View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by CONICET Digital

Journal of Clinical Toxicology

Persia et al., J Clin Toxicol 2016, 6:5
DOI: 10.4172/2161-0495.1000326

Commentary OMICS International

Overview of Genus *Prosopis* Toxicity Reports and its Beneficial Biomedical Properties

Persia FA[1], **Rinaldini E**[1], **Hapon MB**[1,2] **and Gamarra-Luques C**[1,3*]

[1]*Laboratorio de Reproducción y Lactancia, Instituto de Medicina y Biología Experimental de Cuyo-CONICET, Mendoza, Argentina*

[2]*Laboratorio de Reproducción y Lactancia, Facultad de Ciencias Exactas y Naturales, Universidad Nacional de Cuyo, Mendoza, Argentina*

[3]*Laboratorio de Toxicología Experimental, Facultad de Ciencias Médicas, Universidad Nacional de Cuyo, Mendoza, Argentina*

[*]**Corresponding author:** Carlos Gamarra-Luques, Laboratorio de Toxicología Experimental, Instituto de Medicina y Biología Experimental de Cuyo-CCT Mendoza. Av Ruiz Leal s/n. Casilla de Correo 0855, CP 5500, Mendoza Capital, Provincia de Mendoza, Argentina, Tel: (54+261)5244198; E-mail: cgamarraluques@gmail.com

Received date: October 14, 2016; **Accepted date:** October 31, 2016; **Published date:** November 02, 2016

Copyright: © 2016 Persia FA, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Secondary plant metabolites are regarded as promising sources of plant-protecting substances and they are one of the most important lines of plant defense against pests. The range of cellular targets for these substances is very wide and covers metabolic pathways, macromolecules and organelles. In consequence, the plant derivatives study represents a critical situation in which toxic effects against other organisms need to be evaluated in relation to its biological benefits. The genus *Prosopis* (Fabaceae) include 44 species and is considered among the world's most damaging invasive species. The genus had been found in 129 countries globally and many more countries are climatically suitable. *Prosopis* physiology evidences a wide range of adaptability, shows the capability to growth in several adverse conditions, accumulates heavy metals and synthetizes chemical defences. Curiously, since antiquity, some *Prosopis* species around the world were described as important source of ethnopharmacological treatments for several illnesses. Toxicity against prokaryote microorganisms, fungus, parasites, mosquitoes, vertebrate animals and humans is revised in the current work. In accordance to the reviewed literature, it is possible to conclude that more specific research could make *Prosopis* species an important source of nutraceuticals and phytopharmaceutical compounds. Moreover, by its selective toxic effects, plant derivatives can be used as important source of new and successful bioactive molecules.

Keywords: *Prosopis*; Toxicity; Nutraceuticals; Phytopharmaceutical

Introduction

Plants are constantly challenged by environmental fluctuations. In response, they have developed a wide range of morphological and biochemical adaptations committed to ameliorate the effects of abiotic stress [1]. Secondary plant metabolites, such as alkaloids, glycoalkaloids, terpenoids, organic acids or alcohols, are regarded as promising sources of plant-protecting substances. These compounds are produced by a variety of plant species in practically all their organs, and they are one of the most important lines of plant defence against pests. The range of cellular targets for these substances is very wide and covers metabolic pathways, macromolecules and organelles. By modification in cellular targets, plant metabolites can affect the functioning of entire organisms [2]. In accordance to this, the plant derivatives study represents a critical situation in which toxic effects against other organisms need to be evaluated in relation to its biological benefits. Moreover, in many cases, exerted toxicity represents a desirable biological effect. Because it properties, natural products, remain an important source of new drugs, new drug leads, and new chemical entities [3]. Scrutiny of medical indications by source of compounds has demonstrated that natural products and related drugs are used to treat 87% of all categorized human diseases, including as antibacterial, anticancer, anticoagulant, antiparasitic, and immunosuppressant agents, among others [4].

The gender *Prosopis* include many species which are worldwide distributed. Some of the species are used since antiquity by native population and several ethnopharmacologic properties have been described. However, more scientific research about the gender is necessary to promote it use as source of natural medicines, insecticidal compounds and nutrients supplies.

The present work reviews *Prosopis* species research focused on its reported toxic effects and consequent beneficial medical properties with the goal to promote deep research destined to support its nutraceutical and phytopharmaceutical use.

Distribution, abundance and characteristics of genus *Prosopis* (Fabaceae): Invasive species cause ecological, economic and social impacts and are key drivers of global change. This is the case for the genus *Prosopis* (Fabaceae) where several taxa are among the world's most damaging invasive species. *Prosopis* had been found in 129 countries globally and many more countries are climatically suitable. Several *Prosopis* species have substantial impacts on biodiversity, ecosystem services, and local and regional economies [5].

Prosopis taxon is present in most of the world's hot arid and semi-arid regions as native or introduced species [6]. The genus as was described by Burkart (1976) consists of 44 species [7]. Factors that make many *Prosopis* species successful invaders include the production of large numbers of seeds that remain viable for decades, rapid growth rates, ability to coppice after damage [8,9], root systems that allow them to efficiently utilize both surface and ground water [10,11], and allelopathic and allelochemical effects on other plant species [12]. Many *Prosopis* species can also withstand climatic extremes such as very high temperatures and low rainfall, and they are not limited by alkaline, saline or unfertile soils [6,9]. Interspecific

hybridization also enhances invasiveness in many introduced regions [13]. Since a toxicological point of view, it is important to remark the capability of some species to accumulate heavy metals as chromium, lead, arsenic, cadmium, manganese, molybdenum and zinc [14,15]. Moreover, chemical defenses, as protease inhibitors, have been described as anti-herbivore mechanism of defense into the taxa [16].

The mentioned physiological plasticity implicates the production of a variety of successful secondary metabolites. Inside the context of natural products research, metabolites can be isolated and used by its beneficial selective toxic effects. The current status of toxic effects related to genus *Prosopis* and its beneficial biomedical properties are presented below [17,18].

Toxicity of genus *Prosopis* against bacterial taxa: The potential for developing antimicrobials from plants is one of the most explored fields in phytomedicine. Plant based antimicrobials have enormous therapeutic potential as they can serve the purpose without any adverse effects that are often associated with synthetic compounds; hence isolation and purification of phytoconstituents from these plants may yield significant novel antimicrobials [19].

There are only 6 species of *Prosopis* with reported antimicrobial effect (Table 1). These studies were performed against a wide number of GRAM positive and negative bacteria species, including drug resistant and multidrug resistant strains. The most common experimental approach to study the antimicrobial activity was the calculation of minimum inhibition concentration (MIC) and minimum bactericidal concentration (MBC). The antibacterial plant material derivatives better characterized were the indolizidines juliprosopine, juliprosine and prosoflorine [20,21].

Specie	Bacteria	Plant source	Cite
P. strombulifera	*Escherichia coli* *Salmonella typhi*	Fruit.	Anesini and Perez [17]. Perez and Anesini [18].
P. spicigera	*Escherichia coli* *Streptococcus mutans* *S. bovis*	Aerial parts, positive for: alkaloids, aminoacids and proteins.	Khan et al. [19]
P. glandulosa	*Mycobacterrium intracellulare*	Indolizidines from leaves.	Rahman et al. [20]
P. juliflora	*Micrococcus luteus* *Staphylococcus aureus* *Streptococcus mutans* *Bacillus subtilis* *Escherichia coli* *Enterococcus faecalis* *Klebsiella pneumoniae* *Pseudomonas aeruginosa* *Staphylococcus epidermidis* *Streptococcus pyogenes* *Salmonella typhi* *Salmonella typhimurium*	Chloroformic extract of pods. Alkaloids, Glycosides, Flavonoids and Terpenoids from leaves. Aqueos and organic extract of seed pods.	Dos Santos et al. [21] Thakur et al. [22] Tajbakhsh et al. [23]
P. cineraria	*S. aureus* *E. faecium*	Phenolic compounds derived from aerial parts.	Neghabi-Hajiagha et al. [24]
P. laevigata	*K. pneumoniae* *E. faecalis* *E. coli* *S. aureus*	Triterpenes, steroids, coumarins, alkaloids, tannins, carbohydrates and flavonoids derived from bark and leaves.	Sánchez et al. [25]

Table 1: Antibacterial toxicity of *Prosopis sp.*

Other experimental approach different from the conventional antimicrobial study is represented by the Ames´Test [26], which has been extensively used to measure the mutagenic potential of many compounds. Assays use strains of *Salmonella typhimurium* which have point mutations in the histidine biosynthetic operon that render them unable to grow in the absence of histidine. Cultures of bacterial strains in the presence of mutagenic compounds drive mutations that make microorganisms able to grow and form detectable colonies without adding histidine to the culture agar. Consequently, increased capability to grow and form colonies is indicative of mutagenic activity. In the mentioned conditions, mature pods flour of *P. alba* and aqueous extract of *P. strombulifera* were assayed and both species were described as no genotoxic [27,28].

In accordance to revised literature, the plant derivatives presented could be an appropriate source of pharmacological compounds that makes the gender *Prosopis* a promising basis for further studies and development of new antibacterial agents.

Toxicity of genus *Prosopis* against fungus taxa: Within the fungi regarded as human pathogens, members of the genus *Candida* are the most frequently recovered from fungal infections and these *Candida* infections are collectively referred to as candidiasis. The genus is an extremely heterogeneous group of over 150 species, but it is well established that only a few of these are implicated in human infectious diseases. Most cases of candidiasis have been attributed to *Candida albicans*, but other *Candida* species designated as non *C. albicans* Candida (NCAC), have been identified as frequent human pathogens [29]. On other hand, the human fungal pathogen *Cryptococcus neoformans* undergo a number of elaborate interactions with their hosts, including survival and proliferation within phagocytes as well as dissemination to the central nervous system and other tissues; almost half of these infections and has an associated mortality of over 60% [30].

Alkaloids derived from two species of genus *Prosopis*, *P. spicigera* and *P. glandulosa*, were reported as active against C. *albicans*, *C. glabrata*, *C. krusei*, *C. tropicalis* and *C. neoformans* [19,20]. The antifungal plant derivatives more precisely described were juliprosopine and juliprosine, which minimum fungicidal concentration (MFC) against *C. neoformans* was equipotent to amphotericin B. Taken together, reported activity of *Prosopis* plant derivatives make the genus an important source of compounds with a potential to solve inconveniences related to multidrug resistant and emergent species of pathogenic fungus.

Toxicity of genus *Prosopis* against parasites: Protozoal infections are a worldwide health problem, particularly in underdevelop countries [31-34], which account for approximately 14% of the world population whom are at risk of infection. Therefore, a great concern has been expressed by the WHO, as they are considered neglected tropical diseases [35]. Various studies have been conducted on protozoal diseases, including *leishmania*sis, malaria and chagas. These diseases are considered as *major* killing factors, particularly in view of the fact that various difficulties are associated with controlling the sources of infection, the high cost of treatment/prevention and poor compliance. Additional difficulties include drug resistance, low efficacy and poor safety, which may retard treatment [36]. Therefore, there is always need for the development of new and more effective drugs [37]. In this respect, natural products offer good sources for new drug discovery. It is estimated that approximately 60% of the world population still use traditional remedy methods, mainly medicinal plants or their products, because they cannot afford the cost of pharmaceutical products [38,39].

Against protozoal parasites, 3 different species of *Prosopis* demonstrate efficacy. While lectins derived from *P. farcta* are able to agglutinate *in vitro* cultured promastigotes of *Leishmania major*; alkaloids of *P. glandulosa* are toxic against promastigotes, axenic amastigotes and amastigotes in THP1 macrophage culture with a reported activity superior to pentamidine [20,40]. Antimalarial activity was reported by the capability of *P. glandulosa* and *P. juliflora* to affect *in vitro* cultures of chloroquine sensitive and resistant strains of *Plasmodium falciparum* [20,41]. And finally, intracellular amastigotes of *Trypanosoma cruzi* and free trypomastigotes of *T. brucei* are affected by the fruit methanol extract of *P. juliflora* [41].

Altogether, *Prosopis* derivatives antiprotozoal activity could be considered as a promissory field of research and drug development to control the mentioned neglected diseases.

Toxicity of genus *Prosopis* against arthropoda: Mosquitoes are well known as vectors of several disease causing pathogens. The extensive use of synthetic insecticides in the mosquito control strategies resulted to the development of pesticide resistance and fostered environmental deterioration. Hence in recent years plants become an alternative source of mosquito control agents.

Only *P. juliflora* was studied for its toxic properties against mosquitoes. Leaf organic extracts were able to exert larvicidal and oviposition altering activities. Whereas the methanolic extract is able to be toxic in larvae of *Anopheles stephensi*, *Culex quinquefasciatus*, Aedes aegypti and *A. albopictus* [42,43]; acetone extract affects oviposition of *A. albopictus* [44].

The mentioned studies would be of great importance while formulating vector control strategy based on alternative plant based insecticides in hot arid and semi-arid regions. Moreover, vectors control is one of the methods to manage, by transmission interruption, emergent diseases as dengue and chikungunya.

Toxicity of genus *Prosopis* against whole animals: The unique report about *Prosopis* sp toxicity is related to its phytoestrogenic effects on female and male Wistar rats. The study was performed to determine how pods of mesquite (*Prosopis sp*) affect animal agriculture when are used as pasture. On intact females, mesquite pod extract, altered estrous cyclicity, decreased lordotic quotient and intensity of lordosis; in ovariectomized rats, treatment induce vaginal estrus, increased vaginal epithelium height, and induced lordosis [45]. Moreover, several aspects of behavior and reproductive physiology were reported in males. Sexual behavior was disrupted after 40 days of treatment. Plant derivatives also increased testicular germ-cell apoptosis, decreased sperm quality, testicular weight, and testosterone levels [46]. Female and male effects were similar to those observed after the phytoestrogen isoflavones daidzein and genistein treatments.

Only one study was specifically performed to evaluate induced oral toxicity of *P. strombulifera* aqueous extract on BALB/c mice. Oral sub-chronic administration, 28 days dose-repeated, did not induce lethality, neuro-behavioral, anatomo-pathological, serological or biochemical alterations at 150 mg/animal/day [28].

Although, there are not similar reports about specific toxicity studies for others *Prosopis* species, an elevated number of beneficial biomedical properties were reported on different animal species (Table 2). None of these studies mentioned toxic, adverse or undesirable effects in vertebrates.

Specie	Plant source	Specie/strain	Activity	Cite
P. cineraria	Ethanolic extract of bark	Swiss albino mice	Antihyperglycemic, antihyperlipidemic and antioxidative	Sharma et al. [47]
	Alkaloids, phenolic	Swiss albino mice	Antitumoral (Ehrlich ascites carcinoma)	Robertson et al. [48]

	compounds, saponins, flavonoids and phytosterol obtained from leaves and stem bark			
	Methanolic extract from stem bark	Rabbit	Antispasmodic activity, bronchodilator and vasoconstrictive activity. (isolated tissues)	Janbaz et al. [49]
P. glandulosa	Alkaloids, glycosides, triterpenes, flavonoids and phenolic compounds obtained from leaves.	Swiss albino mice	Antitumoral (Ehrlich ascites carcinoma)	Raju et al. [50]
	DiaviteTM (dried and ground pods of P. glandulosa)	Wistar rats and obese Zucker fa/fa rats	Hypoglicemic, stimulates insulin secretion, leads to the formation of small β-cells and improves insulin sensitivity of isolated cardiomyocytes.	George et al. [51]
	Dried and ground pods	Wistar rats	Cardioprotective and infarct sparing as well as anti-hypertensive	Huisamen et al. [52]
	Dry-milled pods	Wistar rats	Suppression of the neutrophil response to contusion injury	George et al. [53]
P. strombulifera	Ethanol extract of plans	Swiss mice	Antinociceptive	Saragusti et al. [54]
P. farcta	Beans	Struthio camelus	Increased HDL cholesterol, total protein, and globulins levels; and decreases LDL cholesterol, inorganic phosphorus, and γ-GT activity.	Omidi et al. [55]
	Roots	Rabbits	reduced total cholesterol, triglyceride, high-density lipoprotein, low-density lipoprotein, and very low density lipoprotein levels.	Saidi et al. [56]
	Beens	Rabbits	Reduced the blood glucose levels.	Dashtban et al. [57]
P. chilensis	Ethanolic extract of aerial plants.	Wistar rats	anti-inflammatory and analgesic	Abodola et al. [58]
P. juliflora	Pods	Holstein-Zebu	Not significantly influence treatments regarding nutrients intake, animal performance, and feeding behavior. (84 days).	De Oliveira Moraes et al. [59]

Table 2: Beneficial biomedical properties of *Prosopis sp* described in animals.

Summarizing, with the exception of phytoestrogenic effects on Wistar rats, there are no other toxic effects related to the administration of *Prosopis* in several animal species. Altogether, evidence supports the plant derivatives research and use on whole animal models.

Reported activity of *Prosopis* on humans and human cell lines: Most of the scientific reported activities were based on ethnopharmacological and popular use of *Prosopis* plants. Mentioned folkloric uses are biased by popular available information about plant treatment benefits making a dissimilar valuation of it use around different geographical regions. As consequence of plants worldwide popular consume, it is possible to discard severe human toxicity. The reported ethnopharmacological properties, discriminated by species, are presented in Table 3. According to our research, there is just one pharmaceutical presentation of *Prosopis* derivatives; Diavite TM is a dried and ground pods of *P. glandulosa* which is prescribed as hypoglycemic agent [51].

Specie	Popular name	Properties	Cite

P. cineraria	Khejri, ghaf, jand, jandi, kalpa plant.	Antidiabetic, miscarriage preventive, malnutrition preventive, eye infections, asthma, bronchitis, dysentery, leukoderma, leprosy, muscle tremors, piles, reumathism, cardiovascular disorders.	NAS, Firewood crops [60], ICFRE [61], Shalini [62], Toky [63], Robertson et al., Janbaz et al. [49]
P. glandulosa	Honey mesquite	Dyspepsia, eruptions, eyes infections, hernias, skin ailments, throat, umbilical ailments, antidiabetic.	Kay [64], Powell [65], George et al. [51]
P. farcta	Mesquite	Colds, diarrhea, inflammation, measles, diabetes, skin diseases, prostate disorders, wound healing, chest pain, interrupt urine.	Al-Aboudi and Afifi [66], Omidi et al. [55]
P. juliflora	Algaroba, mesquite	Culinary purposes as beverages and jellies, toothache, asthma, bronchitis, conjunctivitis and skin/blood/venereal diseases.	Felkner [67], Tapia et al. [68], Hebbar et al. [69], Agra et al. [70], Senthilkumar et al. [71], Malik and Kalidhar [72]
P. alba	Unknown	Food source, dissolve gallstones, anti-bronchitic, laxative, astringent, eye infections.	Pasiecznik et al. [73]
P. strombulifera	Retortuño, retortón, mastuerzo.	Astringent, anti-inflammatory, odontalgic, anti-diarrheic.	Roig [74], Hadad and Ribas [75]
P. chilensis	Algarrobo	Protein and fiber dietary source, astringent, antiseptic.	Singh et al. [76], Rani et al. [77]

Table 3: Ethnopharmacological properties of some *Prosopis* species.

One special mention inside this section is required to the novel report about *P. strombulifera* cytotoxicity on human tumoral cell lines. Leaf aqueous extract evidenced cytotoxicity against colorectal and breast cancer cells affecting proliferation and viability in a dose and time-response manner; moreover, treatment induces clonogenic survival diminution [28]. The above mentioned research constitutes the unique report of oncologic relevance inside genus *Prosopis*.

Conclusion

Despite the numerous reports about *Prosopis* toxic and biomedical properties; only 20% of the species were scientifically analysed. Because of the bio geographical distribution and abundance of the plant material, the potential contribution of the genus as precursor of natural derivatives could be considered as under evaluated. More research need to be destined to expand the number of scientifically studied species, as well as to describe the cellular and molecular mechanisms related to the described properties.

Considering the genus biomedical potential, it is a priority to focus the research efforts to elucidate the new chemical entities provided by *Prosopis* plants to ensure its clinical applications. Chemical-analytical characterization of these natural derived products (secondary plant metabolites) and its derived natural products mimics (synthetic compounds derived from natural products) need to be considered as a priority in future investigations. The description of plant derived specific molecules represent a promissory field to develop new drugs. According to the current review, *Prosopis* derivatives could represent an important source of antimicrobial, antiparasitic, insecticidal, even anti neoplastic compounds. Moreover, chemical characterization of biological active compounds will facilitate its clinical research as alternative or complementary agents to the current available drugs.

In relation to the biological properties related to the genus, it is possible to conclude that more specific research could make *Prosopis* species an important source of nutraceuticals and phytopharmaceuticals compounds.

Acknowledgement

This work was supported by CGL and MBH grants from Secretaría de Ciencia, Técnica y Postgrado (SeCTyP) - Universidad Nacional of Cuyo – Argentina (2016-2018); PICT2014-1877 grant, from Agencia Nacional de Promoción Científica y Tecnológica (ANPCyT) and Instituto Nacional del Cáncer (INC) grant, both from Ministerio de Ciencia, Tecnología e Innovación Productiva - Argentina.

Conflict of Interest

The authors report no conflicts of interest.

References

1. Matus JT (2016) Transcriptomic and metabolomic networks in the Grape berry illustrate that it takes more than flavonoids to fight against ultraviolet radiation. Front Plant Sci 30: 1337.
2. ChowaÅski S, Adamski Z, Marciniak P, RosiÅ ski G, et al. (2016) A Review of Bioinsecticidal Activity of Solanaceae Alkaloids. Toxins (Basel) 1: 8.
3. Balunas MJ, Kinghorn AD (2005) Drug discovery from medicinal plants. Life Sci 78: 431-441.
4. Chin YW, Balunas MJ, Chai HB, Kinghorn AD (2006) Drug discovery from natural sources. AAPS J 8: E239-253.
5. Shackleton RT, Le Maitre DC, Pasiecznik NM, Richardson DM (2014) Prosopis: a global assessment of the biogeography, benefits, impacts and management of one of the world's worst woody invasive plant taxa. AoB PLANTS 6: plu027.
6. Pasiecznik NM, Felker P, Harris PJC, Harsh LN, Cruz G, et al. (2001) The Prosopis juliflora - Prosopis pallida Complex: A Monograph. HDRA, Coventry, UK. p.172.
7. Burkart A (1976) A monograph of the genus Prosopis (Leguminosae subfam. Mimosoideae). Part 1 and 2. Catalogue of the recognized species of Prosopis. Journal of the Arnold Arboretum 57: 219-249.
8. Felker P (1979) Mesquite: an all-purpose leguminous arid land tree. In: Eitchie GA, ed. New agricultural crops, American Association for the

Advancement of Science Symposium Proceedings, Vol. 38. Boulder: Westview Press, 89-132.

9. Shiferaw H, Teketay D, Nemomissa S, Assefa F (2004) Some biological characteristics that foster the invasion of Prosopis juliflora (Sw.) DC. at Middle Awash Rift Valley Area, north-eastern Ethiopia. J Arid Environ 58:135-154.
10. Nilsen ET, Sharifi MR, Rundel PW, Jarrell WM, Virginia RA (1983) Diurnal and seasonal water relations of the desert phreatophyte Prosopis glandulosa (honey mesquite) in the Sonoran Desert of California. Ecol 64: 1381-1393.
11. Dzikiti S, Schachtschneider K, Naiken V, Gush M, Moses G, et al. (2013) Water relations and the effects of clearing invasive Prosopis trees on groundwater in an arid environment in the Northern Cape, South Africa. J Arid Environ 90: 103-113.
12. Elfadl MA, Luukkanen O (2006) Field studies on ecological strategies of Prosopis juliflora in a dry land ecosystem. J Arid Environ 66: 1-15.
13. Zimmermann HG (1991) Biological control of Prosopis, Prosopis spp. (Fabaceae), in South Africa. Agriculture, Ecosystems and Environ 37:175-186.
14. Asomugha RN, Udowelle NA, Offor SJ, Njoku CJ, Ofoma IV, et al. (2016) Heavy metals hazards from Nigerian spices. Rocz Panstw Zakl Hig 67: 309-314.
15. Román-Ponce B, Ramos-Garza J, Vásquez-Murrieta MS, Rivera-Orduña FN, Chen WF, et al. (2016) Cultivable endophytic bacteria from heavy metal(loid)-tolerant plants. Arch Microbiol 198: 941-956.
16. Lima TE, Sartori AL, Rodrigues ML (2016) Plant antiherbivore defenses in Fabaceae species of the Chaco. Braz J Biol .
17. Anesini C, Perez C (1993) Screening of plants used in Argentine folk medicine for antimicrobial activity. J Ethnopharmacol 39: 119-128.
18. Pérez C, Anesini C (1994) In vitro antibacterial activity of Argentine folk medicinal plants against Salmonella typhi. J Ethnopharmacol 44: 41-46.
19. Khan R, Zakir M, Afaq SH, Latif A, Khan AU (2010) Activity of solvent extracts of Prosopis spicigera, Zingiber officinale and Trachyspermum ammi against multidrug resistant bacterial and fungal strains. J Infect Dev Ctries 4: 292-300.
20. Rahman AA, Samoylenko V, Jacob MR, Sahu R, Jain SK, et al. (2011) Antiparasitic and antimicrobial indolizidines from the leaves of Prosopis glandulosa var. glandulosa. Planta Med 77: 1639-1643.
21. Dos Santos ET, Pereira MLA, da Silva CFPG, Souza-Neta LC, Geris R, et al. (2013) Antibacterial activity of the alkaloid-enriched extract from Prosopis juliflora pods and its influence on in vitro ruminal digestion. Int J Mol Sci. 14: 8496-8516.
22. Thakur R, Singh R, Saxena P, Mani A (2014) Evaluation of antibacterial activity of Prosopis juliflora (SW.) DC. leaves. Afr J Tradit Complement Altern Med 11: 182-188.
23. Tajbakhsh S, Barmak A, Vakhshiteh F, Gharibi M (2015) In vitro antibacterial activity of the Prosopis juliflora seed pods on some common pathogens. J Clin Diagn Res 9: DC13-DC15.
24. Neghabi-Hajiagha M, Aliahmadi A, Taheri MR, Ghassempour A, Irajian G, et al. (2016) A bioassay-guided fractionation scheme for characterization of new antibacterial compounds from Prosopis cineraria aerial parts. Iran J Microbiol 8: 1-7.
25. Neghabi-Hajiagha M, Aliahmadi A, Taheri MR, Ghassempour A, Irajian G, et al. (2016) A bioassay-guided fractionation scheme for characterization of new antibacterial compounds from Prosopis cineraria aerial parts. Iran J Microbiol 8: 1-7.
26. Sánchez E, Rivas Morales C, Castillo S, Leos-Rivas C, García-Becerra L, et al. (2016) Antibacterial and antibiofilm activity of methanolic plant extracts against nosocomial microorganisms. Evidence-Based Compl Alter Med: 8
27. Maron DM, Ames BN (1983) Revised methods for the Salmonella mutagenicity test. Mutat Res 113: 173-215.
28. Cattaneo F, Sayago JE, Alberto MR, Zampini IC, Ordoñez RM, et al. (2014) Anti-inflammatory and antioxidant activities, functional properties and mutagenicity studies of protein and protein hydrolysate obtained from Prosopis alba seed flour. Food Chem 161:391-399.
29. Hapon MB, Hapon MV, Persia FA, Pochettino A, Lucero GS, et al. (2014) Aqueous Extract of Prosopis strombulifera (LAM) BENTH Induces Cytotoxic Effects against Tumor Cell Lines without Systemic Alterations in BALB/c Mice. J Clin Toxicol 4: 222.
30. Araújo D, Henriques M, Silva S (2016) Portrait of Candida species biofilm regulatory network genes. Trends Microbiol: 30136-30136.
31. Taylor-Smith LM, May RC (2016) New weapons in the Cryptococcus infection toolkit. Curr Opin Microbiol 34: 67-74.
32. Kondrashin AV, Baranova AM, Morozova LF, Stepanova EV (2011) Global trends in malaria control. Progress and topical tasks in malaria control programs. Med Parazitol (Mosk): 3-8.
33. Tengku SA, Norhayati M (2011) Public health and clinical importance of amoebiasis in Malaysia: a review. Trop Biomed 28: 194-222.
34. Kondrashin AV, Baranova AM, Morozova LF, Stepanova EV (2011) Urgent tasks of malaria elimination programs. Med. Parazitol (Mosk) 3: 3-9.
35. Ferrari BC, Cheung-Kwok-Sang C, Beggs PJ, Stephens N, Power ML, et al. (2011) Molecular epidemiology and spatial distribution of a waterborne cryptosporidiosis outbreak in Australia. Appl Environ Microbiol 77: 7766-7771.
36. World Health Organization (WHO) (2010) Working to overcome the global impact of neglected tropical diseases: First WHO report on neglected tropical diseases. WHO: Geneva, Switzerland, No. 1.
37. Nwaka S, Ridley RG (2003) Virtual drug discovery and development for neglected diseases through public-private partnerships. Nat Rev Drug Discov 2: 919-928.
38. Looareesuwan S, Chulay JD, Canfield CJ, Hutchinson DB (1999) Malarone. (atovaquone and proguanil hydrochloride): A review of its clinical development for treatment of malaria. Malarone Clinical Trials Study Group. Am J Trop Med Hyg 60: 533-541.
39. Clardy J, Walsh C (2004) Lessons from natural molecules. Nature 432: 829-837.
40. Tagboto S, Townson S (2001) Antiparasitic properties of medicinal plants and other naturally occurring products. Adv Parasitol 50: 199-295.
41. Jacobson RL, Schlein Y (1999) Lectins and toxins in the plant diet of Phlebotomus papatasi (Diptera: Psychodidae) can kill Leishmania major promastigotes in the sandfly y and in culture. Ann Trop Med Parasitol 93: 351-356.
42. Al-Musayeib NM, Mothana RA, Al-Massarani S, Matheeussen A, Cos P, et al. (2012) Study of the in vitro antiplasmodial, antileishmanial and antitrypanosomal activities of medicinal plants from Saudi Arabia. Molecules 17: 11379-11390.
43. Bansal SK, Singh KV, Sharma S, Sherwani MR (2012) Laboratory observations on the larvicidal efficacy of three plant species against mosquito vectors of malaria, dengue/dengue hemorrhagic fever (DF/DHF) and lymphatic filariasis in the semi-arid desert. J Environ Biol 33: 617-621.
44. Yadav R, Tikar SN, Sharma AK, Tyagi V, Sukumaran D, et al. (2015) Screening of some weeds for larvicidal activity against Aedes albopictus, a vector of dengue and chikungunya. J Vector Borne Dis 52:88-94.
45. Yadav R, Tyagi V, Tikar SN, Sharma AK, Mendki MJ, et al. (2014) Differential larval toxicity and oviposition altering activity of some indigenous plant extracts against dengue and chikungunya vector Aedes albopictus. J Arthropod-Borne Dis 8: 174-185.
46. Retana-Márquez S, García Aguirre F, Alcántara M, García-Díaz E, Muñoz-Gutiérrez M, et al (2012) Mesquite pod extract modifies the reproductive physiology and behavior of the female rat. Hormones and Behavior 61: 549-558.
47. Retana-Márquez S, Juárez-Rojas L, Hernández A, Romero C, López G, et al. (2016) Comparison of the effects of mesquite pod and Leucaena extracts with phytoestrogens on the reproductive physiology and sexual behavior in the male rat. Physiol Behav 164: 1-10.

48. Sharma N, Garg V, Paul A (2010) Antihyperglycemic, antihyperlipidemic and antioxidative potential of Prosopis cineraria bark. Indian J Clin Biochem 25: 193-200.
49. Robertson S, Narayanan N, Raj Kapoor B (2011) Antitumour activity of Prosopis cineraria (L.) Druce against Ehrlich ascites carcinoma-induced mice. Nat Prod Res 25: 857-862.
50. Janbaz KH, Haider S, Imran I, Zia-Ul-Haq M, DeMartino L, et al. (2012) Pharmacological evaluation of Prosopis cineraria (L.) Druce in gastrointestinal, respiratory, and vascular disorders. Evidence-Based Complementary and Alternative Med: 7.
51. Raju SK, Balasubramanian R, Perumal P, Thangavel D, Manonmani AJ, et al. (2011) Antitumor activity of Prosopis glandulosa Torr. on Ehrlich Ascites Carcinoma (EAC) Tumor Bearing Mice. Iran J Pharm Res 10: 505-510.
52. George C, Lochner A, Huisamen B (2011) The efficacy of Prosopis glandulosa as antidiabetic treatment in rat models of diabetes and insulin resistance. J Ethnopharmacol 137: 298-304.
53. Huisamen B, George C, Dietrich D, Genade S (2013) Cardioprotective and anti-hypertensive effects of Prosopis glandulosa in rat models of pre-diabetes. Cardiovasc J Afr 24: 10-16.
54. George C, Smith C, Isaacs AW, Huisamen B (2015) Chronic Prosopis glandulosa treatment blunts neutrophil infiltration and enhances muscle repair after contusion injury. Nutrients 7: 815-830.
55. Saragusti AC, Bustos PS, Pierosan L, Cabrera JL, Chiabrando GA, et al. (2012) Involvement of the L-arginine-nitric oxide pathway in the antinociception caused by fruits of Prosopis strombulifera (Lam.) Benth. J Ethnopharmacol 140: 117-122.
56. Omidi A, Ansari nik H, Ghazaghi M (2013) Prosopis farcta beans increase HDL cholesterol and decrease LDL cholesterol in ostriches (Struthio camelus). Trop Anim Health Prod 45: 431-434.
57. Saidi MR, Farzaei MH, Miraghaee S, Babaei A, Mohammadi B, et al. (2016) Antihyperlipidemic effect of Syrian Mesquite (Prosopis farcta) root in high cholesterol diet–fed rabbits. J Evid Based Complementary Altern Med 21: 62-66.
58. Dashtban M, Sarir H, Omidi A (2016) The effect of Prosopis farcta beans extract on blood biochemical parameters in streptozotocin-induced diabetic male rats. Adv Biomed Res 5: 116.
59. Abodola MA, Lutfi MF, Bakhiet AO, Mohamed AH (2015) The anti-inflammatory and analgesic properties of Prosopis chilenses in rats. Int J Health Sci (Qassim) 9: 265-271.
60. De Oliveira Moraes GS, Oliveira de Souza EJ, Chaves Véras AS, de Paula Almeida M, Vieira da Cunha M, et al. (2016) Total replacement of corn by mesquite pod meal considering nutritional value, performance, feeding behavior, nitrogen balance, and microbial protein synthesis of Holstein-Zebu crossbred dairy steers. Trop Anim Health Prod 7: 1415-1420
61. NAS, Firewood crops (1980) Shrub and tree species for energy production. National Academy of Sciences, Washington D C.
62. ICFRE, (Indian Council of Forestry Research and Education) (1993) Khejri (Prosopis cineraria) ICFRE, Dehradun, India.
63. Shalini (1997) Vedic Leguminous Plants. Shalini Ed. pp57-58.
64. Toky OP (1999) Medicinal values of Prosopis cineraria in arid and semiarid India. Society of chemical industry I.
65. Kay MA (1996) Healing with Plants in the American and Mexican West. Tuscon: The University of Arizona Press pp. 221-224.
66. Powell AM (1998) Trees and shrubs of Trans-Pecos and adjacent areas. Austin: The University of Texas Press pp. 177-179.
67. Al-Aboudi A, Afifi FU (2010) Plants used for the treatment of diabetes in Jordan: A review of scientific evidence. Pharm Biol 49: 221-239.
68. Felker P (1981) Use of tree legumes in semiarid regions. Econ Bot 35: 174-186.
69. Tapia A, Egly Feresin G, Bustos D, Astudillo L, Theoduloz C, et al. (2000) Biologically active alkaloids and a free radical scavenger from Prosopis species. J Ethnopharmacol 71: 241-246.
70. Hebbar SS, Harsha VH, Shripathi V, Hegde GR (2004) Ethnomedicine of Dharwad district in Karnataka, India--plants used in oral health care. J Ethnopharmacol 94: 261-266.
71. Agra MF, Silva KN, Basilio IJLD, Freitas PF, Barbosa-Filho JM (2008) Survey of medicinal plants used in the region Northeast of Brazil. Rev Bras Farmacogn 18: 472-508.
72. Senthilkumar N, Varma P, Gurusubramanian G (2009) Larvicidal and adulticidal activities of some medicinal plants against the malarial vector, Anopheles stephensi (Liston). Parasitol Res 104: 237-244.
73. Malik A, Kalidhar SB (2005) A review of the chemistry and biological activity of Prosopis species. J Med Arom Plant Sci 27: 675-705.
74. Pasiecznik NM, Harris PJC, Smith SJ (2004) Identifying tropical Prosopis species a field guide. Managing 44. UK: HDRA, Coventry.
75. Roig F (2002) Flora medicinal mendocina. Las plantas medicinales y aromáticas de la provincia de Mendoza, EDIUNC Serie Manuales Nº 33, Mendoza, Argentina.
76. Hadad MA, Ribas YA (2010) Raíces Huarpes: Uso medicinal de plantas en la comunidad de Lagunas del Rosario, Mendoza, Argentina. (1stedn) Eds María Cecilia Montani y Cecilia Vega Riveros, San Juan, Argentina.
77. Singh M, Khatoon S, Singh S, Kumar V, Rawat AK, et al. (2010) Antimicrobial screening of ethnobotanically important stem bark of medicinal plants. Pharmacognosy Res 2: 254-257.
78. Rani B, Singh U, Sharma R, Gupta A, Ayushi A, et al. (2013) Prosopis cineraria (L) druce: a desert tree to brace livelihood in rajasthan. Asian J Pharm Res Health Care 5: 58.