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Research Paper

A Systematic Review on Prunus africana (Hook.f.) Kalkman

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Abstract
Prunus africana (Hook.f.) Kalkman (syn. PygeumafricanumHook.f.), a large tree of the Afromontane family Rosaceae, has received a lot of scientific, commercial and conservation attention within the last several decades. Bark of this tree has become one of the most traded medicinal plant products in Africa which is highly sought after because of its effectiveness in managing benign prostatic hyperplasia (BPH). The review compiles the existing body of knowledge regarding the taxonomy of P. africana, botanical features, ecology, phytochemical profile, pharmacological functions, clinical evidence, and the conservation status. Phytochemical studies have found various bioactive compounds such as phytosterols (especially 8-sitosterol), pentacyclic triterpenes (ursolic acid, oleanolic acid), ferulic acid esters and polyphenolic compounds. Anti-inflammatory, antiprolliferative, antiandrogenic, and antioxidant activity has been proven through pharmacological studies all of which support the basis of using it based on the therapy of BPH. The answer to this is moderate evidence in clinical trials and meta-analyses that its use is supportive in the case of urological symptoms, but the methodological weaknesses in the prime literature require larger, well-designed randomized controlled trials. Conservation Conservationist In terms of conservation P. africana appears at Appendix II of the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) because of mounting pressure on its harvesting of barks and loss of habitat over its range. The review critically evaluates the existing body of knowledge and identifies major voids to be filled by future research, such as sustainable domestication practices, herbal preparation standardisation and long-term clinical effectiveness data.

Keywords: *Prunus africana; Pygeumafricanum; benign prostatic hyperplasia; Afromontane; bark harvesting;*

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I. Introduction

Medical plants remain the main source of healthcare in a significant percentage of the global population, especially in the low- and middle-income countries with poor access to conventional pharmaceuticals (World Health Organization [WHO], 2019). Prunus africana (Hook.f.) Kalkman, the most internationally recognised, commercially important medicinal tree of the African continent, takes a unique place among them. This Afromontane species, which is also referred to as African cherry, red stinkwood, African plum and pygeum, is found in highlands forests in sub-Saharan Africa and in a number of offshore island groups (Cunningham &Mbenkum, 1993).

The healing value of P. africana had been determined by local people throughout its distribution and was known to the world pharmaceutical industries well before experts discovered its potential. Historically, traditional healers across most part of Central and East Africa used to prepare decoctions out of barks to treat urinary disorders, chest complaints, fever, and many more (Ndung'u et al., 2024). It was in the 1960s and 1970s that commercial exploitation of international medicines/pharmaceutical industries took off as European pharmaceutical firms came up with proprietary formulations of lipidosterolic bark extracts which were standardised to treat BPH-related LUTS - a disease which is said to affect over 50% of men over 50 years of age worldwide (Wilt et al., 2002). Towards the end of 1990s the pharmaceutical products established on the basis of P. africana bark extract became commercially valued and contributed to the annual revenue of several hundreds of millions of USD (Kadu et al., 2012), creating great pressure on the wild population.

The result of this growing business pressure has been disastrous to wild P. africana populations. In the late 1990s, a total of more than 3,300 tonnes of bark was harvested every year to meet the world pharmaceutical production needs (Cunningham et al., 2016). The species were listed on the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) at the convention in 1995 under the Appendix II as a response to recorded declines in its population. In 2007, a European Union (EU) ban on imports of bark was implemented, which was later lifted in 2011, and in 2023, the CITES Plants Committee started a formal Review of Significant Trade in P. africana, which made it clear that continued concern was being expressed about the sustainability of international trade in this species (CITES, 2023).

The review will combine existing evidence in the entire range of scientific fields applicable to P. africana such as taxonomy, ecology, ethnobotany, phytochemistry, pharmacology, clinical medicine and conservation biology. The limitations of the methodology in the current literature are critically appraised in the course of this, and potential areas of priority in future research are established.

II. Taxonomy and Botanical Description

2.1 Taxonomic Classification

It was William Jackson Hooker the younger (Hook.f.) who in 1867 formally described Prunus africana as Pygeumafricanum. After exhaustive revision of Old World species under subgenus Prunus Laurocerasus, Cornelis Kalkman (1965) transferred this species to genus Prunus. Pygeumafricanum still exists significantly within pharmacological and clinical texts. Its full taxonomic name is: Kingdom Plantae; Division Magnoliophyta; Class Magnoliopsida; Order Rosales; Family Rosaceae; Subfamily Amygdaloideae (syn. Prunoideae); Genus Prunus; Species P. africana (Hook.f.) Kalkman (Ndung'u et al., 2024).

2.2 Morphological Characteristics

Prunus africana is a medium to large evergreen tree usually 10-25 m high, however, with some recorded to be as high as 40 m. Full grown trunks can have a diameter at the height of the breast that is more than one meter. Diagnostic features of the bark include; rough, cracked, brown to black in colour, and when cut, exudes a reddish resin, which adds to the vernacular name of red stinkwood (Cunningham and Mbenkum, 1993). There are simple, alternate, petiolate, and elliptic to oblong-elliptic (5-20 cm long) leaves, finely serrated, dark-green and glossy on the upper surface. The petiole (1-2 cm) is often reddish. The odour of the crushed leaves resembles an almond-like smelling that is in line with the cyanogenic glycoside chemistry of genus Prunus (Ndung'u et al., 2024).

Flower is small, whitish cream, and in tight axillary racemes 5-15 cm. The plant is bisexual and has five petals and many stamens. The fruits are drupes that measure 8-12 mm in diameter, they are ripe, turning dark purple-black in color and have a single dark seed. Critical importance Frugivorous birds, monkeys and elephants are key seed dispersers and therefore their presence is vital in the process of natural regeneration (Cunningham and Mbenkum, 1993).

III. Geographic Distribution and Ecology

3.1 Distribution

Prunus africana is fragmented in character with a montane distribution throughout sub-Saharan Africa and some groups of islands. It covers the countries of Ethiopia and the East African highlands, the Democratic Republic of the Congo, Rwanda, Burundi, Uganda, Kenya, Tanzania, Malawi, Zambia, Zimbabwe, and South Africa, and West and Central African states, such as Cameroon, Nigeria, and Equatorial Guinea (Ndung'u et al., 2024). They are found on Bioko (Equatorial Guinea), Sao Tome and Principe, the Comoro Islands and Madagascar (Cunningham and Mbenkum, 1993). The presence of geographic difference in the phytochemical composition among 20 populations along this range has been reported and ursolic acid exhibited the greatest interpopulational variation (66) of the significant constituents in the barks (Kadu et al., 2012).

3.2 Habitat and Ecology

Prunus africana is highly related to the Afromontane forest, and it is found at altitude of between 900 and 3,300 above sea level, with the highest growth at 1,200-3,000 m in the tropics (Cunningham et al., 2016). It needs an annual rainfall of 900-3400 mm, is a moderate frost-tolerant species, and prefers deep and well-drained soils that are rich in humus. It is a shade-tolerant species during early development but a light-demanding species at maturity. In the forest canopy, it has been linked with Podocarpus spp., Hageniaabyssinica and Juniperus procera. During fragmented populations, there is a lower level of dispersal effectiveness, and genetic isolation is elevated (Cunningham et al., 2016).

IV. Ethnobotanical Uses and Traditional Medicine

4.1 Traditional Medicinal Uses

Varied pharmacopoeias based on the bark of P. africana have evolved in traditional communities that are distributed throughout the distribution range of the species. In Cameroon, Kenya, Uganda, Tanzania, and Rwanda, the widespread use of the decoctions of barks as a treatment method in urinary conditions, BPH, prostate diseases, fever, malaria, gastrointestinal disorders, chest pain, gonorrhoea, kidney disease, wound healing, and diabetes mellitus (Ndung'u et al., 2024; Komakech et al., 2017). In Uganda, the plant is the most common one in the treatment of the health conditions of men including prostate diseases in 23 African countries surveyed (Ndung'u et al., 2024). In Madagascar, the preparation of urinary issues of the prostate by use of bark preparations is specifically used by the traditional healers (Cunningham &Mbenkum, 1993). The wood is also dense and sturdy and is also useful in construction, furniture and in the form of a fuel source.

4.2 Entry into Global Pharmaceutical Trade

Commercialisation of P.*africana* to manufacture pharmaceutical products worldwide started in the 1960s. Firms in Europe (in France and Italy, in the first instance), produced proprietary lipidosterolic extracts sold as Tadenan(r) and Pygeum(r), mainly to treat BPH (Wilt et al., 2002). The bark of P. africana became one of the most commercially important medicinal plant commodities in Africa by the 1970s to 1990s, mostly traded centrally in Cameroon. In 2012, Cameroon increased its share of total bark exports, which was 38 percent (1995-2004 average) to 72.6 percent (658.6 metric tonnes) with sales restrictions on exports by CITES in Burundi, Kenya and Madagascar (Cunningham et al., 2016).

V. Phytochemical Composition

5.1 Phytosterols

The most common phytosterol is b-sitosterol and b-sitostone with a mean concentration in the bark of 490mg/kg and 198mg/kg respectively across populations in Africa (Kadu et al., 2012). Other phytosterols are campesterol and stigmasterol. b-Sitosterol has been accredited with the anti-inflammatory effects which prevent swelling of the prostate and is the key element in the disease-rationalisation in BPH treatment (Kadu et al., 2012; Ndung'u et al., 2024). Recent in silico investigations have also revealed that b-sitosterol has binding affinity to the androgen receptor ([?]8.9 kcal/mol) which is greater than that of the reference drug flutamide ([?]8.6 kcal/mol), implying that it can be used as an antiprostate cancer agent (Ndung'u et al., 2024).

5.2 Pentacyclic Triterpenes

Ursolic acid (mean 743 mg/kg) is the most common bioactive component in P. africana bark in its regional occurrence and is the most interpopulational variable (Kadu et al., 2012). There is also the presence of oleanic acid, a-amyrin and b-amyrin. The pentacyclic triterpenes are linked to anti-inflammatory, anti-oedematous, antiproliferative and anticancer effects (Komakech et al., 2017). It has also been demonstrated that oleanic acid can inhibit cell viability, induce apoptosis and arrest cell cycle of G0/G1 in prostate cancer PC-3, DU145 and LNCaP cell lines through inhibition of PI3K/Akt signalling pathway (Komakech et al., 2017).

5.3 Ferulic Acid Esters and Related Compounds

Ferulic acid esters are one of the most diagnostically unique constituents in the P. africana barks. The average ferulic acid content of sampled populations is 49 mg/kg, and the n-docosanol is 25 mg/kg (Kadu et al., 2012). These compounds are thought to have antitumour and hypocholesterolaemic effects on the prostate and the level of n-docosanol was highly significantly correlated with all other analysed analytes throughout the populations indicating that it can be used as a chemical marker to determine the quality of the bark (Kadu et al., 2012).

5.4 Tannins, Alkaloids, Flavonoids, and Fatty Acids

Polar part of P. africana bark has large amounts of tannins, saponins, alkaloids, and flavonoids (Ndung'u et al., 2024). Among the simple phenolic acids, gallic acid, caffeic acid, and ellagic acid were detected in aqueous extracts of barks. The fatty acids present in the bark are also lauric acid (mean 18 mg/kg) and myristic acid (22 mg / kg) (Kadu et al., 2012). Other bioactive compounds that were extracted in the bark are b-sitosterol-3-O-glucoside, N-butylbenzenesulfonamide, tartaric acid, and benzoic acid (Komakech et al., 2022). Cyanogenic glycosides are also consistent with the wider phytochemistry of the Prunus genus of cyanogenic glycosides.

VI. Pharmacological Properties

6.1 Anti-inflammatory Activity

P. africana extracts are very well documented in terms of their anti-inflammatory action. An anti-inflammatory effect on the production of pro-inflammatory prostaglandins by the inhibition of the arachidonic acid cascade by phytosterols, especially b-sitosterol, and an anti-oedematous effect of pentacyclic triterpenes (Kadu et al., 2012; Ndung'u et al., 2024). Ursolic acid and oleanolic acid inhibit nuclear factor kappa-B (NF-kB) signalling, which is a key axis in inflammation; inhibition of NF-kB is also important in halting cancer cell proliferation and works as an antimutagenic (Komakech et al., 2022). The combination of these anti-inflammatory processes is pharmacologically pertinent to the BPH pathogenesis, where inflammatory processes are gradually becoming a significant factor (Wilt et al., 2002).

6.2 Antiproliferative and Antiandrogenic Activity

The epidermal growth factor (EGF) and insulin-like growth factor (IGF) binding to prostate cell membrane receptors is prevented by the ferulic acid ester portion of P. africana, which suppresses growth factor-mediated growth. The extract also prevents the intake of testosterone by prolactin-stimulated prostate cells and this decreases the androgenic drive (Wilt et al., 2002). In even more recent molecular investigations, four phytochemicals, b-sitosterol, campesterol, prunetrin, and stigmastan-3,5-diene, showed greater affinity of antiandrogen effects by molecular docking than the anti-androgenic standard flutamide in molecular docking studies, with a solid argument in favor of their antiandrogenic action (Ndung'u et al., 2024).

6.3 Anticancer Activity

The emerging evidence is making P. africana a promising chemoprevention and chemotherapy agent of prostate cancer. Transgenic adenocarcinoma of the mouse prostate (TRAMP) mice fed on P. africana exhibited a statistically significant decrease in the incidence of prostate cancer, as compared to the control animals ($p = 0.034$; Komakech et al., 2022). In vitro experiments have proved that PC-3 human prostate cancer cells are about 50 percent growth inhibited by the use of the bark extracts and significant apoptosis is also produced (Komakech et al., 2022). Namely, the IC50 of the extracts of 52.30 mg/mL (stem bark extract) and 82.40 mg/mL (micropropagated root extract) against PC-3 cells have been presented, and dose-dependent apoptosis has been verified using annexin-V and propidium iodide staining and caspase-3 activation (Komakech et al., 2022). They include the anticancer effect of inducing cell apoptosis, cell growth and proliferation arrest, and inhibition of signalling factors that promote invasion, migration, and metastasis (Ndung'u et al., 2024).

6.4 Antioxidant Activity

The polyphenolic fraction — including tannins, catechins, and phenolic acids — exhibits significant free radical scavenging capacity as measured by DPPH and FRAP assays. Ursolic and oleanolic acid contribute further to the overall antioxidant profile (Ndung'u et al., 2024). These antioxidant properties may also contribute indirectly to the anti-inflammatory and antiproliferative effects, and are relevant to the recently documented anti-dipeptidyl peptidase-4 (anti-DPP-4) activity of *P. africana* extracts, which has implications for diabetes management (Ndung'u et al., 2024).

Of the polyphenolic fraction, which comprises tannins, catechins involving phenolic acids, the free radical scavenging ability is high with DPPH and FRAP methodologies. The antioxidant profile is also supplemented by ursolic and oleanolic acid (Ndung'u et al., 2024). These anti-oxidant possibilities come into play indirectly in the anti-inflammatory and anti-proliferative impact and is also applicable in the recently identified anti-dipeptidyl peptidase-4 (anti-DPP-4) effect of P. africana extracts, which have implications in the management of diabetes (Ndung'u et al., 2024).

6.5 Antimicrobial Activity

P. africana bark extracts have been shown to be inhibitor of numerous bacterial pathogens, which is in line with the old practice of using it against infectious diseases. Mwitari et al. (2013) found significant antimicrobial activity against the relevant Kenyan clinical isolates, and the most likely mechanisms were membrane disruption and enzyme inhibition, which could be ascribed to the tannin and phenolic fractions. The antifungal against dermatophytes and Candida spp. has also been reported (Ndung'u et al., 2024). Also, the anticholinesterase activity is associated with the neuroprotective properties of stem bark and leaf extracts, which could be relevant to managing the Alzheimer disease (Ngai et al., 2022 as cited in Ndung'u et al., 2024).

VII. Clinical Evidence for Benign Prostatic Hyperplasia

7.1 BPH: Clinical Background

BPH is a non-malignant swelling of the prostate gland, which occurs in an estimated 50 percent of men beyond the age of 50 and over 80 percent beyond the age of 80 and presents in the form of LUTS comprising of nocturia, urinary hesitancy, weak stream, incomplete bladder emptying and urinary frequency (Wilt et al., 2002). The condition severely deteriorates the quality of life, and it causes immense health system burdens in health systems worldwide.

7.2 Systematic Review and Meta-Analysis Evidence

The Cochrane systemic review and meta-analysis by Wilt et al. (2002), which also combined clinical evidence data from 18 randomised controlled trials (RCTs) including 1,562 men, is the most authoritative synthesis of clinical evidence of P. africana in the management of BPH. The pooled analysis established that men under the P. africana extract reported a large improvement in overall urological symptoms and urinary flow measures, decrease in nocturia by 19%, improvement in residual urinary volume by 23, and the increase in peak urine flow rate by 23, relative to placebo (Wilt et al., 2002). The adverse events were not severe and were mainly gastrointestinal. Another literature also supports the pharmacological activity of the anti-BPH effects of P. africana: Jena et al. (2016, cited in Ndung'u et al., 2024) found that the bark extract was effective against testosterone-induced BPH in animal models, and the authors attribute the efficacy to the synergistic effects of pentacyclic triterpenoids, ferulic acid esters, and phytosterols.

7.3 Limitations of the Clinical Evidence

Wilt et al. (2002) found that there are high methodological limitations that limited the strength of the conclusions made in the incorporated trials. These consisted of small study periods (the majority of studies ≤60 days); small sample sizes; insufficient reporting on randomisation and allocation concealment; imprecision in extract preparation and dosing schedule; imprecision in outcome measures; and inadequate reporting on adverse events. Lack of head-to-head comparative trials with existing pharmacotherapies of BPH (alpha-blockers, 5-alpha-reductase inhibitors) is a serious gap. The authors specifically suggested bigger and extended-period, rigorously designed trials with the utilisation of standardised tooling like the International Prostate Symptom Score (IPSS). This cry is still more or less unheard even 20 years later.

7.4 Standardisation of Preparations

Differences in the composition of phytochemicals between commercial preparations are a necessary obstacle to clinical research and regulatory approval. The bulk of clinical evidence is based on trials that utilize the proprietary extract Tadenan® (200 mg two times a day), standardised on the content of defined phytosterol and ferulic acid esters (Wilt et al., 2002). Geographic and seasonal differences in the composition of the barks - ursolic acid has a maximum interpopulational variation of 66 percent, which points to the need to have strong quality control standards (Kadu et al., 2012). The field has a priority of developing internationally recognisedpharmacopoeial monographs that include validated methods of analysis of key marker compounds.

VIII. Conservation Status and Threats

8.1 CITES Listing and Regulatory History

Prunus africana was annexed under CITES to Appendix II in the Ninth Conference of the Parties (CoP9, 1994; entering force 1995) and needed to have export permits issued depending on non-detriment findings (NDFs) (CITES, 1995). In 2007, a European Union ban on importing bark was enforced on barek imports due to evidence of unsustainable trade, but lifted in 2011 on the basis of Cameroon promises to have a National Management Plan in place on the species (Cunningham et al., 2016). Various studies have found that the management plan was undermined with an incomplete scientific foundation and failed to capture conservation research results (Cunningham et al., 2016). This accelerates the ongoing tensions around unsustainable levels of trade, with the CITES Plants Committee having been given the first in-person committee review of the species since CoP19 in Panama in 2023 (CITES, 2023).

8.2 Scale of Exploitation and Population Impacts

This was at the height of reaching more than 3,300 tonnes of barks harvested at one time of year with a retail market value of USD 220 million (Cunningham et al., 2016). In 2012, Cameroon was leading the trade in the world by contributing 72.6 percent of the world exports (658.6 metric tonnes) (Cunningham et al., 2016). Informally, commercial harvesting persists in the Mount Cameroon National Park and in various forest reserves in Cameroon where there is also minimal enforcement (Cunningham et al., 2016). The harvesters employed to work in the National Park in 2012 were paid less than USD 1 per day, 33 cents per kg, because of structural inequities of the value chain, in sharp contrast with the USD 6/kg price in the European market (Cunningham et

al., 2016). The use of matrix population modelling has shown that the population growth rates of P. africana are the most responsive to the survival of large and mature seed-bearing trees (Stewart, 2003) - the specific individuals that bark harvesters are attracted to (Cunningham et al., 2016).

8.3 CITES Non-Detriment Findings and National Inventories

CITES non-detriment purpose national inventories have been carried out in a number of range states. In 2022, an inventory of harvestable trees (trees above 30 cm dbh) was made on privately owned land that was located off of the protected areas in Uganda, from which a new calculation of export quota was made (CITES, 2023). The inventory of Uganda was an express recognition that the conversion of private forest to agricultural land posed a higher risk than commercial harvesting of the barks in that country, and that sustainable trade was an incentive to keep the species on the land of the private owners (CITES, 2023). A 2021 survey in TchabalMbabo forest (25,671 ha), Cameroon, found 6.23 stems/ha (358 stems/57.5 ha), and population data was used to make new harvesting recommendations (Ndedy-Bile et al., 2023).

8.4 Habitat Loss and Additional Threats

The agricultural activity, small-scale farming, cattle grazing, illicit logging, and charcoal burning still diminish and dissect Afromontane forest homes throughout the P. africana variety (Cunningham et al., 2016). Even in some areas formally designated as part of the protected places in Burundi, Cameroon, the DRC, and Madagascar, wild populations are still at risk (Cunningham et al., 2016). Specifically, the eastern forests of the DRC are exceptionally difficult in terms of conservation due to the political instability (Cunningham et al., 2016). Climate change is another threat, which is getting increasingly bigger and the changes in the temperature and precipitation regime in montane areas are projected to affect the range of the species in question, their phenology, and their reproductive success.

IX. Sustainable Harvesting, Domestication, and Policy

9.1 Transition to Cultivation

The overall policy implication of the modern P. africana literature is that sustainable wild harvest will not be sufficient to ensure the long-term supply of medicinal bark and that cultural transformation of bark supply chains to cultivated ones is needed. Cunningham et al. (2016) specifically requested CITES and EU to create distinct, traceable supply chains founded on cultivated stocks, as virtually all commercially traded tree barks in the world majorly (i.e., cinnamon and cassia) have switched to agroforestry production. P. africana is already grown by more Cameroonian smallholder farmers than any other country, and on-farm production would work to the benefit of thousands of farmers, including women whose physical capacity to harvest wild P. africana makes it onerous (Cunningham et al., 2016).

9.2 Propagation and Agroforestry

Major studies have been put into propagation biology of P. africana in order to facilitate domestication. There are recalcitrant seed behaviour and low and fluctuating germination rates that limit seed germination. Mist propagation conditions of vegetative propagation using cuttings has been experimentally demonstrated to be technically viable and it can be used to multiply high-performing genotypes (Cunningham &Mbenkum, 1993). Such progresses as the introduction of a validated micropropagation protocol that retains genetic fidelity of targeted P. africana lines have led to the mass production of elite planting material (Komakech et al., 2022). Micropropagated root extracts have also proven to have the same in vitro antiprostate cancer activity as stem bark extracts, which indicates that root-based sources may act as a supplement or even alternative to the primary pharmaceutical raw material, bark, and this would help to decrease the amount of harvest pressure of standing trees (Komakech et al., 2022).

9.3 Community-Based Conservation and Benefit Sharing

The ongoing injustice of the P. africana value chain where local harvesters are paid a small percentage of the European market price but have to pay the cost of conservation and sustainable management is a root cause of failure of governance (Cunningham et al., 2016). Sustainable management can best be attained in cases where local communities are empowered as the main managers of resources, equitably enjoy the commercial activity and also given technical assistance to sustainability in harvesting and cultivating crops (Stewart, 2003). It is also important to integrate fair-trade certification, clear royalty-sharing and community forest governance schemes. In Uganda, a policy of the government restricting commercial harvesting to privately owned land not under protection with an export quota based on inventory can be presented as an example of regulatory integration of trade and conservation goals (CITES, 2023).

X. Safety Profile and Toxicology

The P. africana bark extract has been assessed both preclinically and clinically in terms of safety profile. Standardisedlipidosterolic extract was not toxic in acute or subacute doses in rodents many times higher than the full therapeutic dose in humans, and did not exhibit any mutagenic activity in bacterial reverse mutation (Ames) assays (Ndung'u et al., 2024). The histopathological alterations in the key organs were not detected in subchronic oral toxicity studies at the clinically relevant dosages.

The adverse events in clinical trials were in general mild, temporary and mostly gastrointestinal, such as nausea, diarrhoea, and abdominal discomfort (Wilt et al., 2002). None of the clinically significant changes in hormonal parameters were reported, which further differentiated P. africana with 5-alpha-reductase inhibitors that are linked to sexual dysfunction. Most trials last a comparatively short time, meaning that it is impossible to make long-term safety conclusions. Cytotoxic effects of the extracts spread on the normal cells need to be carefully dose-optimised, and the IC50 on the cross-comparisons of the activity on cancerous and non-tumorigenic cell lines should be conducted to come up with sufficient safety margins (Komakech et al., 2022). There are no current peer-reviewed publications of systematic post-marketing pharmacovigilance data of P. africana preparations.

XI. Future Research Directions

A number of research gaps have been established regarding the literature on the P. africana. The evidence based clinical pharmacology requires large, sufficiently powered, long-term, RCTs comparing standardised P. africana extract with placebo or active comparators (alpha-blockers; 5-alpha-reductase inhibitors) using validated outcome measures (IPSS, quality-of-life indices) to develop a strong evidence base and air regulatory approval in the global markets.

Phytochemically speaking, metabolomic mapping using high-resolution mass spectrometry and NMR spectroscopy would facilitate the knowledge of the complete chemical diversity of the bark extracts within geographic areas and guide standardisation. Since the n-docosanol concentration is associated with all other significant analytes (Kadu et al., 2012), its potential use as a quality standard is worth consideration.

Research into the use of P. africana as an anticancer agent is growing at a very fast rate, but at the preclinical phase. The next steps include systematic dose-finding trials, mechanistic pathway trials and phase I/II trials on prostate cancer chemoprevention. The possibility of the micropropagated root extracts to substitute the bark as a source material of pharmaceutical is especially promising and requires faster exploration (Komakech et al., 2022).

To conserve the species, population genetic research on contemporary molecular markers is necessary to determine genetic diversity and genetic flow between fragmented populations within the species range. Adaptive conservation planning will need predictive modelling of effects of climate change on species distribution, phenology, and bark phytochemistry. Lastly, socioeconomic studies that would have the levels of equitable allocation of value-chain advantages to local harvesting communities, and assess the viability of fair-trade supply chain frameworks are essential in aligning commercial and conservation drives.

XII. Conclusion

Prunus africana is a species with a phenomenal scientific, pharmacological, commercial, cultural and conservation value. Its bark is one of the most globally traded pharmacological commodities in Africa, and has a long history of pharmacological foundation to its efficacy of managing BPH due to a wide array of phytochemical profile that includes b-sitosterol, ursolic acid, ferulic acid esters, tannin, alkaloid and flavonoid. There is clinical evidence to support efficacy of LUTS/BPH but is limited due to the methodological limitations of the original trials in the literature. Emerging preclinical data is also quickly accumulating to make P. africana a promising source of anticancer phytochemicals, especially prostate cancer.

The management of medicinal plant resources around the world is a warning lesson to the conservation path of this species. CITES Appendix II was listed since 1995, but more than 40 years of international trade have not yet led to sustainable management of wild populations, and the CITES Review of Significant Trade initiated in 2023 exudates the urgency of the situation (CITES, 2023; Cunningham et al., 2016). Scientific community, the regulatory bodies, pharmaceutical industry and the local communities should all engage in switching the wild harvest to cultivated supply chains, instating a decent benefit-sharing system, and upholding the current regulatory frameworks. Technical instruments of this shift have already been developed in micropropagation (Komakech et al., 2022) and agroforestry domestication, now only the political and commercial will to do so is asked.

According to this review, a sustainable future of P. africana as an ecological resource and source of safe and effective medicines can only be achieved through further integration of scientific disciplines and

through a consistent interdisciplinary cooperation between scientists, conservationists, policy-makers, and people in its distribution range.

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