Review Article

Potential of extracts and piperidine alkaloids from *Prosopis* spp. to the control of plant pests and diseases

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ABSTRACT

The genus *Prosopis* comprises 44 species of spiny small trees adapted to arid and semiarid regions of the planet that have been used by human populations as a source of wood, food and medicine. *Prosopis* spp. possess high quantities of phenolic compounds and piperidine alkaloids with antioxidant, neurotoxical, antimicrobial, antimalarial, insecticidal and allelopathic activities. Juliprosopine **(1)** is the major and more characterized piperidine alkaloid present in the genus *Prosopis*. In this review we present the potential of *Prosopis* spp. extracts and piperidine alkaloids for the control of plant pests and diseases and discuss the possibility of their use as an alternative in the organic agriculture.

Keywords: Prosopis spp. extracts; piperidine alkaloids; phytopathogen; plant diseases.

1. INTRODUCTION

Since agriculture emerged, weeds, insects, and microorganisms, which co-evolved with plants in the ecosystem, have turned out in plant pests and diseases. The ability of pathogenic microorganism to colonize the host have increased with the domestication, and systematic-extensive monoculture of plants. Today, these pests and diseases have become a threat to our-food-production safety. This due to the natural phenomena of resistance present in weeds [1], insects [2], bacteria [3], and fungi [4] as a consequence of the indiscriminate application of bactericides, fungicides and pesticides agents (frequently mixed and applied together) in crops over time [5, 6]. All these practices have conducted to the creation of global programs oriented to reducing and making rational use of synthetic biocides in plant pests and diseases control, such as the Integrated Pest Management (IPM, FAO), the International Plant Protection Convention (IPPC, FAO) and the Fungicide Resistance Action Committee (FRAC).

Natural products emerge as an alternative to the control of insects and phytopathogenic microorganisms with minimal residuality and low environmental impact [7]. In addition, natural biocides appear as the main option in the growing organic agriculture market (USDA Organic). According to the Research Institute of Organic Agriculture (FiBL), 71.5 million hectares were organically managed in 2018, and the offer for biopesticides is increasing every year (OMRI). In this respect, plants represent a vast source of new compounds with biocidal properties due to they have an extraordinary ability of synthetizing organic molecules to cope with phytopathogens [5, 8].

This review provides a summary of the available biological activities of the extracts of *Prosopis* spp., such as antibacterial, antifungal, insecticide and allelopathic activity, as well as information about the bioactive compounds that have been identified in the genus.

2. CHARACTERISTICS FEATURES OF PROSOPIS SPP.

The genus *Prosopis* belongs to the family Leguminoseae (Fabaceae), subfamily Mimosaceae, and is composed of 44 species usually distributed in arid, tropical and subtropical regions from Asia, Africa, and the Americas [9, 10, 11]. Members of *Prosopis* spp. have been used with different purposes such as; wood as a source of fuel; the pods as a source of carbohydrates and protein for livestock and human populations, and the leaves, seeds, and gum as a medicinal source [12, 13, 14]. Ecologically, *Prosopis* spp. are ever green xerophyte trees or shrubs well adapted to arid zones that spread and multiply easily, and they might become invasive species in the places where they are introduced if not properly controlled [15, 16]. *P. juliflora* is the most studied species from a pharmacological ad phytochemical point of view. Its alkaloids display a wide range of biological activities [17, 15, 18, 19, 20]. Nevertheless, the emphasis on *Prosopis* spp. extracts as a potential source of biopesticides has not been recently reviewed. Piperidine alkaloids have also been identified in leaves, pods, roots, and flowers of others *Prosopis* species, such as *P. glandulosa* [21, 22] *P. ruscifolia* [23], *P. africana* [24], *P. affinis* [11], *P. alpataco*, *P. argentina*, *P. chilensis*, *P. flexuosa* and *P. pugionata* [9]. Two kinds of piperidine alkaloids could be found in *Prosopis* spp. based on presence or absence of an indolizidine ring in their structures.

2.1 *Prosopis juliflora*

Prosopis juliflora is an evergreen shrub or tree commonly called “mesquite” o “algarroba”, originally from America and nowadays introduced and widespread in many countries around the world. *P. juliflora* is an important species in semi-desert areas, playing an important role as shelter, improving soils via nitrogen fixation, increasing organic matter via leaf litter addition, changing soil structure and microbial populations. Its flowers produce a large amount of pollen as such as they are highly melliferous [12, 25, 26]. For humans, it is used as a revegetation species [27], as a source of wood for fuel and construction [28] and the pods are used as cattle food [29]. In the countries where *P. juliflora* is introduced, it can become an insidious species [17, 16] due to the allelochemicals present in the different tissues that can change the native ecosystem structure [14]. In traditional medicine, the leaves and bark have been employed to treat cold, sore throat, inflammation, digestive problems, skincare and wound healing [30, 31, 32]. Its extracts displayed antioxidant [26, 33, 31], antimalarial [34], antibacterial [35, 36, 37], antifungal [38, 30], antimites [39], and herbicidal [40] activities. Also, the pharmacological properties of its extracts, alkaloid fractions and compounds have been extensively reviewed [41, 42, 13, 14, 43].

2.2 *Prosopis africana*

P. africana, commonly known as African mesquite, is the only *Prosopis* species that grows in the African continent. It is a small to large tree with thornless twigs and a fast-growing root system [44]. The pods and leaves have been used as a source of animal food due to their high protein content; the wood, as a source of charcoal, construction poles, and wooden tools; and the roots and bark as a source of medicine for human ailments, such as toothache, [45, 46, 20], gingivitis and periodontal disease treatment [24], as well as wound healing [47]. Ecologically is an important soil fixing nitrogen plant [46]. The stem, bark and root extracts have shown several biological activities, such as antibacterial, antifungal [24, 47, 48] and antimalarial activity [44]. Some studies have described the presence of alkaloids and phenolic compounds in this species [24, 49].

Unlike other *Prosopis* species, *P. africana* has a low germination rate of seeds and low fruit production [45]. Its use has been so extensive, that in some regions of Africa it is a threatened species.

2.3 *Prosopis glandulosa*

Prosopis glandulosa, popularly known as honey mesquite, is a medium sized tree with spiny branches native from the north of Mexico to the south of EE.UU [50]. *P. glandulosa* has been employed as firewood and in the traditional medicine for eye infections, open woods, dermatological and stomach ailments. There exist two varieties of *P. glandulosa*; var. *glandulosa* and var. *torreyana*. The former is present in the more humid areas toward Gulf of Mexico and the latter prefers the drier climate near the Pacific. Anatomically, *P. glandulosa* var. *glandulosa* present larger leaves than var. *torreyana* and there exist thorny populations of *P. glandulosa* var. *glandulosa* that can be classified as var. *prostrata* [10]. The polar extracts (ethanolic and aqueous) of the leaves have displayed antifungal activity and the alkaloid rich fraction derived of the extracts recorded higher activity [50, 21, 22]. Besides, the aqueous extract has been used to generate silver nanoparticles with antibacterial and antifungal activity [51, 52].

2.4 *Prosopis ruscifolia*

Prosopis ruscifolia, also known as “vinal” in South America, is a thorny tree native to northern Argentina [23]. The methanolic bark extract exhibits antibacterial activity against *Staphylococcus aureus* (ATCC 8095 and INEI 2213), *Enterococcus faecium* (INEI2464), *Klebsiella pneumoniae* (ATCC 10031) [53] and the methanolic leaf extract shows antifungal activity. The antifungal components were identified as juliflorine (**1**), prosoflorine (**4**), cyclitol and a triterpene saponin [54, 55]. Indolizidine alkaloids have been detected in situ in the cuticle and palisade mesophylls of the leaflets, as well as in petiole and rachis parenchyma. On the other hand, in pods, are present in the cuticle, epidermal cells, mesocarp parenchyma cells and the phloem [23].

3. PROSOPIS SPP. CHEMICAL CONSTITUENTS

3.1 Stem bark

Characterization of the bark extracts from *P. juliflora* have revealed the presence of high content of flavonoids, as 4’-O-methyl-gallocatechin, (+)-catechins and (-)-mezquitol, the latter is the most abundant [56, 57]. Also, the 7,3’,4’-trihydroxy-3-methoxyflavanone was identified in the *P. africana* bark [49]. Additionally, *Prosopis* spp. bark contains alkylated piperidine alkaloids (Fig. 1). [58] isolated the N-methylcassine (**12**) from methanolic bark extract of *P. nigra*, *P. ruscifolia and P. vinalillo* through an acid-base extraction followed of preparative Thin Layer Chromatography (TLC). Besides, [11] isolated by first time and structurally characterized the N-methyl-2-isocassine (**12b**), N-methyl-6-isocassine (**12c**), and N-methyl-6-isocarnavaline (**13**) from *P. affinis* bark, using mass spectrometry (MS), infra-red (IR) and nuclear magnetic resonance (NMR) data. In addition, juliprosopine (**1**) and juliprosine (**2**) have been found in *P. flexuosa* exudate [9].

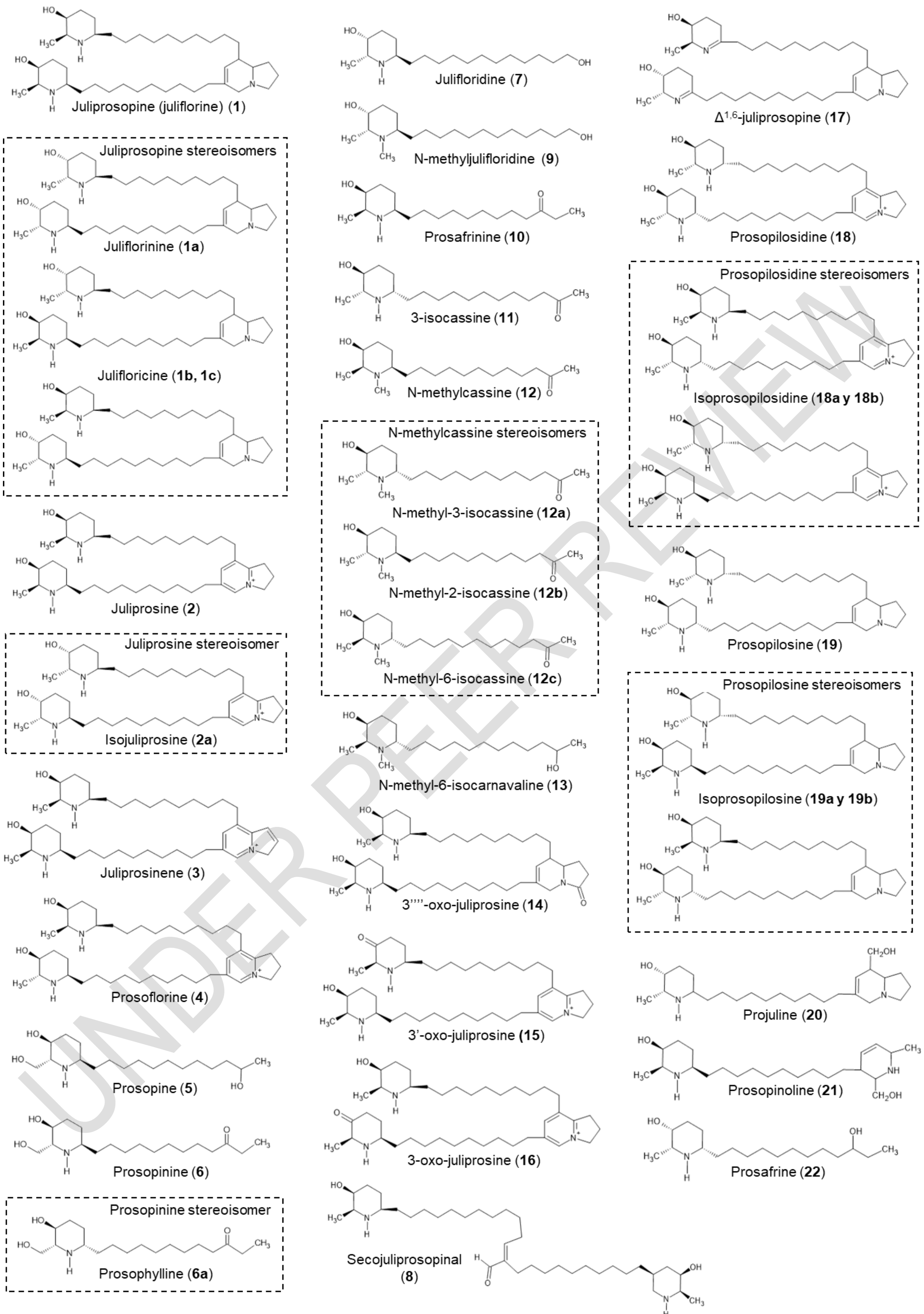

Fig. 1. Piperidine alkaloids from *Prosopis* spp.

3.2 Flowers and Pollen

The flowers of *Prosopis* spp. are highly melliferous since they produce an enormous pollen quantity. Phytochemical studies using Dragendorff’s reagent and direct analysis in real time (DART)-MS of ethanolic flower extract from *P. juliflora*, showed the presence of the alkaloids juliflоridine (**7**), prosopine (**5**), prosopinine (**6**) and prosafrinine (**10**) (Fig.1) [59]. Also, a wide variety of phenolic compounds have been detected in the hydroethanolic pollen extract, such as apigenine, luteolin and cinnamic acid derivatives, as well as flavonol, quercetin and genistein glycosides [26], making *P. juliflora* pollen an interesting source of natural antioxidant compounds and alkaloids.

3.3 Root

[21] identified the alkaloids 3-isocassine (**11**), N-methyl-3-isocassine (**12a**) and N-methylcassine (**12**) from the ethanolic root bark extract of *P. glandulosa* var. *torreyana* using IR spectra and 1H- 13C NMR (Fig. 1). Also, alkaloids have been detected in the methanolic, ethanolic and aqueous root extract of *P. africana* with Dragendorff’s, Mayer’s and Wagner’s reagents [44, 24].

3.4 Leaves

Most of the phytochemical studies have been carried out in the aerial parts of *Prosopis* spp. In *P. juliflora* leaves extracts have been detected alkaloids, flavonoids, tannins, saponins, anthraquinones, and coumarins [60, 41, 33, 61, 31, 62, 37, 43]. Similarly compounds that are present in the leaves are also present in the *P. juliflora* spines. [32] reported the presence of flavonoids, saponins, glycosides, terpenoids and coumarins in the aqueous and ethanolic thorn extracts by colorimetric methods, and alkaloids were found only in the aqueous extract. Studies of the relative abundance reveal that flavonoids (16%), pectin substances (4.9%) and alkaloids (3.6%) are the three main compounds in *P. juliflora* leaves [41].

Alkaloids have been found in *P. alba* [63], *P. laevigata* [64], *P. glandulosa* [22], *P. ruscifolia* [23], *P. alpataco*, *P. argentina*, *P. chilensis*, *P. flexuosa* and *P. pugionata* [9]. *Prosopis* spp. alkaloids have attracted more research interest that all other secondary metabolites detected in *Prosopis* spp. leaves due to their pharmacological and biological activities [41].

Characterization of *P. juliflora* leaf alkaloids through spectroscopic and spectrometric techniques has been carried out. The analysis of MS, IR as well as 1H and 13C NMR spectra revealed the structure of juliflorine (juliprosopine) (**1**) and their stereoisomers juliflorinine (**1a**) and julifloricine (**1b**; **1c**), as well as the jullifloridine (**7**) and the juliprosinene (**3**) [65, 66]. Using the same techniques, [67] elucidated the juliprosine (**2**) and the isojuliprosine (**2a**) structures. Later, [68] reported the structures of secojuliprosopinal (8), 3’’’’-oxo-juliprosopine (**14**), 3-oxo-juliprosine (**15**) 3’-oxo-juliprosine (**16**) using Electrospray ionization (ESI)-MS and 1H-13C NMR and julifloravizole was described by 1H-13C NMR correlations [69]. In recent years, [35] and [59, 70] identified the alkaloids prosoflorine (**4**), prosopine (**5**), prosopinine (**6**), projuline (**20**), prosafrinine (**10**) and N-methyl julifloridine (**9**) with DART-MS. The juliprosopine (**1**) was also identified in the aerial parts of *P. pugionata* using NMR and MS techniques [9]. [22] isolated and identified by IR, ESI-HRMS and 1H-13C NMR the prosopilosidine (**18**) and their stereoisomers isoprosopilosidine (**18a**, **18b**) as well as the prosopilosine (**19**) and their stereoisomers isoprosopilosine (**19a**, **19b**), all compounds from the ethanolic leaf extract of *P. glandulosa* var. *glandulosa*. Tryptamine and juliprosopine (**1**) were also present, the latter is the representative alkaloid of the genus *Prosopis* [21]. In addition, the alkaloids prosopine (**5**), prosopinine (**6**) and its stereoisomer prosophylline (**6a**), prosafrinine (**10**) and prosafrine (**20**) were isolated from *P. africana* leaves (Fig. 1) [71].

3.5 Pods

The *Prosopis* spp. pods have been used as a source of protein to feed cattle and human populations, nevertheless, if they are used as the only source of nourishment, could provoke a neurotoxic disease called "twisted face" o "cara torta", especially in ruminant cattle [72, 73]. Nevertheless, *Prosopis* spp. pods are a rich source of polyphenolic compounds with antioxidant activity and a high variety of piperidine alkaloids [20]. In *P. juliflora* pods have been detected the same alkaloids that those found in the leaves but in different concentrations. The relative abundance with DART-MS in *P. juliflora* showed that the major alkaloid in leaves is juliprosopine (**1**) followed by juliprosine (**2**), both alkaloids with indolizidine moiety; while in pods and flowers the most abundant is julifloridine (**7**) followed by prosopinine (**6**) belonging to the group of alkaloids without indolizidine moiety [35, 59]. It is important to point out that prosopinoline (**21**) was only detected in pods, while N-methyl julifloridine (**9**) was found only in the leaves [59]. In *P. flexuosa* pods, juliprosine (**2**) and juliprosopine (**1**) are the major alkaloids according with HPLC-HRMS analysis [72] (Fig. 1).

In addition to alkaloids, *Prosopis* spp. pods are a rich source of polyphenolic compounds. *P. alba* pods contains Q-dihexoside rhamnoside, vitexin and isovitexin, and in *P. nigra* pods are present anthocyanins like cyanidin rhamnosyl hexoside, peonidin-3-hexoside, malvidin dihexoside and vicenin II [20]. The total phenols and flavonoid contents in *P. farcta* pods were estimated as 61.5 mg gallic acid equivalent and 17 mg quercetin equivalent per gram of dry plant material, respectively. The major volatile constituents are the palmitic acid, 9,12-octadecadienoic acid ethyl ester, cembrene A, myristic acid, farnesyl acetate, nonanal and the α-terpinyl acetate [74].

4. BIOLOGICAL ACTIVITIES OF PROSOPIS SPP. EXTRACTS AND PHYTOCHEMICALS

Plants are adapted to naturally produce secondary metabolites to deal with biotic and abiotic stress. Compounds like terpenes, flavonoids, phenols, and alkaloids are responsible of this plant chemical defense to cope with adverse conditions. Phytochemicals are biologically active and the antimicrobial metabolites are especially interesting since they could reduce the antimicrobial resistance (AMR) effect with a low environmental residually [75, 8].

4.1 Antifungal activity

Despite plants have naturally developed a defense mechanism to avoid fungal diseases, crops around the world are infected by several phytopathogenic fungi that overcome those defenses causing plant disease, low productivity, and crop losses. Synthetic fungicides are currently used to reduce this problem with the disadvantages of resistance phenomena [4]. In this context, *Prosopis* spp. derived compounds and extracts could represent another natural alternative to reduce the use of synthetic fungicides to the control of the pathogenic fungi. [48] showed that the aqueous bark extract of *P. Africana*, and to a lesser extent the aqueous leaf extract, inhibited the in vitro mycelial growth and reduced the sporulation and spore length of *Curvularia lunata* isolated from *Jatropha curcas* (Table 1). [76] used aqueous extract of *P. juliflora* leaves (2% w/v) to the control late leaf spot (LLS; *Phaeoisariopsis personata*) and rust (*Puccinia arachidis*) in groundnut (*Arachis hypogaea*) under greenhouse conditions and in the field. Foliar application of *P. juliflora* leaf extract reduced foliar disease severity in the greenhouse, whereas the combination of the extracts with chlorothalonil increased the pod yields by 81-98% in the field. This strategy reduced three times the use of chlorothalonil and allowed the management of these diseases in field conditions. [77] tested seven commercial fungicides amended with the *P. juliflora* alkaloid fraction against the seed-borne *Fusarium verticillioides* isolated from maize, and the use of the alkaloid fraction significantly reduced the percentage of the synthetic fungicides to reach the same mycelial inhibition as that produced by the highest concentration of the pure fungicide. The application of *P. juliflora* aqueous extracts to seeds and seedlings grown in pots showed potential to reduce root infecting fungi (*Fusarium* spp., *Rhizoctonia solani*, and *Macrophomina phaseolina*) and improves germination in cowpea (*Vigna unguiculata*) and mungbean (*Vigna radiata*) [78]. Furthermore, the leaf powder added to the soil was effective in controlling the root rot disease in okra plants [79] (Table 1).

Table 1. Antimicrobial, insecticide and allelopathic activities from *Prosopis* spp. tissues, extracts and alkaloids.

Tissue and extracts	Activity	Assays	Ref
Prosopis africana			
Aqueous bark extract Aqueous leaf extract	Antifungal against: *Curvularia lunata* isolated from *Jatropha curcas*	***In vitro*** Mycelial growth by food poison method	[48]
Prosopis juliflora			
Leaf powder; alone and mixed with *Verticillium chlamydosporium*, *Paecilomyces lilacinus*, and *Bacillus subtilis*	Antifungal against: *Macrophomina phaseolina*, *Rhizoctonia solani*, and *Fusarium solani*	***In vivo*** Fungal development in Okra plants growth in soil amended after infection.	[79]
Aqueous leaf extract and methanolic leaf extract	*Colletotrichum musae* isolated from banana	***In vitro*** Mycelial growth by disk diffusion method and conidia germination	[38]
Aqueous leaf extract, methanolic leaf extract and acetone leaf extract	Antifungal against: *Colletotrichum gloeosporioides* isolated from mango	***In vitro*** Mycelial growth by food poison method and conidia formation ***In vivo*** Disease severity on mango (*Mangifera indica*) fruits infected	[85]
Aqueous leaf extract and aqueous leaf extract + chlorothalonil	Antifungal against: *Phaeoisariopsis personata* and *Puccinia arachidis* from groundnut	***In vitro*** Conidial germination ***In vivo*** Disease severity in groundnut (*Arachis hypogaea* cv. TMV 2) plants on greenhouse and field	[76]
Successive extraction: Petroleum ether leaf extract (N/A), hexane leaf extract (N/A), chloroform leaf extract (N/A), methanolic leaf extract Combination of methanolic leaf extract or alkaloid fraction + fungicide	Antifungal against: Seed-borne *Fusarium verticilloides* from maize	***In vitro*** Mycelial growth by food poison method	[77]

(Copper oxychloride, methyl-thiophanate, chlorothalonil, carbendazim and strobilurins)			
Aqueous leaf extract Aqueous stem extract Aqueous flowers extract	Antifungal against: *Fusarium* spp., *Rhizoctonia solani*, and *Macrophomina phaseolina*	***In vivo*** Disease severity in Cowpea (*Vigna unguiculata*) and Mungbean (*Vigna radiate*) seeds and plants in greenhouse	[78]
Aqueous leaf extract Successive extraction: Petroleum ether extract (N/A), benzene extract (N/A), chloroform extract (N/A), ethanolic extract, methanolic extract Alkaloid fraction	Antifungal against: *Alternaria alternata* from tobacco	***In vitro*** Mycelial growth by food poison method	[69]
Ethanol leaf extract	Antibacterial against: *Pseudomonas* sp., *P. aeruginosa*, *Salmonella typhimurium*, *Klebsiella pneumonia*, *E. coli*, *Staphylococcus epidermis, S. aureus*, *Micrococcus luteus*, *Streptococcus* sp., *B. subtilis*.	***In vitro*** Agar disk diffusion method	[60]
Methanol, ethanol and butanol leaf extract Methanol leaf extract, petroleum spirit fraction (N/A), chloroform fraction, ethyl acetate fraction, aqueous fraction	Antibacterial against: *P. aeruginosa*, *B. subtilis*, *Enterococcus faecalis*, *E. coli*, *K. pneumonia*, *Salmonella typhi*, *S. typhimurium*, *S. aureus*, *S. epidermidis*, *Streptococcus pyogenes*.	***In vitro*** Agar disk diffusion method	[88]
80% Ethanol leaf extract 80% Ethanol root bark extract	Antibacterial against: *P. aeruginosa*, *E. coli*	***In vitro*** Agar disk diffusion method	[89]
Aqueous leaf extract	Antibacterial against: *Xanthomonas campestris* pvs. *malvacearum*, *phaseoli* and *vesicatoria* from cotton, french bean and tomato, respectively.	***In vitro*** Agar well diffusion method	[90]
Methanol, ethanol, ethyl acetate (N/A), hexane, chloroform, dichloromethane and petroleum ether leaf extracts.	Antibacterial against: *Xanthomonas campestris* pv. *vesicatoria* from tomato	***In vitro*** Agar disk diffusion method	[91]
Aqueous leaf extract	Antibacterial against:	***In vitro***	[92]

	Xanthomonas campestris, Agrobacterium rhizogenes and Aspergillus fumigatus	Agar well diffusion method	
Methanol leaf extract	Antibacterial against: *Klebsiella* sp., *S. aureus*, *Streptococcus* sp., *Bacillus* sp., *E. coli*.	***In vitro*** Agar well diffusion method	[36]
Hexane leaf extract	Insecticidal against: *Macrotermes* spp.	***In vitro*** No-choice bioassay method	[62]
Aqueous leaf extract	Insecticidal against: *Tetranychus bastosi*	***In vitro*** No-choice bioassay method ***In vivo*** Counting of adult females and control efficiency on the fecundity and residual efficiency on the fecundity and mortality of adult females in *Jatropha curcas* plants under nursery conditions	[39]
Aqueous leaf extract	Insecticidal against: *Nephotettix virescens*	***In vivo*** Counting population of *N. virescens* and percentage of rice tungro disease incidence in nursery and field	[94]
Aqueous leaf extract Ether leaf extract Leaf powder Leaf smoke	Insecticidal against: *Callosobruchus chinensis*	***In vitro*** Control efficiency on the egg laying, adult emergence, rate of development and adult mortality in *Phaseolus mungo* grains	[95]
Methanol seed extract Methanol seed extract + *Bacillus thuringiensis kurstaki* (Btk) HD1 strain	Insecticidal against: *Helicoverpa armigera* from non *Bt* cotton fields	***In vitro*** Lethal concentration (LC_{50}), antifeedant bioassay, control efficiency on insect development	[96]
Aqueous leaf extract Aqueous bark extract Aqueous root extract	Allelopathic against: *Mimosa tenuiflora*	***In vitro*** Seedlings emergency percentage, stem height and diameter, leaves number and dry matter weight of *Mimosa tenuiflora* seedlings	[97]
Aqueous leaf extract	Allelopathic against: *Cynodon dactylon*	***In vitro*** Seedlings germination percentage and early seedling development	[98]
Aqueous leaf extract Aqueous stem extract	Allelopathic against: Wheat (*Triticum aestivum*)	***In vivo*** Weed density, fresh weed	[40]

Aqueous root extract		biomass, dry weed biomass, chlorophyll content, leaf area index, leaf area duration, crop growth rate, net assimilation rate, plant height and number of tillers, spike length, number of grains, 1000-grain weight, grain yield, biological yield, harvest index and grain protein content	
Methanol leaf extract Alkaloid fraction (3´´´´-oxo-juliprosopine, secojuliprosopinal and 3-oxo-juliprosine/3´-oxo-juliprosine)	Allelopathic against: *Lepidium sativum*	***In vitro*** Determination of roots and shoots growth and IC50.	[68]
Prosopis ruscifolia			
Leaf and steam extracts Successive extraction: Hexane extract (N/A), dichloromethane extract (N/A), ethyl acetate extract (N/A), methanol extract Fraction with juliflorine, juliprosinene, pinitol, and a triterpene saponin	Antifungal against: *Aspergillus fumigatus*, *A. niger*, *A. nomius*, *A. flavus*, and *A. parasiticus*	***In vitro*** Mycelial growth by bioautography and plate microdilution	[54]
Prosopis glandulosa			
Aqueous leaf extract	Antifungal against: *Colletotrichum gloeosporioides, Fusarium oxysporum, Rhizopus oryzae* and *R. stolonifer*	***In vitro*** Mycelial growth by food poison method ***In vivo*** Disease severity in strawberry (*Fragaria x ananassa*), cherry, tomato (*Solanum lycopersicum* var. *cerasiforme*) and baby carrot (*Daucus carota*)	[50]
Ethanol leaf extract; Alkaloid fraction; juliprosopine Ethanol root extract; Alkaloid fraction; 3-isocassine (N/A), *N*-methyl-3-isocassine (N/A), N-methylcassine(N/A)	Antifungal against: *Cryptococcus neoformans* (ATCC90113), *A. fumigatus* (ATCC 90906)	***In vitro*** Mycelial growth by plate microdilution	[21]
Ethanol leaf extract; Alkaloid fraction; prosopilosidine, prosopilosine, isoprosopilosine, isoprosopilosidine,	Antifungal against: *C. neoformans* (ATCC90113), *A. fumigatus* (ATCC 90906)	***In vitro*** Mycelial growth by plate microdilution ***In vivo*** Male mice (Swiss Webster strain) infected with *C.*	[22]

juliprosopine		*neoformans*	
Nanoparticles from the aqueous leaf extract	Antifungal against: *Fusarium solani* (T-ICA04) from transgenic insect-resistant cotton	***In vivo*** Determination of physiological and morphological parameters and disease severity in Bollgard® cotton transgenic seedlings	[52]

N/A; no activity.

In addition, aqueous extract of *P. glandulosa* leaves at 5% completely inhibited the radial growth of *C. gloeosporioides* and dramatically reduced to *F. oxysporum*, *R. oryzae*, *R. stolonifera* (Table 1). At this concentration, the extract also decreased the disease symptoms (necrosis, soft rot, dehydration) produced by *C. gloeosporioides*, *F. oxysporum*, *R. oryzae*, and *R. stolonifer* on strawberry, cherry tomato, and baby carrot [50]. *Colletotrichum* spp. is an important genus of plant pathogens that generates pre and post-harvest losses in a wide variety of crops [80, 81]. Resistance reports to the benzimidazoles fungicides benomyl, thiabendazole, and thiophanate methyl had been noticed in *C. musae* isolated from banana and *C. gloeosporioides* from mango [82, 83]. Additionally, *C. gloesporioides* resistance to the post-harvest application of imazalil fungicide has been reported in mango [84]. Also, isolated strains of *C. cereale* and *C. coffeanum* had presented benzimidazole resistance, and there exist reports of *C. graminicola* resistant to strobilurin related to QoI fungicides. [38] tested the in vitro antifungal activity of methanolic leaf extracts (10% w/v) of several plant species against *C. musae* isolated from banana, and *P. juliflora* extract displayed the highest inhibitory effect on conidial germination and mycelial growth. In a similar way, [85] reported the in vitro antifungal activity of methanolic and acetone extract (10-20% w/v) from *P. juliflora* leaves against *C. gloeosporioides* isolated from mango, as well as a reduction in the anthracnose disease symptoms on mango fruits (Table 1). In addition, the aqueous extract (24% w/v) and the alkaloid rich fraction from *P. juiliflora* leaves inhibited in vitro radial growth of *Alternaria alternata* isolated from tobacco plants [69].

Finally, the methanolic extract of the aerial parts (leaves and limbs) of *P. ruscifolia* displayed antifungal activity against *Aspergillus fumigatus*, *A. niger*, *A. nomius*, *A. flavus*, and *A. parasiticus*. Further analysis of this extract revealed the presence of alkaloids, such as juliprosopine (**1**) and juliprosinene (**3**) (Fig. 1); pinitol and a triterpene saponin [54]. The juliprosopine (**1**) and prosopilosidine (**18**) isolated from *P. glandulosa* var. *glandulosa* showed in vitro antifungal activity against *Cryptococcus neoformans* (ATCC90113) and *A. fumigatus* (ATCC 90906), respectively [22, 86].

The potential of *Prosopis* spp. extracts or chemical constituents to the control of phytopathogenic fungi could be potentiated through the formulation of nanoparticles. Silver nanoparticles (AgNPs) obtained from aqueous leaf extract of *P. glandulosa* inhibited the in vitro and in vivo growth of *F. solani* in cotton plants [52], and zinc oxide nanoparticles (ZnONPs) synthesized with aqueous extract from *P. farcta* pods exhibited antifungal activity against 10 clinical isolates of *C. albicans* [87].

4.2 Antibacterial activity

The inhibitory effect of *Prosopis* spp. extracts against plant pathogenic bacteria is not as wide as that showed against fungi. In vitro antibacterial activity from leaves and root alcoholic extracts of *P. juliflora* have been reported against *Pseudomonas aureginosa* at doses of 10% (w/v) [60, 88, 89]. [90] also reported in vitro antibacterial activity of aqueous leaf extract against *Xanthomonas campestris* pathovars *malvacearum*, *phaseoli* and *vesicatoria* from cotton, French bean and tomato, respectively. Also, the *P. juliflora* methanolic extract inhibited the growth of *X. campestris* [91, 92], and *Agrobacterium rhizogenes* [92]. Other studies have shown the antibacterial activity of the *P. juliflora* leaf methanolic extract [36], the *P. juliflora* alkaloid fraction [73] and the *P. farcta* pod ethanolic extract against human pathogenic bacteria, suggesting that *Prosopis* spp. extracts could display activity against many other phytopathogenic bacteria. Furthermore, the AgNPs from *P. glandulosa* leaf extract has potential antibacterial activity as well [51].

4.3 Insecticide activity

Plants produced secondary metabolites to cope with the frequent interactions with the environment, including herbivores (insects, nematodes, vertebrates) [5]. Insects cause the major crop losses that have increased since the green-revolution [2]. In a similar way as in fungi, bacteria, and weeds, pesticide resistance emerged as early as the synthetic insecticide control was massively implemented [93], this accompanied with the residual toxicity and the non-target organism effect. The hexane leaf extract of *P. juliflora* was lethal against *Macrotermes* spp. at 25, 50, 75 and 100 mg L-1. The mortality percentage increased with the concentration in a time dependent manner [62]. In nursery conditions, the aqueous leaf extract is efficient in the control of *Tetranychus bastosi* on *Jatropha curcas* at LC50 and LC90 values of 53.4% and 85.3%, respectively. Low residuality of the extract and absence phytotoxic effects were observed in *J. curcas* plants [39]. Aqueous leaf extract applied in the field can restrain the population of the green leafhopper (*Nephotettix virescens*), that transmits the rice tungro virus (RTV) in rice plants [94]. [95] reported a deterrent effect of the aqueous and ether extracts from leaves, bark, and fruits of *P. juliflora* against *Callosobruchus chinensis* beetle. The ether leaf extract (10% w/v) displayed the highest adult mortality percentages (66.6%), the smoke treatment from fruit and leaves powder induced 70% of mortality while the aqueous bark extract (10%) reduced the egg laying. The methanolic seed extract from *P. juliflora* increased the mortality of *Helicoverpa armigera* larvae from 10 to 80% at 1 and 80 mg L-1, respectively. The combination of seed extract and spore-crystal mixture of *Bacillus thuringiensis* kurstaki had a synergistic effect increasing larvae mortality and decreasing adult longevity and fecundity [96].

4.4 Allelopathic activity

The *P. juliflora* extracts also displayed allelopathic activity that could be exploited to control weeds in some crops. The aqueous extracts (25%, p/v) of leaves, bark, and roots from *P. juliflora* reduced the seedling emergence of *Mimosa tenuiflora* around 30%. Additionally, the leaves extract also reduced the seedlings height and stem diameter [97]. Also, [98] reported the reduction in the germination rate of *Cynodon dactylon* seeds and the radicle length in seedlings with the exposition of aqueous leaf extract from *P. juliflora* (10-60 g L-1) in a concentration dependent manner. [40] assessed the application of aqueous extracts from *P. juliflora* leaves, steam, and bark on wheat plants (*Triticum aestivum*) cultivated in the field to the control of weeds. All extracts reduced the weeds density 60 days after sowing, but the wheat yield and quality parameters were reduced as the extract concentration increased (up to 40%). This pointed out that *P. juliflora* extracts cannot be used in all kinds of crops, and it is necessary to establish the maximum doses to inhibit the growth of the weed without affecting the growth of the crop. [68] tested the effect of some alkaloids isolated from *P. juliflora* leaves, such as secojuliprosopinal (**8**), 3’’’’-oxo-juliprosopine (**14**), and the mix 3-oxo-juliprosine (**16**)/3’-oxo-juliprosine (**15**) on seeds germination and seedlings growth of *Lepidium sativum* (Fig. 1). All alkaloids inhibited the shoots and roots growth, whereas the mixture of 3-oxo-juliprosine/3’-oxo-juliprosine displayed the strongest activity on shoots

(MIC50: 200 µM) and roots (MIC50: 100 µM). These results suggest that both piperidine alkaloids with and without indolizidine ring are responsible for the allelopathic activity of the *Prosopis* spp. extracts.

4. CONCLUSION

Prosopis spp. are small spiny trees adapted to growth on semiarid areas. All parts of these species are widely used by human populations as a source of wood, medicine, and food for cattle. Besides, the antifungal, antibacterial, insecticidal, and allelopathic activities of their extracts and piperidine alkaloids against some causal agents of plant pests and diseases highlights the potential of phytochemicals of these plant species as an alternative to decrease the use of synthetic biocides and the environmental pollution related to their application. Although the synergism of *Prosopis* spp. extracts with fungicides or beneficial microorganisms allows the efficient use of compounds with biocidal characteristics, studies in the field conditions are necessary.

In the market, there exist a wide variety of plant derived biocides and their demand is increasing since the spread of the organic agriculture and the necessity of an integrated pest management for a healthy agriculture. Hence, the evaluation of pure compounds and the standardization of extracts based in bioactive compounds are imperative to the formulation of *Prosopis* spp.-derived biocides products.

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