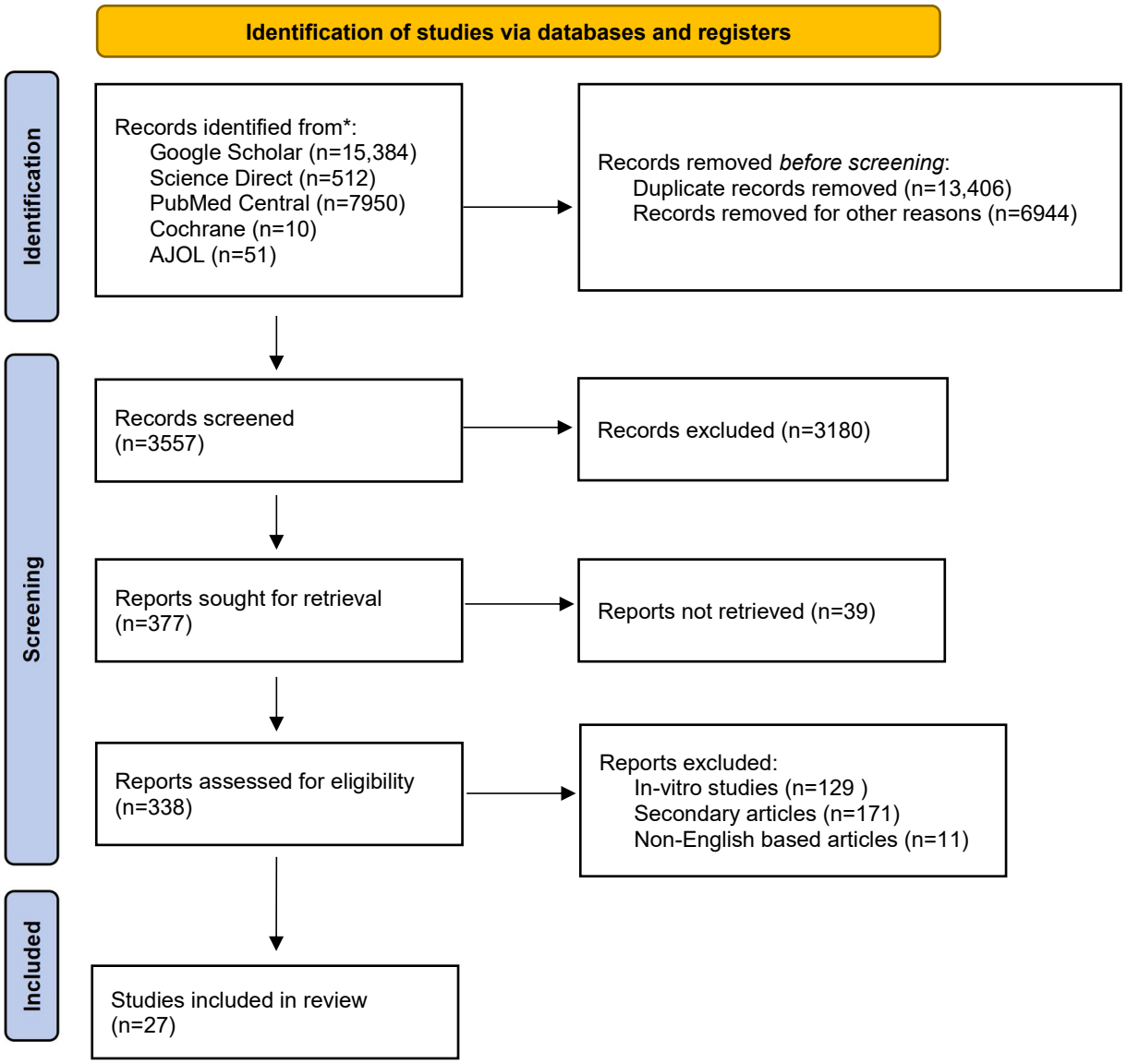

Figure 1. PRISMA flowchart showing the screening of results.

Table 4. Objective 1: Identify and synthesise evidence on the use of herbal medicines in the management of prostate cancer.

Authors and Year	Herbal Preparation	Study Design	Sample Size	Cancer Stage	Study Setting/Country	Citation
van Die et al. (2017)	Turmeric, resveratrol, green tea, broccoli sprouts	Placebo-controlled RCT	22	Biochemically recurrent prostate cancer	Australia	[38]
Dorff et al. (2014)	Prostate Health Cocktail	Phase II trial	40	Biochemically recurrent prostate cancer	USA	[39]
Pendleton et al. (2008)	Soy milk with isoflavones	Phase II trial	20	Biochemically recurrent prostate cancer	USA	[40]
Thomas et al. (2014)	Polyphenol-rich supplement	Double-blind RCT	199	Localised prostate cancer	UK	[41]
Grainger et al. (2008)	Tomato and soy diet	Randomised dietary intervention	41	Recurrent, asymptomatic prostate cancer	USA	[42]
Paller et al. (2015)	Muscadine grape skin extract	Phase I/II trial	14	Biochemically recurrent prostate cancer	USA	[43]
Swanson et al. (2015)	*Phellodendron amurense* bark extract	Tolerance study	21	Prostate cancer (surgery/radiation)	USA	[44]
Cheon and Ko (2020)	SH003 (*Astragalus, Angelica, Trichosanthes*)	Phase I dose-escalation	11	Solid cancers	South Korea	[45]
Pang et al. (2015)	Qianlie Xiaozheng Tang	Pilot study	70	Castration-resistant prostate cancer	China	[46]
Henning et al. (2015)	Green/black tea	Randomised clinical trial	113	Localised prostate adenocarcinoma	USA	[47]
Paller et al. (2018)	Muscadine grape skin extract	Randomised, placebo-controlled	125	Biochemically recurrent prostate cancer	USA	[48]
Keizman et al. (2023)	Modified citrus pectin	Phase II study	39	Non-metastatic biochemically relapsed	Israel	[49]
Cipolla et al. (2015)	Stabilized sulforaphane	Double-blind RCT	78	Biochemical recurrence post-prostatectomy	France	[50]
Bunani et al. (2025)	Traditional herbs	Qualitative study	15	Prostate cancer (varied stages)	Uganda	[51]
Cai et al. (2024)	Curcuma longa, Boswellia, Pinus pinaster, Urtica dioica	Randomised controlled trial	162	Biopsy-confirmed prostate cancer	Italy	[52]
Demark-Wahnefried et al. (2008)	Flaxseed+low-fat diet	Randomised controlled trial	161	Prostate cancer (pre-surgery)	USA	[53]
Stenner-Liewen et al. (2013)	Pomegranate juice	Phase IIb RCT	19	Advanced prostate cancer	Switzerland	[54]
Lokeshwar et al. (2024)	Fermented soy beverage	Double-blind RCT	19	Localised prostate cancer	USA	[55]
Pantuck et al. (2006)	Pomegranate juice	Phase II trial	46	Rising PSA post-surgery/radiation	USA	[56]
Bosland et al. (2013)	Soy protein isolate	Double-blind RCT	177	Biochemical recurrence risk	USA	[57]
Alumkal et al. (2015)	Sulforaphane-rich broccoli sprouts	Phase II single-arm	20	Recurrent prostate cancer	USA	[58]
Freedland et al. (2013)	Pomegranate extract	Double-blind RCT	70	Prostate cancer	USA	[59]
Twardowski et al. (2015)	White button mushroom powder	Phase I trial	36	Biochemically recurrent prostate cancer	USA	[60]
Wyatt et al. (2016)	Saw palmetto	Exploratory RCT	21	Early-stage prostate cancer	USA	[61]
deVere White et al. (2010)	Genistein combined with polysaccharide	Double-blind RCT	53	Localised prostate cancer	USA	[62]
Chawatama (2017)	Zimbabwean Traditional Medicines	Mixed methods study	40	Prostate cancer (not specified)	Zimbabwe	[63]
Osei & Gyamerah (2025)	CAM	Qualitative exploratory	16	Prostate cancer (not specified)	Ghana	[64]

Table 4 Summarises the studies reviewed under Objective 1, focusing on identifying and synthesising evidence on the use of herbal medicines in the management of prostate cancer. A broader depiction of the study details including specific biomarker values are shown in the supplementary data for this research.

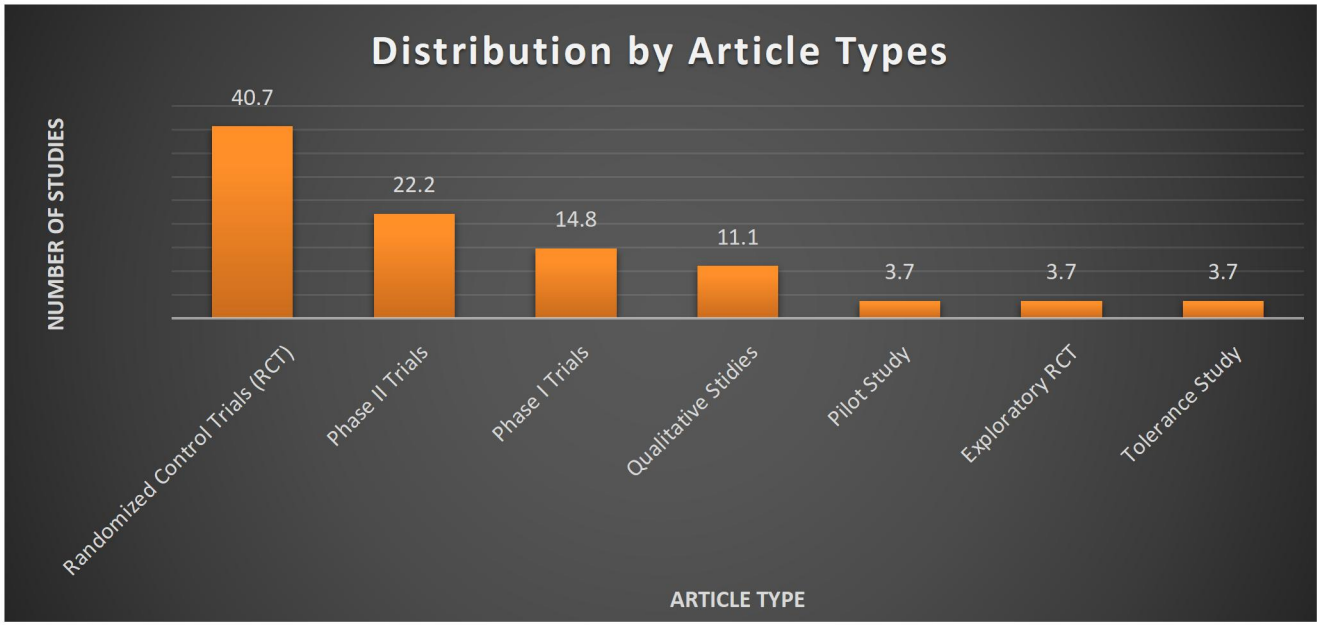

Figure 2. Distribution of study designs selected for review.

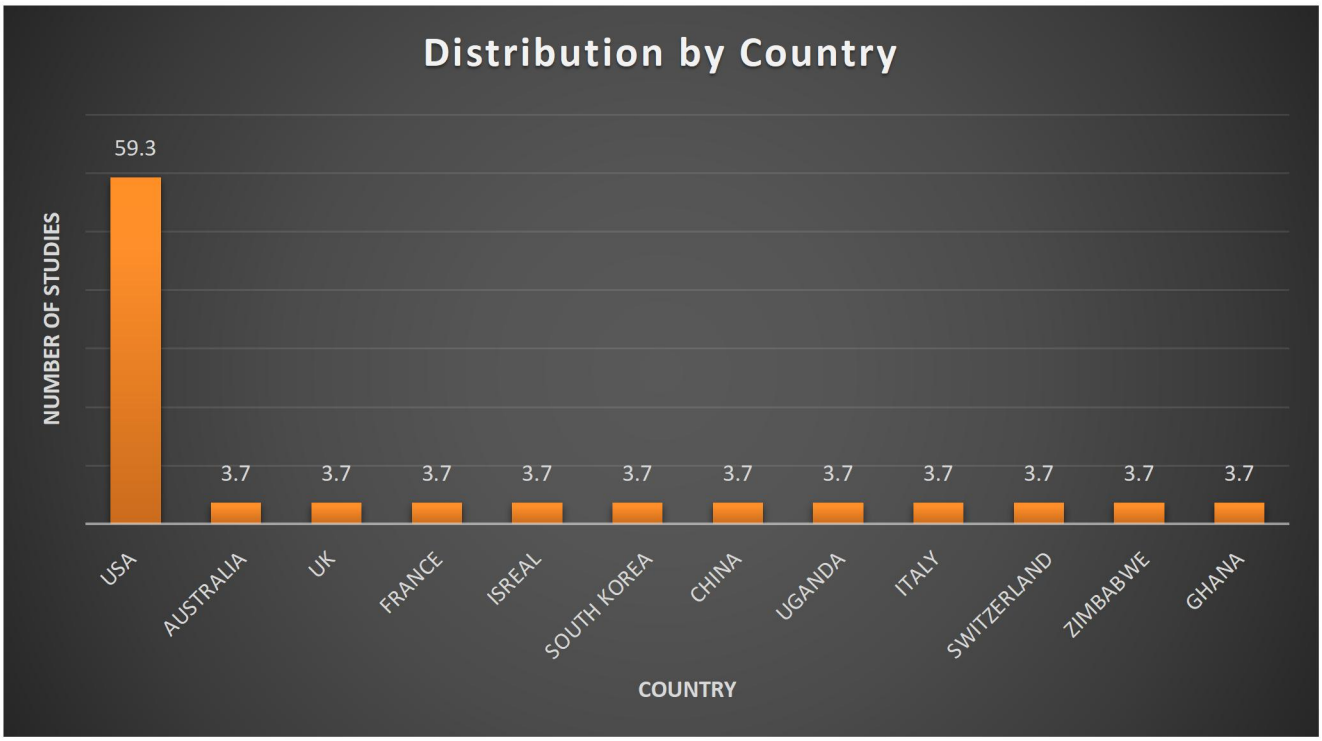

Figure 3. Distribution of country/ study setting for the 27 studies included in the review.

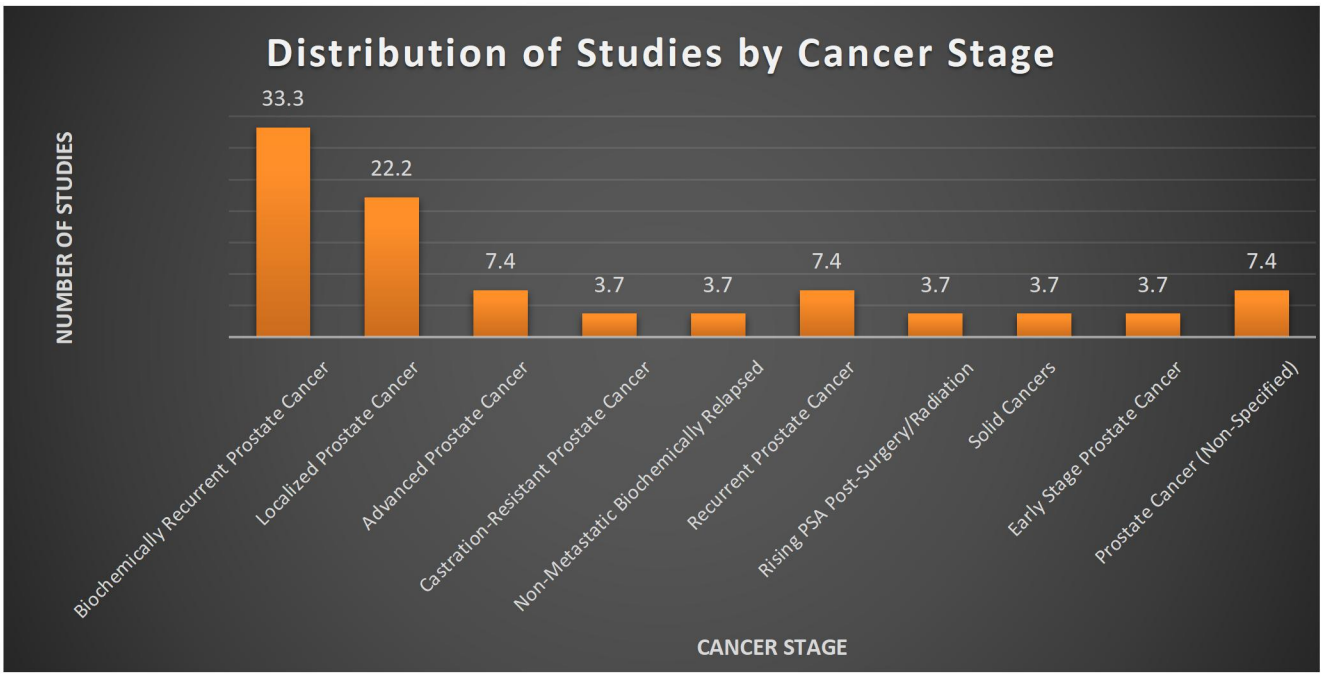

Figure 4. Different cancer stages researched among the included studies.

The Table 4 presents details of each study, including the specific herbal preparation used, study design, sample size, cancer stage, and geographical setting. "Biochemically recurrent prostate cancer" refers to prostate cancer recurrence indicated by a rise in prostate-specific antigen (PSA) levels following primary treatment (surgery or radiotherapy) [38,39,40,43,48,50,57,60]. Localised prostate cancer refers to those cancer that are still confined within the prostate gland identified in the study by [41,47,55,62]; including those described as early stage prostate cancer [61], and prostate cancer presurgery [53]. "Not specified" denotes instances where the study did not clearly report cancer staging [63,64] or methodological details in the original publication. The bar graph from Figure 2. shows that RCTs were the most included, followed by non-randomised controlled trials, then qualitative studies. On the other hand, Figure 3 shows that the United States of America has the highest number (59.3%) of clinical studies on herbal intervention for prostate cancer while the rest have 3.7% each. Similarly, Figure 4 showed that biochemically recurrent cancer followed by localised prostate cancers were the most studied. On the other hand, Figure 3 exposed the paucity of data from Africa, with only three countries (Ghana, Zimbabwe and Uganda) at about 11% while the United States of America had the most studies at 59.3%. Asian countries produced 7.4% of the pooled data alongside Europe, with Israel and the United Kingdom at 3.7% each.

Objective 2: To evaluate clinical efficacy using PSA Levels

Table 5. Summary table of T-test results for articles that reported mean values of PSA (pre and post).

Herbal Intervention	Pre-PSA (ng/mL)	Post-PSA (ng/mL)	Mean Difference (ng/mL)	Sample Size	p-value	Conclusion	Citation
Curcuma longa, Boswellia, Pinus, Urtica	6.7	3.1	-3.6	162	<0.05 (estimated)	Significant PSA reduction	[52]
Flaxseed+low-fat diet	5.7	4.9	-0.8	161	<0.05 (estimated)	Possible significant PSA reduction	[53]
Green tea	9.6	8.4	-1.2	~37	<0.05 (estimated)	Likely significant PSA reduction	[47]
Fermented soy beverage	8.98	8.02	-0.96	19	≈0.05 (estimated)	Possible significant PSA reduction	[55]
Stabilized sulforaphane	0.78	0.879	+0.099	78	>0.05 (within group)	No significant PSA reduction	[50]

Table 5 presents the summary of studies that reported mean pre- and post-intervention PSA values, allowing for quantitative comparison through an independent-sample T-test analysis. "Pre-PSA" refers to the mean baseline PSA value prior to herbal intervention, while "Post-PSA" represents the mean value after treatment. The specific value of the pre- and post-intervention PSA values of all the selected studies are shown in Tables 1 and 2 of the supplementary data of this study.

Table 6. Summary table of combined T-test result.

Analysis	Mean Difference (ng/mL)	SEM (ng/mL)	T-statistic	p-value	Conclusion
Combined (5 studies)	-1.678	0.0774	-21.68	<0.0001	Highly significant PSA reduction

Table 6 summarises the pooled T-test analysis of five studies that provided sufficient quantitative data on pre- and post-intervention PSA levels. The combined mean difference (-1.678±0.0774 ng/mL) demonstrates a statistically significant reduction in PSA following herbal interventions, with a highly significant overall p-value (<0.0001). "SEM" denotes the standard error of the mean, and the "T-statistic" reflects the magnitude of difference relative to sample variability.

From Table 6 the statistical significance of PSA reductions was calculated for studies that reported pre- and post-intervention PSA levels. The "Mean Difference" was calculated as (post-pre), with negative values indicating a reduction in PSA levels. P-values marked "estimated" were inferred from available summary statistics when raw data were not provided. Excluded studies either lacked quantitative PSA data, reported only PSA doubling time or percentages, or presented non-comparable control group outcomes. For instance, studies like [38,48,49,56] were excluded due to missing post-intervention PSA values or reporting only PSA doubling time or percentages. Qualitative studies [51,63,64] lack numerical PSA data. Studies with only control group comparisons [41] or unclear PSA changes (e.g., [59] were also excluded. Nevertheless, the combined analysis depicted in Table 6 indicates that the included herbal preparations–*Curcuma longa*, flaxseed, green tea, fermented soy, and sulforaphane–collectively contribute to a meaningful reduction in PSA levels among prostate cancer patients [47,50,52,53,55]. This supports the potential role of phytochemical-rich interventions as complementary strategies in prostate cancer management.

Across included studies, herbal and phytochemical therapies exhibited favourable safety profiles, with most adverse events being mild to moderate (Grades 1-2). A small number of studies reported isolated Grade 3 events (e.g., transient hypokalemia, transaminitis, or hyperglycemia), which resolved without intervention. No dose-limiting toxicity, treatment-related mortality, or serious long-term effects were observed, indicating that herbal therapies for prostate cancer are generally safe and well-tolerated under studied conditions (Table 7).

Table 7. Objective 3: Assess safety and reported adverse effects.

Herbal Preparation	Adverse Effects	Severity	Citation
Turmeric, resveratrol, green tea, broccoli	Mild-to-moderate events	Grade 1-2	[38]
Prostate Health Cocktail	Grade 2/3 transaminitis, hyperglycemia, hypercalcemia, flatulence	Grade 2-3	[39]
Soy milk with isoflavones	Minimal; one withdrawal due to diarrhoea	Grade 1	[40]
Polyphenol-rich supplement	Some gastrointestinal events	Grade 1	[41]
Tomato and soy diet	Minimal gastrointestinal complaints	Grade 1	[42]
Muscadine grape skin extract	Grade 1 gastrointestinal symptoms	Grade 1	[43]
Phellodendron amurense bark extract	Transient Grade 3 (hypokalemia, urinary incontinence); mostly Grade 2	Grade 2-3	[44]
SH003	Hot flashes, diarrhoea	Grade 1-2	[45]
Qianlie Xiaozheng Tang	No severe effects; some dropouts	Grade 1	[46]
Green/black tea	No serious adverse events	None	[47]
Muscadine grape skin extract	Grade 1 or 2; no serious adverse events	Grade 1-2	[48]
Modified citrus pectin	Grade 1 toxicity in 30%	Grade 1	[49]
Stabilized sulforaphane	Mild gastrointestinal side effects	Grade 1	[50]
C*urcuma longa, Boswellia, Pinus, Urtica*	Minimal side effects	Grade 1	[52]
Flaxseed+low-fat diet	Minimal side effects	Grade 1	[53]
Pomegranate juice	Mild bowel disturbances	Grade 1	[54]
Fermented soy beverage	One serious adverse events (unrelated)	Grade 1	[55]
Pomegranate juice	No serious adverse events	None	[56]
Soy protein isolate	No significant adverse events; palatability issues	Grade 1	[57]
Sulforaphane-rich broccoli sprouts	Grade 1; one Grade 2 constipation	Grade 1-2	[58]
Pomegranate extract	Mild gastrointestinal effects	Grade 1	[59]
White button mushroom powder	Grade 1 bloating; one Grade 3 hyponatremia	Grade 1-3	[60]
Saw palmetto	No dose-limiting toxicities	None	[61]
Genistein combined with polysaccharide	Mild gastrointestinal complaints, diarrhoea	Grade 1	[62]

Table 8. Objective 4: Identify the specific part of the plant employed and the specific phytochemical involved.

Herbal Preparation	Plant Part	Phytochemicals	Citation
Pomegranate	Fruit (juice/extract)	Polyphenols, ellagic acid	[54,56,59]
Soy	Milk, protein isolate, fermented beverage	Isoflavones (genistein, daidzein, equol)	[40,55,57]
Muscadine grape	Skin extract	Ellagic acid, quercetin, resveratrol	[43,48]
Green tea	Leaves (brewed/extract)	Catechins (EGCG, EGC, EC, ECG)	[38,41,47]
Broccoli	Sprouts/stabilised extract	Glucosinolates, sulforaphane, isothiocyanates	[38,41,50,58]
Tomato	Fruit	Lycopene	[42]
Flaxseed	Seeds	Lignans, omega-3 fatty acids	[53]
Phellodendron amurense	Bark	Berberine, palmatine, phellodendrine	[44]
White button mushroom	Whole mushroom powder	Not specified	[57]
Saw palmetto	Fruit	Not specified	[61]
Turmeric	Rhizome	Curcumin	[38,41,53]
Modified citrus pectin	Citrus peel	Galectin-3 inhibitors	[49]
SH003	Roots, fruits	Astragaloside, decursin, trichosanthin	[46]
Qianlie Xiaozheng Tang	Not specified	Not specified	[47]
Traditional herbs (African)	Various	Not specified	[51,63,64]

Table 8 summarises findings from Objective 4, which focuses on identifying the specific plant parts and corresponding phytochemicals implicated in various herbal preparations investigated across the cited studies. “Not specified” indicates that the original study did not report the plant part or phytochemical composition in sufficient detail. Study numbers correspond to references listed in the main text.

From Table 7, gastrointestinal anomalies ranging from Grade 1 to Grade 2 were shown to be the predominant adverse effect upon administration of various herbal interventions. However, minor reports from studies [39] and [44] showed a transient effect on electrolyte stability, ranging from hypokalemia and hyperglycemia to hyperglycemia, and urinary incontinence. The majority of the herbal preparations, as shown in Table 8, were derived from fruits and leaves, with fruits being the most frequently utilised plant part (e.g., pomegranate, tomato, muscadine grape, saw palmetto). Commonly identified bioactive compounds included polyphenols, isoflavones, catechins, glucosinolates, sulforaphane, and curcumin, all of which are known for their antioxidant and anti-inflammatory properties relevant to prostate cancer management. Preparations such as pomegranate extracts, soy-based interventions, and green tea catechins appeared most frequently across studies, reflecting their established roles in prostate cancer chemoprevention. In contrast, several traditional herbal formulations (e.g., African traditional herbs, Qianlie Xiaozheng Tang, and saw palmetto) did not provide sufficient detail regarding the specific plant parts or phytochemical constituents, limiting biochemical comparability. Overall, the evidence from Table 8 shows the predominance of phytochemical-rich plant components targeting oxidative and hormonal pathways implicated in prostate carcinogenesis.

4. Discussion

4.1 Effectiveness of Herbal Interventions Using PSA as a Biomarker

PSA is one of the commonest and a readily assessable biomarker for prostate health, especially in prostate cancers, although recommendations have been made against its routine check for prophylaxis [65,66]. The standard value for the PSA of a healthy man ranges from 1.5ng/ml to 4.5ng/ml, depending on the age, as described by the National Cancer Institute of the United States of America [65] The findings from this systematic literature review reveal that several herbal interventions can be of immense benefit as an alternative, and in some cases, a complement in the management of prostate cancer at different stages. Although biochemically recurrent prostate cancer and localised prostate cancer appear to be the most predominant. Nevertheless, research like that of [39,41,42,44,47,49,50,52,53,55,56,58,60], from table 4 and buttressed in the intervention and outcome variable table, all recorded a favourable decrease in the PSA value after treatment with different herbal interventions. It is also noteworthy that studies by [49,56,58] recorded an increased PSA doubling time. The PSA doubling time is a validated research and clinical factor which determines the time it takes for a patient’s PSA to double from a baseline value. Hence, the longer the time it takes, the more effective the intervention, and by extension, the healthier the prostate gland [67,68]. On the other hand, studies by [38,40,46] recorded an increase in the PSA value after intervention, while [38] also recorded a decrease in PSA doubling time, indicating little to no positive effect on the health of the prostate gland. Similarly, various articles also recorded a stable or insignificant increase in PSA value at the intervention arm of their study, including [54,57,59,61,62].

Furthermore, the significance of these reductions was analysed using the pooled mean difference and a descriptive T-test. Table 5 showed varying degree of PSA reductions with studies [47,52,53,55], all showing significant reductions using estimated p-values.The pooled mean difference of (-1.678±0.0774 ng/mL) as shown in tables 5 and 6 indicates a significant reduction in PSA levels across the five studies that reported mean PSA changes, suggesting that herbal interventions (*Curcuma longa*, flaxseed, green tea, fermented soy, and sulforaphane) collectively reduce PSA levels in prostate cancer patients [47,50,52,53,55]. The T-statistic (-21.68) and p-value (<0.0001) confirm a highly significant effect, driven by large sample sizes (total n=457) and consistent PSA reductions in most studies (except [50], which had a small positive difference). [52] contributed the largest effect (-3.6-3.6-3.6 ng/mL, n=162), followed by [47] (-1.2-1.2-1.2 ng/mL), [55] (-0.96-0.96-0.96 ng/mL), and [53] (-0.8-0.8-0.8 ng/mL). In [50], a slight increase (+0.099 ng/mL) is outweighed by larger studies due to weighting.

Several extant literature have researched the effects of different herbal interventions on PSA values, as a test for the quality of prostate health following cancer detection. A systematic review on the effect of green tea on PSA levels showed no significant change; however, subgroup analysis revealed a significant decrease among the USA population [69]. The studies [38,41,47] included in this current review made use of green tea as their interventions, and although they did not report a change in PSA values, the studies recorded an improved prostate-specific antigen doubling time (PSADT), which indicated that it takes a longer time for PSA values to increase in the treated group when compared to the control/placebo groups. Moreso, the studies were conducted in Australia, the United Kingdom and the United States, indicating that demographic differences may have no effect as reported by [69]. Another review involving RCTs recorded a positive impact on PSA by phytochemicals. While the study mentioned pharmaceutically synthesised agents like Finasteride and Dutasteride as major agents, they pointed out that Saw palmetto (*Seronoa repens)* has a positive effect in reducing PSA values among prostate cancer patients. However, this is not significant [70]. The study by [61], which was also included in this current review, recorded an insignificant difference in the test group when compared to the placebo group, although the authors recommended it for prostate cancer patients.

It is important to point out that these herbal formulations function through different mechanisms to produce their effect on PSA and inadvertently, on prostate cancer cells. For instance, a class of phytochemicals referred to as phytoandrogens have been implicated in modulating the role of androgen in prostate health [71]. Generally, prostate cancer cells rely heavily on testosterone and dihydrotestosterone (DHT) to grow. This is why current orthodox treatments like androgen deprivation therapy (ADT)–work by reducing these androgens or blocking their receptors especially for metastatic prostate cancer [72]. However, prostate cancer cells have the ability to develop androgen receptor hypersensitivity, and intratumoral androgen synthesis. This confers them the ability to activate cancer cell growth even upon the most minute of androgen secretion, as well as the ability to synthesise androgens, making it difficult to manage [73]. Nevertheless, these phytochemicals have been shown through research to weakly bind with androgen receptors thereby providing competitive partial agonist effect [71]. Similarly, a review of the modulatory effect of phytoandrogens showed that they have the ability to influence the activities of co-regulators of androgen receptors including co-activators and co-repressors [74]. This gives them the ability to reduce the expression of these receptors thereby reducing the activities of androgens intricate in the growth of prostate cancer cells. However, it is important to point out that their role is debated and some expert posit that some have the ability to mimic, or enhance androgen activity thereby encouraging tumour growth [75].

Nonetheless, key herbal interventions which showed reduction PSA level or increase in PSA doubling time have be implicated in modulatory activities of androgens and their receptors. Green tea shown by study [38,41,47] have shown to contain catechins that has the ability to suppresses AR expression, and decreases DHT-induced growth [76]. Similarly, the isoflavones from Soy bean shown by studies [40,55,57], have been implicated in weak AR modulation,and in the inhibition of 5-α-reductase. This enzyme is critical in the conversion of testesterone to dihydrotestesterone, a more potent androgen promoting prostate cancer growth [77]. On the other hand, it is important to point out that other herbal interventions function through other patways to prevent tumourogenesis and cancer growth. For instance, pomegranate polyphenols have been shown to be a potent antioxidant and reduce inflammatory markers. This is critical in preventing oxidative DNA damage, a precursor of oncogene formation [78]. Similarly, Lycopenes from tomatoes, soy isoflavones, curcumin from tumeric, and sulforaphanae from broccoli have all been shown to exert antioxidant effects with others implicated in anti-proliferation and inhibition of tumour progression pathways [79,80]. However, there is a need for further studies to fully understand the biochemical pathways of these physiological activities.

4.2 Effectiveness Using Reported Adverse Effects

On the other hand, the selected studies also recorded various degrees of adverse effects, ranging from Grade 1 to Grade 3. Grade 1 side effects appeared the most with 11 of the 15 studies, which reported adverse effects, pointing out mild to moderate gastrointestinal disturbances as the major side effects. These studies as shown in table 7 employed either Soy isoflavones**,** polyphenol-rich blends (pomegranate+green tea+broccoli+turmeric)**,** tomato+soy diet**,** muscadine grape skin extract**,** SH003 (Astragalus/Angelica/Trichosanthes), sulforaphane (both stabilized and broccoli-sprout forms), pomegranate

juice/extract**,** white button mushroom powder**,** and/or genistein combined polysaccharide as their interventions [38,40,41,42,43,45,50,54,56,58,59,60,62]. This suggests that the vast majority of the extracts and herbal interventions used for the management of prostate cancer result in gastrointestinal disturbances. A non-empirical literature review on the various complications and adverse effects that bedevil different therapies employed in prostate cancer management (chemotherapy, radiotherapy, thermal therapy, prostatectomy, hormone therapy and immunotherapy) recorded rectal injury/bleeding, bowel problems, urinary incontinence, erectile dysfunction, and kidney, and liver problem as the major and most recurring side effects regardless of the choice of therapy [81].

Furthermore, severe (Grade 3) adverse effects were recorded by [39,44,60], which include transaminitis, hyperglycemia, hypercalcemia, transient Grade 3 (hypokalemia, urinary incontinence), and hyponatremia. These were studies in which *Phellodendron amurense* bark extract, Prostarate Health Cocktail, and white button mushroom powder were administered. However, research evidence suggests that these grade three adverse effects may be related to gastrointestinal and kidney disturbances caused by these herbal interventions. Thus, diarrhoea or vomiting, and kidney dysfunction through the activation of metabolo-tubular functions of the kidney as noted by [44] in their *Phellodendron amurense* bark extract study, can lead to loss of key electrolytes, leading to hypokalemia and hypocalcemia [44,82]. Nevertheless, the qualitative studies included in this review all recorded positive perceptions, with participants from all three studies making positive and favourable remarks on the use of herbal interventions/traditional medicine compared to other standard therapies used in managing prostate cancer [51,63,64]. Although these qualitative studies mostly sought the perceptions of patients, with only [63] seeking the perceptions of both patients and health workers. In the same vein, the qualitative studies were all conducted in Africa, indicating a demographic homogeneity which may influence this perception. For instance, studies have shown that people from the African continent are inclined to practice traditional medicine as opposed to their counterparts in Europe and the Americas. This may be as a result of anthropological or historical ties to the use of these medicines before the advent of orthodox medications [83,84,85].

4.3 Implications for African Healthcare and Clinical Practice

Of the 27 studies that made it to this review, only 3 (~11%) were conducted in Africa [51,63,64]. This suggests that Africa is lagging in the push to achieve integrative and holistic healthcare management in the fight against prostate cancer. However, it is important to point out that while three articles were conducted in Africa, none of them mentioned the use of a particular herbal intervention. Nevertheless, evidence suggests that most of the phytochemicals, herbal extracts or natural products pointed out among other studies are botanically available in Africa. For example, turmeric (*Curcuma longa*), green tea (*Camellia sinensis*), and Broccoli (*Brassica oleracea*) are widely cultivated in East and West Africa for culinary and medicinal purposes [86,87]. Similarly, Soy (*Glycine max*) is cultivated extensively in Nigeria, Ghana, Uganda, and Zambia as a high-protein legume. Tomato (*Solanum lycopersicum*) is cultivated throughout Africa, while Falxseed (*Linum usitatissimum*) and Pomegranate are both cultivated in Northern Africa (Egypt) and some parts of South Africa [88-90]. This suggests that most of these plants and their products are readily available for various uses in Africa. Although one of the study [61] made use of Saw palmetto (*Serona repens*), which is not native to Africa but gets imported and used in African herbal medicine markets [91].

The World Health Organisation recommends a holistic and multidisciplinary approach centred on the patient and their needs. This suggests that the use of herbal interventions, although not explicitly stated, can be used in the management of prostate cancer [92]. However, the prevalence of its use in Africa, although widely acknowledged across multiple studies [93-95], appears not to be backed by research evidence obtained within the African setting. The data provided by the World Health Organisation on cancer research and development across its member countries showed that Africa is the least represented in clinical trials, ranking as low as 1-500 (total registered trials) from 1999 to 2022 [96]. Consequently, while prevalence studies may show that Africans are among the highest adopters of the use of herbal interventions as an alternative or complement in the management of various cancers, or specifically to prostate cancer [93,95], the lack or paucity of research evidence from clinical studies suggests that Africa's healthcare providers and traditional medicine givers may have been putting a square peg in a round hole. The adoption of a treatment plan based on the clinical evidence presented from a different demographic may not be the ideal strategy to follow. Especially when considering that race and genetic factors of an individual are major risk factors for consideration in the development of prostate cancer, and by extension, the management of prostate cancer [3].

In context, none of the studies conducted in Africa involved a clinical trial, rather they are either qualitative exploratory studies or mixed method design. This reinforces the evidence presented by the World Health Organisation on the paucity of clinical evidence from Africa. Clinical research serves as the bridge between scientific discovery and real-world healthcare improvement. It involves the systematic study of health interventions–such as drugs, medical devices, or public health strategies–to determine their safety, effectiveness, and applicability in patient care [97,98]. Findings from well-conducted clinical studies inform evidence-based policies, guiding national and international health authorities in setting treatment standards, allocating resources, and developing preventive strategies [99]. By translating research outcomes into clinical

guidelines and health policies**,** clinical research ensures that medical practice evolves from reliable data rather than tradition or opinion, ultimately improving patient outcomes and population health Therefore, for Africa to improve in the management of prostate cancer and by extension, reduce the mortality through the use of CAM (natural products, and herbal interventions), there is a need to improve the quality and rate of clinical research from the region [100]. Also, governmental agencies and non-governmental agencies like the African Organisation for Research and Training in Cancer (AORTIC) should make moves to standardise, streamline and empiricise the different herbal interventions that can be applied in African healthcare, for the management of not just prostate cancer, but all cancers [100]. This should include policies and awareness creation to reduce the stigma associated with its use, as pointed out by the qualitative studies selected for this review [51,64].

Furthermore, the clinical implications of these findings are significant for both patients and healthcare providers managing prostate cancer. Although reductions in PSA levels and prolonged PSA doubling times suggest that certain herbal interventions, such as green tea catechins, cucumin, boswellia, pinus, urtica, pomegranate extracts, and phytosterol-rich botanicals, sulforaphane, flaxseed oil+low fat diet, and fermented soy beverage may exert biological effects on prostate tissue, these outcomes should be interpreted cautiously. PSA changes alone do not equate to tumour regression or improved survival, but they can serve as adjunct indicators of biochemical response when monitored alongside imaging and clinical evaluation [101,102]. Integrating standardised herbal preparations as complementary agents may therefore offer supportive benefits in delaying biochemical progression or enhancing the tolerability of conventional therapies [103-105]. Clinicians should, however, ensure careful monitoring of PSA kinetics and potential herb-drug interactions to prevent misinterpretation of disease status [106]. Importantly, the observed PSA modulation highlights the need for larger, well-controlled clinical trials to validate these effects and determine whether they translate into meaningful improvements in progression-free or OS for prostate cancer patients.

4.4 Limitations of the Study and Recommendations for Future Research

This study encountered several limitations inherited mostly from the quality and design of the selected studies. For instance, the majority of studies included in this systematic review were conducted in countries outside of Africa, with only a small fraction (3 out of 27) originating from African nations. Although the search process employed only AJOL as the only African-specific database for clinical studies. This limited geographical representation may affect the generalisability of the findings to African populations, where cultural, environmental, and genetic factors may influence the efficacy and safety of herbal interventions. Similarly, there was an inconsistency in the measurement and reporting of the PSA values. Some studies did not report post-intervention PSA values or provided only PSA doubling times, which limits the ability to assess the direct impact of herbal interventions on PSA levels. This inconsistency complicates the evaluation of treatment efficacy. Others reported PSA median values, making the study sample incorporated for the T-test very small, although statistical significance was recorded. On the other hand, the vast majority of the studies did not report tumour progression rate or survival outcomes after interventions were administered, which makes it difficult to holistically determine the clinical efficacy of these extracts on prostate cancer. These limitations highlight the need for further research, particularly high-quality clinical trials conducted within African contexts, to establish the efficacy and safety of herbal medicines in the management of prostate cancer.

5. Conclusion

In conclusion, this systematic review highlights the promising role of herbal medicines in managing prostate cancer, particularly in African contexts where access to conventional treatments may be limited. The findings indicate that various herbal interventions can lead to significant reductions in PSA levels, suggesting potential efficacy in slowing disease progression. However, the review also reveals critical limitations, including the predominance of studies conducted outside Africa, which may hinder the applicability of results to local populations. Additionally, inconsistencies in PSA measurement and reporting, along with insufficient data on tumour progression and survival outcomes, complicate the assessment of clinical efficacy. This is because PSA progression is not a definite marker of tumour therapeutics. These findings highlight the urgent need for high-quality clinical trials within African settings to validate the safety and effectiveness of herbal therapies, ultimately aiming to enhance treatment options and outcomes for patients with prostate cancer in the region.

Conflict of Interest

The authors declare that there are no competing interests whatsoever. This study was independently executed by the authors without any funding from any institution, or private individuals.

Generative AI statement

The authors declare that no Gen AI was used in the creation of this manuscript.

Abbreviations

ADT: Androgen deprivation therapy

AORTIC: African organisation for research and training in cancer

BPH: Benign prostatic hyperplasia

CAM: Complementary and alternative medicines

CASP: Critical appraisal skills programme

CTCAE: Common terminology criteria for adverse events

DHT: Dihydrotestosterone

JBI: Joanna briggs institute

OS: Overall survival

PEO: Population, exposure, outcome

PFS: Progression-free survival

PICO: Population, intervention, comparison, outcome

PRISMA: Preferred reporting items for systematic reviews and meta-analyses

PSA: Prostate-specific antigen

PSADT: Prostate-specific antigen doubling time

PSA-PFS: Prostate-specific antigen progression-free survival

RCTs: Randomised controlled trials

ROBINS-I: Risk of bias in non-randomised studies of interventions

SEM: Standard error of mean

WHO: World Health Organisation

Reference

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