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Review Article

A REVIEW OF BOTANY, MEDICINAL USES, AND BIOLOGICAL ACTIVITIES OF *PENTANISIA PRUNELLOIDES (RUBIACEAE)*

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ABSTRACT

This study is aimed at providing a critical review of the botany, biological activities and medicinal uses of P. prunelloides. Documented information on botany, biological activities, and medicinal uses of *P. prunelloides* was collected from several online sources which included BMC, Scopus, SciFinder, Google Scholar, Science Direct, Elsevier, PubMed, and Web of Science. Additional information on the botany, biological activities, and medicinal uses of *P. prunelloides* was gathered from book chapters, books, journal articles, theses, and scientific publications sourced from the University of Fort Hare Library. The study showed that the leaves and roots of *P. prunelloides* are used as herbal medicines for bodily pains, burns, cancer, diabetes, fever, gastrointestinal problems, heartburn, heart problems, respiratory problems, retained placenta, rheumatism, sexually transmitted infections, skin infections, snakebite, sores, wounds, toothache, and vomiting. Pharmacological research revealed that P. prunelloides extracts have antibacterial, antimycobacterial, antifungal, antiviral, antidiabetic, anti-inflammatory, analgesic, antioxidant, uterotonic and cytotoxicity activities. Future studies should focus on evaluating the phytochemical, pharmacological, and toxicological activities of *P. prunelloides* crude extracts as well as chemical compounds isolated from the species.

Keywords: Herbal medicine, Indigenous pharmacopeia, *Pentanisia prunelloides*, Pharmacology, Phytochemistry, *Rubiaceae*.

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INTRODUCTION

Pentanisia prunelloides (Klotzsch ex Eckl. and Zeyh.) Walp. is a member of the Rubiaceae family and an important component of the grassland biome in south-central Africa. The fleshy, tuberous root is mainly used as herbal medicine, but sometimes also the leaves. The roots of *P. prunelloides* are ingredients of a herbal concoction referred to as "isihlambezo" consisting of *Agapanthus africanus* (L.) Hoffmans (roots), *Callilepis laureola* DC. (roots), *Clivia miniata* (Lindl.) Bosse (leaves), *Combretum erythrophyllum* (Burch.) Sond. (roots), Crinum spp. (bulb), *Gomphocarpus fruticosus* (L.) W.T. Aiton (roots), *Gunnera perpensa* L. (rhizomes), *Gymnanthemum corymbosum* (Thumb.) H. Rob. (roots), *Rhoicissus tridentata* (L.f.) Wild and R.B. Drumm. subsp. *cuneifolia* (Eckl. and Zeyh.) Urton (roots), *Scadoxus puniceus* (L.) Friis and Nordal (bulb), and *Typha capensis* (Rohrb.) N.E.Br. (rhizome) [1-4]. Isihlambezo is used to induce or augment labor, is used as a postnatal medication to expel afterbirth, is administered to animals to expel the placenta, and is also used in the treatment of endometritis [3,4]. The roots of *P. prunelloides* are ingredients of another herbal concoction known as "sejeso" (Ingwe® brand), made up of *Elephantorrhiza elephantina* (Burch.) Skeels, *Alepidea amatymbica* Eckl. and Zeyh., *Hypoxis obtusa* Burch. ex Ker Gawl., deionized water, and potassium sorbate as a preservative, which is used as a remedy for constipation, heartburn, indigestion, loss of appetite, stomach ailments, and vomiting [5-7]. Research by Famewo *et al*. [8,9] revealed that *P. prunelloides* is an ingredient of a polyherbal medicine mixed with *Centella eriantha* (A.Rich.) Drude (rhizome), *Hypoxis argentea* Harv. ex Baker (corm), *Kniphofia drepanophylla* Baker (root), *Rapanea melanophloeos* (L.) Mez (bark), and *Strychnos decussata* (Pappe) Gilg (bark) which is used as a herbal medicine for tuberculosis.

Due to the popularity of the species as a herbal medicine, the roots of *P. prunelloides* are sold in informal herbal medicine markets in the Eastern Cape [10,11], KwaZulu-Natal province [12], and Western Cape [11] provinces in South Africa. *P. prunelloides* is also one of the important medicinal plants in South Africa, included in the book "Medicinal Plants of South Africa," a photographic guide to the most commonly used plant medicines in the country, including their botany, main traditional uses, and active ingredients [13]. According to Arnold *et al*. [14] and Van Wyk [15,16], the roots and leaves of *P. prunelloides* have commercial potential as remedies for headache, pain, and wounds and act as a purgative in South Africa. Therefore, *P. prunelloides* is an integral part of traditional pharmacopoeia in South-Central Africa with potential contribution to primary health care of local communities in the region [17,18]. Therefore, this is the rationale behind the current study, aimed at providing a critical appraisal of the existing ethnomedicinal uses, phytochemistry, and biological activities of *P. prunelloides*.

DESCRIPTION AND TAXONOMY OF *P. PRUNELLOIDES*

The genus name *Pentanisia* is derived from the Greek word "penta" meaning five and "anisos" which means unequal, in reference to the calyx lobes. The specific epithet "*prunelloides*" means resembling members of the genus *Prunella* L. (*Lamiaceae* family) derived from the Latin word "prunus" which means purple [19]. *P. prunelloides* is divided into two subspecies, namely *P. prunelloides* subsp. *latifolia* (Hochst.) Verdc. and *P. prunelloides* subsp. *prunelloides* [20,21]. In South Africa, both subspecies have height ranging from 10 cm to 45 cm and have been recorded at an altitude ranging from 10 m to 2200 m above the sea level [21]. However, most ethnobotanical and ethnopharmacological literature do not separate *P. prunelloides* into specific subspecies, but rather *P. prunelloides sensu lato*, and this is the approach that has been adopted in the current review. Synonyms associated with *P. prunelloides* include *Diotocarpus prunelloides* (Klotzsch) Hochst., *P. variabilis* Harv. var. intermedia Sond., and *P. variabilis* Harv. var. *latifolia* (Hochst.) Sond. [20,21]. The species has been recorded in Lesotho, Malawi, Mozambique, South Africa, Swaziland, Tanzania, and Zambia [20,21].

P. prunelloides is a perennial herb of about 0.6 m in height and 0.6 m wide [13,22]. *P. prunelloides* is a multi-stemmed herb often trailing in the grass or erect. The leafy, hairy, stout, and spreading branches sprout from a thick and tuberous rootstock [13]. The leaves are without stalks, with waxy margins; are oblong in shape; are borne in pairs; are narrow; and are usually hairless. The tubular blue or lilac flowers are borne in heads on stalks above the leaves on the branch ends. *P. prunelloides* has

been recorded in well-drained sandy and loamy soils. *P. prunelloides* is long lived and dormant in the winter months [13]. The English common names of the species are wild verbena and broad-leaved pentanisia; other vernacular names include sooibrandbossie and wild verbena (Afrikaans), khatoane and setimamollo (Sotho), icikamlilo, icimamlilo, and icishamlilo (Xhosa), icimamlilo, icishamililo-elincane, incishamlilo, and umakuphole (Zulu) [13,19,22,23].

MEDICINAL USES OF *P. PRUNELLOIDES*

A wide range of medicinal uses of *P. prunelloides* have been reported in literature (Table 1). Its major uses have been reported in at least two countries and literature records include its treatment of bodily pains, burns, cancer, diabetes, fever, gastrointestinal problems, heartburn, heart problems, respiratory problems, retained placenta, rheumatism, sexually transmitted infections, skin infections, snakebite, sores, wounds, toothache, and vomiting. In South Africa, the roots of *P. prunelloides* are mixed with those of *Jatropha zeyheri* Sond. and *Warburgia salutaris* (Bertol.f.) Chiov. as herbal medicine for blisters, bruises, burns, and cuts [24,25]. The roots of *P. prunelloides* are mixed with those of *E. elephantina* as herbal medicine for eczema [7,24-27]. According to Bryant [28] and Hutchings *et al*. [23], the roots of *P. prunelloides* are mixed with those of *Withania somnifera* (L.) Dun. as herbal medicine for gangrenous rectitis. Research by Bisi-Johnson *et al*. [29] and Mpofu *et al*. [6] revealed that the roots of *P. prunelloides* are mixed with those of *Acokanthera oblongifolia* (Hochst.) Codd and *E. elephantina* as remedy for stomach ailments. The roots of *P. prunelloides* are mixed with those of *Dicoma anomala* Sond. [24-26,30,31] or are mixed with roots of *D. anomala* and bulbs of *Hypoxis colchicifolia* Baker [24,25,27] as remedy for insect and sting bites. According to Masika and Afolayan [32], the leaves of *P. prunelloides* are mixed with those of *Cannabis sativa* L. and glycerin as ethnoveterinary medicine for conjunctivitis and retained placenta.

CHEMISTRY AND PHYTOCHEMISTRY OF *P. PRUNELLOIDES*

Mtunzi *et al*. [79] quantified heavy metals in *P. prunelloides* roots, with copper showing the highest concentration of 0.6 ppm, followed by manganese (0.5 ppm), lead and nickel (0.1 ppm each), and iron (0.008 ppm). The concentrations of the trace elements in *P. prunelloides* roots were below the permissible limits set by Codex Alimentarius Commission [80] and, therefore, Mtunzi *et al*. [79] concluded that the species extracts used as herbal medicines may not result in heavy metal toxicity. Phytochemical compounds that have been identified from the leaves and roots of *P. prunelloides* include alkaloids, anthocyanidins, anthraquinones, cardiac glycosides, flavonoids, glucose, saponins, steroids, sucrose, tannins, and terpenoids [6,31,44,62,81-84]. Other phytochemical compounds that have been identified from the leaves and roots of *P. prunelloides* include alanine, allo-isoleucine, α-aminobutyric acid, arabinose, asparagine, aspartic acid, diosgenin, (-)-epicatechin, epicatechin gallate, epigallocatechin gallate, glucuronic acid, hexoses, kaempferol, oleanolic acid, palmitic acid, quercetin, rhamnose, serine, tormentic acid, and valine [6,42,44,47,62,82,84,85]. Nair *et al*. [5] identified a common plasticizer, di(2-ethylhexyl) phthalate (DEHP), in a herbal mixture known as "sejeso" (ingwe® brand) which also includes the roots of *P. prunelloides* mixed with *A. amatymbica*, *E. elephantina*, *H. obtusa*, deionized water, and potassium sorbate as preservative. DEHP is highly toxic, and there are strict international controls in place for regulation of its consumption, and the amount of 43.3 mg/L from the mixture is unacceptably high [5].

BIOLOGICAL ACTIVITIES OF *P. PRUNELLOIDES*

The following biological activities have been reported from the leaf and root extracts of *P. prunelloides*: antibacterial [25,30,31,42,47,60,61,65,86-89], antimycobacterial [8,61,90,91], antifungal [25,30,31,87-89], antiviral [42], antidiabetic [84], anti-inflammatory [31,42,43,61,83,87,88,90,92], analgesic [83], antioxidant [6,31,43,62,84,87,87], uterotonic [2,92], and cytotoxicity [6,62] activities.

Antibacterial activities

Yff *et al*. [42] evaluated the antibacterial activities of aqueous, ethanolic, and ethyl acetate extracts of the leaves and roots of *P. prunelloides* against *Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus,* using the serial dilution technique with neomycin as the positive control. The extracts exhibited activities with minimum lethal concentration values, ranging from 0.4 mg/ml to 12.5 mg/ml against 0.4 µg/ml to 3.1 µg/ml exhibited by the control [42]. Jäger [86] evaluated the antibacterial activities of aqueous ethyl acetate root extracts of *P. prunelloides* against *S. aureus* and *B. subtilis* using the microtiter plate assay with neomycin as positive control. The extract exhibited activities with minimum inhibitory concentration (MIC) value of >1.0 mg/ml and >2.0 mg/ml against 1.6 µg/ml and 3.1 µg/ml exhibited by the control [86]. Mabona [25] and Mabona *et al*. [30] evaluated the antibacterial activities of aqueous and dichlomethane: methanol (1:1) root and root bark extracts of *P. prunelloides* using the microtiter plate assay against dermatologically relevant pathogens such as *Brevibacillus* agri, *Propionibacterium acnes*, *Pseudomonas aeruginosa*, *S. aureus*, and *S. epidermidis* with ciprofloxacin as a positive control. The extracts exhibited activities with MIC values ranging from 1.0 mg/ml to >16.00 mg/ml. Mabona *et al*. [30] also evaluated the interactive antibacterial activities of *P. prunelloides* root mixed with *E. elephantine* rhizome; *P. prunelloides* root and root bark mixed with *D. anomala* tuber against *P. aeruginosa*, *S. aureus*, and *S. epidermidis.* These combinations produced synergistic effects with MIC values from 0.5 mg/ml to >16.00 mg/ml, with the sum of the ∑fractional inhibitory concentration (∑FIC) values ranging from 0.3 to 4.0 [25,30]. Madikizela *et al*. [60] and Madikizela [61] evaluated the antibacterial activities of dichloromethane, petroleum ether, ethanol, and water extracts of leaves and roots of *P. prunelloides* against *K. pneumoniae*, *S. aureus*, and *Mycobacterium aurum* using the microdilution assay with neomycin and streptomycin as positive controls. The extracts exhibited activities with MIC values ranging from 0.2 mg/ml to 12.5 mg/ml, with the positive controls exhibiting MIC values ranging from 0.05 mg/ml to 0.2 mg/ml [60,61]. Mpofu *et al*. [6] evaluated the antibacterial activities of the methanol and aqueous root extracts of *P. prunelloides* using the microtiter assay against *Bacillus cereus*, *Enterococcus faecalis*, and *E. coli* with ciprofloxacin as a positive control. The extracts exhibited activities with MIC values ranging from 0.4 mg/mL to 16.0 mg/mL. Mpofu *et al*. [6] also evaluated the antibacterial activities of *P. prunelloides* combined with *E. elephantina* in 1:1 ratio which exhibited activities ranging from 0.2 mg/mL to 4.0 mg/mL, displaying synergistic interactions with sum of the values ranging from 0.2 to 1.0 against *B. cereus*, *E. faecalis*, and *E. coli*. Mpofu *et al*. [6] also evaluated the antibacterial activities of (-)-epicatechin and palmitic acid isolated from *P. prunelloides* roots using the microtiter plate dilution technique against *B. cereus*, *E. faecalis*, and *E. coli* with ciprofloxacin as a positive control. The compounds exhibited activities with MIC values ranging from 0.1 mg/mL to 0.6 mg/mL, whereas combination of the two compounds exhibited activities with MIC values ranging from 0.2 mg/mL to 4.0 mg/mL; synergistic interactions were noted against *E. coli* and *E. faecalis* with ΣFIC values of 0.1 and 0.50, respectively [6]. Mugomeri *et al.* [63] used the checkerboard microdilution technique to determine the efficacy of mixing (-)-epicatechin and palmitic acid or any of these two compounds with *P. prunelloides* against *B. cereus*, *S. aureus*, *E. coli*, *K. pneumonia*, and *E. faecalis.* The results demonstrated that the combinations resulted in either additive or synergistic effects, but no antagonistic interactions were observed [65]. Muleya [87] and Muleya *et al*. [88] evaluated the antibacterial activities of crude, hexane, dichloromethane, ethyl acetate, acetone, and methanol root extracts of *P. prunelloides* against *S. aureus*, *E. coli*, *E. faecalis*, and *P. aeruginosa* using serial dilution assay. The extracts exhibited activities with MIC values ranging from 150.0 µg/ml to 650.0 µg/ml [87,88]. Xaba [31] and Xaba and Buwa [89] evaluated the antibacterial activities of methanol, ethanol, acetone, and aqueous root extracts of *P. prunelloides* against *P. aeruginosa*, *Bacillus pumilus*, *S. aureus*, *E. coli*, and *K. pneumonia* using microplate dilution assay. The extracts exhibited activities with MIC values ranging between 0.1 mg/ml and 6.3 mg/ml [31,89].

Table 1: Medicinal uses of *Pentanisia prunelloides*

Medicinal use	Parts of the plant used	Country	References
Blisters, bruises, burns, and cuts	Roots mixed with those of *Jatropha zeyheri* and *Warburgia salutaris*	South Africa	[24,25]
Bodily pains	Roots	South Africa and Swaziland	[33-36]
Burns	Leaves and roots	Lesotho and South Africa	[13,23,25,27,30,31,37-53]
Breast cancer and internal tumors	Leaves and roots	Lesotho and South Africa	[13,37-39,41,45,47,52,54-56]
Constipation	Roots	Lesotho and South Africa	[3,23,35,38,40,45,57,58]
Diabetes	Leaves and roots	Lesotho and South Africa	[35,52,54]
Dysmenorrhea	Roots	South Africa	[34,58]
Eczema	Roots mixed with those of *Elephantorrhiza elephantina*	South Africa	[7,24-27]
Emetic	Roots	Lesotho	[45]
Fever	Roots	Lesotho and South Africa	[6,13,23,34,37,38,44-46,49,50,53,60-63]
Gangrenous rectitis	Roots mixed with those of *Withania somnifera*	South Africa	[23,28]
Gastrointestinal problems (diarrhea, dysentery, and stomach problems)	Leaves and roots	Lesotho and South Africa	[6,23,29,34,36,38,40,44,45,49,62,6465]
Stomach ailments	Roots mixed with those of *Acokanthera oblongifolia* and *Elephantorrhiza elephantina*	South Africa	[6,29]
Hemorrhoids	Leaves and roots	South Africa	[6,13,23,28,34,44,47,49,50,62,65,66]
Heartburn and heart problems	Leaves and roots	Lesotho and South Africa	[6,13,34,37,44-46,49,50,53,54,62,65]
High blood pressure	Leaves and roots	Lesotho	[54]
Immune booster	Bulb	Swaziland	[67]
Insect and sting bites	Roots mixed with those of *Dicoma anomala*	South Africa	[24,25,27,30,31]
Insect and sting bites	Roots mixed with those of *Dicoma anomala* and bulbs of *Hypoxis colchicifolia*	South Africa	[24,25,27]
Liver problems	Leaves and roots	Lesotho	[54]
Magical (good luck, protection)	Roots	Lesotho and South Africa	[23,38,39,45,52,68,69]
Respiratory problems (chest pains, colds, cough, influenza, and tuberculosis)	Leaves and roots	Lesotho and South Africa	[6,13,23,26,37,38,42,44-47,49,50,54,60,62,65,70]
Retained placenta	Leaves and roots	Lesotho and South Africa	[2,13,23,37-39,41,45,50,54,55,71,72]
Rheumatism, swollen and aching foot	Leaves and roots	Lesotho, South Africa, and Swaziland	[6,13,23,25,28-31,35,37,42-44,46,47,49,50,53,62,65,66,69,73,74]
Schizophrenia	Roots	South Africa	[35]
Sexually transmitted infections	Leaves and roots	Lesotho and South Africa	[23,38,44,45,47,75]
Skin infections (boils, itching, infection, inflammation, pimples, rash, and shingles)	Leaves and roots	Lesotho and South Africa	[3,6,13,23,27,31,36-42,45,47,48,50-52,56,62,65,68]
Snakebite	Leaves and roots	Lesotho and South Africa	[13,23,28,44,46,47,49,50,53,66,74]
Sores and wounds	Roots	Lesotho and South Africa	[13,22,23,36-41,44,45,50,51,56,76]
Tonic	Roots	South Africa and Swaziland	[36,73]
Toothache	Roots	Lesotho and South Africa	[13,44,46,47,49,50,53,60,61]
Ulcers	Roots	Lesotho	[6,38,45,47,62,65]
Vomiting	Leaves and roots	Lesotho and South Africa	[13,29,44,46,49,50]
Ethnoveterinary medicine			
Abortion in goats	Roots	South Africa	[77]
Conjunctivitis	Leaves mixed with leaves of *Cannabis sativa* and glycerin	South Africa	[32]
Cough	Leaves	South Africa	[78]
Retained placenta	Leaves mixed with leaves of *Cannabis sativa* and glycerin	South Africa	[32]
Retained placenta	Roots	South Africa	[2,22,37,72]

Antimycobacterial activities

Madikizela [61] and Madikizela *et al*. [90] evaluated the antimycobacterial activities of dichloromethane, petroleum ether, ethanol, water, leaf, root, and whole plant part extracts of *P. prunelloides* using resazurin microplate assay against *Mycobacterium tuberculosis* with rifampicin as a positive control. The extracts exhibited activities with MIC values ranging from 0.8 mg/ml to 12.5 mg/ml which were higher than 0.02 mg/ml exhibited by the positive control [61,90]. Lehasa *et al*. [91] evaluated the antimycobacterial activities of aqueous and ethanol root extracts of *P. prunelloides* against *M. tuberculosis*. The extract exhibited activities with MIC values ranging between 0.8 mg/ml and 0.2 mg/ml [91]. Famewo *et al*. [8] evaluated the antimycobacterial activities of ethanol herbal mixture of *P. prunelloides* with *C. eriantha*, *H. argentea*, *K. drepanophylla*, *R. melanophloeos*, and *S. decussata* against *M. tuberculosis* with isoniazid (0.05 µg/ml) as a positive control. The mixture showed activities at concentrations below 25 µg/ml and exhibited MIC value of 1.6 µg/ml, while the positive control exhibited MIC value of 0.05 µg/ml [8].

Antifungal activities

Mabona [25] and Mabona *et al*. [30] evaluated the antifungal activities of aqueous and dichloromethane:methanol (1:1) root and root bark extracts

of *P. prunelloides* using the microtiter assay against dermatologically relevant pathogens such as *Candida albicans*, *Microsporum canis*, and *Trichophyton mentagrophytes* with amphotericin B as a positive control. The extracts exhibited activities with MIC values ranging from 2.0 mg/ml to >16.00 mg/ml. Mabona *et al*. [30] also evaluated the interactive antifungal activities of *P. prunelloides* root mixed with *E. elephantina* rhizome; *P. prunelloides* root and root bark mixed with *D. anomala* tuber against *C. albicans*. These combinations produced synergistic effects with MIC values of 2.0 mg/ml to 16.00 mg/ml and ∑FIC values ranging from 0.3 to 3.0 [25,30]. Muleya [87] and Muleya *et al*. [88] evaluated the antifungal activities of acetone root extracts of *P. prunelloides* against *C. albicans* and *Aspergillus fumigatus* using serial dilution assay. The extracts exhibited activities with MIC value of 625.0 µg/ml [87,88]. Xaba [31] and Xaba and Buwa [89] evaluated the antifungal activities of methanol, ethanol, acetone, and aqueous root extracts of *P. prunelloides* against *C. albicans* and *Trichophyton mucoides* using microplate dilution assay. The extracts exhibited activities with an MIC value of 0.5 mg/ml [31,89].

Antiviral activities

Yff *et al*. [42] evaluated the antiviral activities of aqueous extracts of leaves and roots of *P. prunelloides* using antiviral assays aimed at assessing replication or inhibition of 1000 $TCID_{50}$ influenza A as a percentage reduction in the number of fluorescent foci on the infected VK cell cultures. The extracts inhibited viral replication of the influenza A virus [42].

Antidiabetic activities

Makhudu [84] evaluated the antidiabetic activities of the water, ethanol, aqueous-ethanol, and hexane root extracts of *P. prunelloides* and tormentic acid isolated from the species against the activities of α-amylase, α-glucosidase, sucrose, and maltase with acarbose as a positive control. The extracts exhibited activities with half-maximal inhibitory concentration (IC_{50}) values ranging from 0.5 µg/mL to 90.5 µg/mL, while the positive control exhibited IC_{50} values of 9.9 µg/mL to 129.4 µg/mL. The tormentic acid inhibited α-amylase and α-glucosidase at 70.5 µg/mL and 28.2 µg/mL, respectively [84].

Anti-inflammatory activities

Lindsey *et al*. [92] evaluated the aqueous and ethanol leaf and root extracts of *P. prunelloides* for prostaglandin synthesis inhibitors using the cyclooxygenase inhibitory bioassay with indomethacin as the positive control. The aqueous and ethanol leaf extracts inhibited cyclooxygenase at 71%–87%, which was higher than 67% inhibition exhibited by the standard, indomethacin [92]. Yff *et al*. [42] evaluated the anti-inflammatory activities of aqueous, ethanolic, and ethyl acetate extracts of leaves and roots of *P. prunelloides* using the cyclooxygenase-1 assay with indomethacin (20 µM) as a positive control. The extracts exhibited activities with percentage inhibition of cyclooxygenase ranging from 65% to 87%, which was comparable to 83% exhibited by the control [42]. Frum and Viljoen [43] and Lehasa *et al* [91] evaluated the anti-inflammatory activities of aqueous and methanol root extracts of *P. prunelloides* through the assessment of 5-lipoxygenase inhibitory activities using a threefold step-wise dilution method with dimethyl sulfoxide and Tween®20 as negative controls and nordihydroguaiaretic acid as a positive control. The methanol extract exhibited 5-lipoxygenase inhibitory activities with IC_{50} value of 32.7 ppm [43]. Madikizela [61] and Madikizela *et al*. [90] evaluated the anti-inflammatory activities of dichloromethane, petroleum ether, ethanol, water, leaf, root, and whole plant part extracts of *P. prunelloides* using the cyclooxygenase-2 (COX-2) inhibition assay with indomethacin as a positive control. The highest COX-2 inhibition was exhibited by petroleum ether against the root extract at 86.9% [61,90]. Muleya [87] and Muleya *et al*. [88] evaluated the anti-inflammatory activities of acetone root extracts of *P. prunelloides* against 15-soybean lipoxygenase enzyme. The lipoxygenase inhibitory activity of 79% indicates high anti-inflammatory activity [87,88]. Mathews *et al*. [83] evaluated the anti-inflammatory activities of leaf and root aqueous extracts of *P. prunelloides* on egg albumin-induced rat paw edema model, with aspirin used as a standard drug. The extracts exhibited dose-dependent anti-inflammatory effects [83]. Xaba [31] evaluated the anti-inflammatory activities of aqueous, acetone, ethanol, and methanol root extracts of *P. prunelloides* using the 5-lipoxygenase enzyme (Cayman) assay with nordihydroguaiaretic acid as a positive control. The extracts exhibited activities with IC_{50} values ranging from 0.2 µg/ml and 0.4 µg/ml, which was comparable to IC_{50} value of 0.6 µg/ml exhibited by the control [31].

Analgesic activities

Mathews *et al*. [83] evaluated the analgesic activities of leaf and root aqueous extracts of *P. prunelloides* in mice using formalin- and acetic acid-induced writhing tests. The extracts significantly reduced paw lickings in the mice compared to vehicle in the neurogenic and formalin-induced nociception phases, indicating significant analgesic activities [83].

Antioxidant activities

Frum and Viljoen [43] evaluated the antioxidant activities of aqueous and methanol root extracts of *P. prunelloides* using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging assay. The aqueous and methanol extracts exhibited activities with IC_{50} values of 38.0 ppm and 11.8 ppm, respectively [43]. Mpofu [62] and Mpofu *et al*. [6] evaluated the antioxidant activities of methanol and aqueous extracts of roots of *P. prunelloides* using DPPH free radical scavenging assay with ascorbic acid and (-)-epicatechin as positive controls. The extracts exhibited activities with the Yen and Duh percentage inhibition values ranging from 4.5% to 33%, while ascorbic acid and (-)-epicatechin showed inhibition of 67.5% and 68.0%, respectively [6,62]. Muleya [87] and Muleya *et al*. [88] evaluated the antioxidant activities of crude, hexane, dichloromethane, ethyl acetate, acetone, and methanol root extracts of *P. prunelloides* using 2,2´-azinobis (3-ethylbenzothiazoline)-6-sulfonic acid and DPPH radicals with trolox as a positive control. The extracts exhibited activities with half-maximal effective concentration (EC_{50}) values ranging from 4.1 µg/ml to 111.9 µg/ml against DPPH and EC_{50} values ranging from 0.1 µg/ml to 3987.3 µg/ml [87,88]. Xaba [31] evaluated the antioxidant activities of acetone, aqueous, ethanol, and methanol root extracts of *P. prunelloides* using DPPH free radical scavenging and the phosphomolybdate assays. The extracts exhibited activities with IC_{50} values ranging from 0.3 µg/ml to 0.4 µg/ml against DPPH and IC_{50} values of 0.03 µg/ml to 1.0 µg/ml against phosphomolybdate assay [31]. Makhudu [84] evaluated the antioxidant activities of water, ethanol, aqueous-ethanol, and hexane root extracts of *P. prunelloides* using iron chelation, DPPH, and hydroxyl and superoxide anion radical scavenging assays with gallic acid as a positive control. The extracts exhibited activities with IC_{50} values of 75.4 µg/mL to 142.7 µg/mL against DPPH, superoxide (0.3 µg/mL to 118.7 µg/mL), hydroxyl (0.5 µg/mL to 43.0 µg/mL), iron chelation (4.2 µg/mL to 64.9 µg/mL), and gallic acid (34.0 µg/mL to 101.7 µg/mL) [84].

Uterotonic activities

Kaido *et al*. [2] investigated the uterotonic activities of the crude decoction of *P. prunelloides* on the isolated rat uterus and ileum preparation. The aqueous extract of *P. prunelloides* initiated contractions in the isolated rat uterus, showed direct smooth muscle activity on the uterus and ileum preparations, and potentiated the initial response of the uterus to oxytocin [2]. Lindsey *et al*. [92] evaluated the uterine-relaxing activities of ethanol leaf and root extracts of *P. prunelloides* using *in vitro* uterine bioassay. The extracts caused mild contraction of the relaxed uterine muscles [92].

Cytotoxicity activities

Mpofu *et al*. [6] and Mpofu [62] evaluated the cytotoxic activities of the aqueous and methanol root extracts of *P. prunelloides* using the brine shrimp lethality test. The aqueous and methanol extracts exhibited moderate cytotoxicity with median lethal dose values of 3.2 and 5.6 ppm, respectively [6,62].

CONCLUSION

P. prunelloides is a well-known plant species in South-Central Africa in traditional and folk medicine which is an important part of indigenous

culture in the region. In many cases, the roots and, sometimes, the leaves are used to manage and treat several human diseases. Detailed phytochemical evaluations are lacking although alkaloids, anthocyanidins, anthraquinones, cardiac glycosides, flavonoids, glucose, saponins, steroids, sucrose, tannins, terpenoids, alanine, allo-isoleucine, α-aminobutyric acid, arabinose, asparagine, aspartic acid, diosgenin, (-)-epicatechin, epicatechin gallate, epigallocatechin gallate, glucuronic acid, hexoses, kaempferol, oleanolic acid, palmitic acid, quercetin, rhamnose, serine, tormentic acid, and valine have been identified from the species. Studies focusing on the biological activities of *P. prunelloides* crude extracts have been conducted *in vitro*. Not much data are available on the biological activities of compounds isolated from the species and toxicity of *P. prunelloides* crude extracts and chemical ingredients isolated from the species. Therefore, there is a need for further studies focusing on the phytochemistry, pharmacological, toxicological, and *in vivo* studies involving the crude extracts and chemical ingredients isolated from the species.

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AUTHORS' CONTRIBUTIONS

The author declares that this work was done by the author named in this article.

CONFLICT OF INTEREST

The author declares that he has no conflict of interest.

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