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Plant Review

Physical, Chemical and Biological Study of Leaf Extracts from *Senna obtusifolia* : Bibliographic Review

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ABSTRACT

Senna obtusifolia (Fabaceae; Synonyms: *Cassia obtusifolia, Cassia humilis*) is a plant widely found in the state of Amapá, popularly known as "Mata-pasto", it is widely used worldwide, being used in local and traditional medicine, for diseases related to rheumatism, headache, hepatitis and diuretic. The research was carried out using the databases of theses, dissertations and indexed articles. Additional information was collected from books, reviews and related documents. The morphometric study of the leaves of *S. obtusifolia* was found in the literature. The analyzes revealed different morphological and anatomical patterns, which are important on the adaxial and abaxial surfaces, since the surface is glabrous and has calcium oxalate druses, unicellular trichomes, epidermal idioblasts. The study of morphology is important in the medicinal activity of the plant since the secondary metabolites in plants are affected by different biotic and abiotic stresses. Thus, stress conditions affect secondary metabolites or the so-called active ingredients and other compounds that plants produce, which are generally the basis of their medicinal activity. According to the literature, several classes of secondary metabolites were found, such as anthraquinones, flavonoids, terpenoids and others in the leaves of *S. obtusifolia*. Current evidence indicates that the secondary metabolites it contains in extracts of *S. obtusifolia* have hypocholesterolemic, antioxidant, allelopathic, antinociceptive, anti-inflammatory, cancer-preventing, arthritis, diabetes, heart disease, kidney and liver toxicity, and urinary tract infections. Detailed information in the literature on *S. obtusifolia* reveals that this species has a wide pharmacological use proven in scientific research.

Key words: *Cassia*, Fabaceae, Fedegoso, Mata Pasto, *Senna.*

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INTRODUCTION

There is little bibliographic information in the literature regarding the physical and morphological study of the surface of the leaves of *S. obtusifolia*, and this type of study has an economic, social, ecological, environmental, taxonomic and pharmacological importance. The growing human need, both in food, medicine and industry, has provided great advances in the biological studies of *S. obtusifolia.*[1] The morphological characterization of plant species uses parameters that range from the macroscopic scale, such as the thickness of structures, size, shape, color, to the microscopic scales, such as the shape of cells, the presence of oil structures and the presence of chemical compounds.[2]

Plants produce secondary metabolites with very diverse chemical and functional characteristics and where they can act in the activity that some have on pathogens or various human diseases, therefore, it is important to study medicinal plants for their pharmaceutical potential.[3,4]

However, in order to better understand the biological activities attributed to the leaf extracts of *S. obtusifolia*, including its anti-inflammatory, antioxidant and antimicrobial activities, it is necessary to know the molecules of their composition and how they act.[5] Considering the importance of investigations about the chemical composition and biological activities of the species *S. obtusifolia*, the present work has contributed to showing the anti-inflammatory, antimicrobial and antioxidant potential of the leaves of this native species, as well as the detection of its secondary metabolites. The chemical composition of *S. obtusifolia* was structurally diverse. Among the compounds already described, include alkaloids, flavonoids and others.[5] Thus, this review aimed to describe the physical, chemical and biological profile of the leaf extracts of *S. obtusifolia* and their possible pharmacological activities, providing the dissemination of results obtained in recent years.

METHODOLOGY

This bibliographic review presents the main researches related to the physical, chemical and biological study of extracts of the species *S. obtusifólia*. To this end, bibliographic references used in this study were based on national and international theses, dissertations and articles indexed in the databases available in the Capes Periodicals (http://www.periodicos.capes.gov),

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Scielo (http://www. scielo.org), Science Direct (http://www.sciencedirect.com), Google Scholar (http://www.scholar.google.com) and Scopus (www.scopus.com), in Portuguese, English and Spanish, based on the corresponding bibliographic reference between the years 1974-2020, but 80% of these correspond between the years 2014-2020.

THE VEGETABLE SPECIES *S. OBTUSIFOLIA*

Botanical description

S. obtusifolia (L.) H.S. Irwin and Barneby (1982) - Taxonomic Serial No.: 505165 according to Integrated Taxonomic Information System (ITIS, 2018), belongs to the Fabaceae family and is a leguminous plant known in English as Java beans or Sicklepod and in Bengali as Achkigard.[6] The plant is invasive and considered a weed in Bangladesh. Most of the time, the plant is found in abandoned lands or on the sides of roads.[7]

S. obtusifolia are sub-shrubs or shrubs of 0.3-1.2 m high; smooth hairless branches, its stipples have dimensions of 8-15 × 0.5-1.2 mm, linear to linear-lanceolate, persistent. Leaves 3.3-6.3 cm long; petiole 1.5-3.5 cm long; fusiform, sessile or subsessile extrafloral nectary, in the first or rarely in the second pair of leaflets; spindles 1.8-2.8 cm long; interfoliolar segments 0.7-1.5 in length; leaflets 2-3 pairs, 2-4.1 × 1.5-2.8 cm, obtuse or rounded and mucronulated apex, glabrous to puberulent adaxial face (where the hair cover is invisible to the eyes, that is to say it is apparently smooth), short-seric abaxial face, ciliated margin, cardiac, brachidodrome nerves, little prominent ribs on both sides.[8]

Ethnobotanical Relevance

The genus *Senna* Mill. with about 350 tropical species, 280 of which are American and about 80 present in Brazil, it is one of the largest genera of the Cassieae tribe, subtribe Cassiinae,[6,9] belongs to the Leguminoseae family (Caesalpiniacea). Leguminosae is cosmopolitan and the third largest family of angiosperms with about 727 genera and 19,325 allocated to the subfamilies Mimosoideae, Papilionoideae and Caesalpinioideae. In Brazil it is the most diverse taxon with approximately 171 genera and 2,694 species,[10] Phylogenetically, Caesalpinioideae is paraphyletic and its generic, tribal and infratribal limits need to be revised.[11] Among the Caesalpinioideae, the Cassieae Bronn tribe stands out with 5 subtribes (Cassiineae Bronn, Ceratoniinae H.S. Irwin and Barneby, Dialiinae H.S. Irwin and Barneby, Duparquetiinae H.S. Irwin and Barneby and Labicheinae H.S. Irwin and Barneby) and 732 species. Caesalpinioideae stands out for the controversial system of many of its taxa, such as *Chamaecrista*, *Cassia* and *Senna* members of the Cassieae subtribe Cassiinae tribe. *Senna* with 350 species, 280 of which American, is a monophyletic genus and very little known taxonomically, especially in Brazil where it is represented by about 80 species.[12]

The Cassinae subtribe comprises three genera: *Cassia* L., *Senna* and *Chamaecrista* Moench.[6] *Senna* is distinguished from *Cassia* mainly by the straight fillets, shorter or even twice the length of the anthers, by the basifix anthers and by the presence of extrafloral nectaries in most species. On the other hand, *Senna* differs from *Chamaecrista* mainly by the absence of bractéolas (exceptionally present), by the zygomorphic androceu and by vegetables that can be indeiscent.[6] *Senna* had his taxonomy studied mainly by De Candolle (1825), Bentham (1870; 1871) and Irwin and Barneby (1981; 1982). However, De Candolle (lc), considered *Senna* as part of *Cassia* (= *Cassia* subg. *Senna*), which was corroborated by Bentham (lc), while Irwin and Barneby (1982) treated him as an independent genre.[12]

The species of *Chamaecrista* and *Senna* were included in *Cassia* L. until the taxonomic treatment of Irwin and Barneby (1981). Previously, *S. obtusifolia* was known as *C.obtusifolia* L. was allocated to the *Senna* genus by Irwin and Barneby (1982). A second species, *C. tora* L., sporadically grows in association with sicklepod in Australia and is commonly confused. Irwin and Barneby (1982) did not consider *C. tora* L. in their review, since it does not occur in the New World, and this species remained, inappropriately, in the genus *Cassia*. However, Randell (1988) accepted the use of three genres to replace *Cassia sensu lato* and, consequently, placed *C. tora* in the genus *Senna*. The correct names are therefore *S. obtusifolia* (L.) Irwin and Barneby (sicklepod) and *S. tora* (L.) Roxb. (*Cassia fetida*).[13]

History and ethnopharmacological use

S. obtusifolia probably originates from the Neotropics, the neotropical region is the biogeographic region comprising Central America, including the southern part of Mexico and the Baja California peninsula, southern Florida, all Caribbean islands and South America, [6,14] but it currently has a pantropical distribution. It is found in Africa (tropical west, central and eastern Africa, Namibia and South Africa), India, Sri Lanka, Pakistan, Malaysia, Philippines, Indonesia, Papua New Guinea, USA (including Hawaii) in Mexico and Central America, the Caribbean and Colombia to Brazil, Paraguay and Argentina, being below 1650 m.[6,15]

S. obtusifolia was probably introduced to Australia in World War II.[14] It was first registered as a weed in the Northern Territory (central-northern Australia) in 1961 and in Queensland (eastern Australia) in 1963.[16] It was declared a harmful plant in Queensland under the Rural Land Protection Act on October 17, 1981.[16] The first record of the occurrence of *S. obtusifolia* in India is that of Roxburgh (1832 as *S. toroides*), which reported that the seeds of the plant were collected in Mysore in 1800.[16]

S. obtusifolia has many traditional, ethno-herbogenic and medicinal properties. Currently, it is used as a nervous tonic, liver stimulant, mild laxative and also as a cardiac tonic. The herb helps the body maintain the normal cholesterol level. Its cream is used to treat skin conditions and also to prevent chronic diseases such as dermatitis. However, the presence of several antinutritional factors, such as trypsin inhibitors, saponins, hemagglutinins, tannins, total polyphenols makes it difficult to use *S. obtusifolia* in animal feed.[17] Since, in western Sudan and eastern Chad, the leaves of *S. obtusifolia* ferment to reduce antinutritional factors, such as phytic acid (52.5%), tannins (6.3%) and polyphenol (20.3%), and increases the fat, protein and ash content, and decreases the fiber content to produce a protein-rich food product called "kawal", which is consumed by many people as a meat substitute.[18,19]

In addition, it synthesizes numerous bioactive compounds and little is known about the nematicidal potential of its extracts and/or essential oils,[20] it is abortive, laxative, sedative, diuretic, antirheumatic, used against headaches, hepatitis, to improve sight, toxic to cattle, antiastenic, neuroprotective, antioxidant, antimicrobial, antiparasitic, insecticide, antitumor and hepatoprotective.[5,21] It also serves to treat colic, diabetes, malaria, pneumonia, headache, constipation, ulcer, candidiasis, burns, dermatitis and gonorrhea. With an emphasis on pharmacological study, with antifungal and antibacterial properties against most of the microorganisms tested, including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Bacillus subtilis* and *Candida albicans*.[22]

According to the literature, the different ethnopharmacological uses of *S. obtusifolia* were obtained in different traditional communities, as shown in Table 1.

With this information, it is possible to observe the great importance of the use of the researched species, since there are reports of diverse biological activities and very diverse and that it is used in various regions of the planet. Thus, this species has great potential for study in search of confirmation of these activities to later propose a possible safe use with proven efficacy and safety.

Physical Study of *S. obtusifolia*

Leaf morphology

There is little bibliographic information in the literature regarding the physical and morphological study of the surface of the leaves of *S. obtusifolia*, and this type of study has an economic, social, ecological, environmental, taxonomic and pharmacological importance.[1] The analyzes revealed different morphological and anatomical patterns, which are important on the adaxial and abaxial surfaces, since the surface is glabrous and has calcium oxalate druses, unicellular trichomes, epidermal idioblasts. The study of morphology is important in the medicinal activity of the plant since the secondary metabolites in the plants are affected by different biotic and abiotic stresses.[34]

Soladoye *et al*. (2010) in their morphometric study of the genus *Senna* Mill. Obtained the following leaf data of *S. obtusifolia*, as shown in Table 2.

The mean and standard deviation of the quantitative characters of the leaf abaxial surface of *S. obtusifolia* are shown in Table 2. Characters such as leaflet length, leaflet width and leaflet length/width ratio contribute significantly to species identification.[35]

The adaxial epidermis is mainly polygonal to irregular in shape, the sizes vary from 27.5 to 55 μm in length and 15 to 30 μm in width. Stomata are present, mainly paracitic, some gradations in relation to the anomocytic type found, the shape is elliptical. With a stomata index of 14.3-17.1%, stoma frequency of 108-165 mm^{-2}. The abaxial surface has irregularly shaped epidermal cells, with slightly wavy walls and narrow, elongated cells with straight walls. The sizes vary from 37.5 to 80 μm in length and 17.5 to 40 μm in width. Stomata are present, mostly paracitic, sometimes anomocytic, in elliptical form, with a stoma index of 18.2-22.8%, stoma frequency of 168-220 mm^{-2}. The non-glandular trichome is present, unicellular and long. The sizes range from 150 to 737.5 μm in length and 7.5 to 12.5 μm in width. Druzes of calcium oxalate are present.[36]

According to Begum *et al*. (2014) in his study of stomatal and trichomal diversity in *Senna* Mill. of Bangladesh obtain the following leaf data for *S. obtusifolia*, as shown in Table 3.

The species *S. obtusifolia* offers different types and amounts of stomata and trichomes; it is important to note that the stomata and trichomes of the adaxial part are different from the abaxial part (Table 3). The adaxial part has unicellular non-glandular trichome and the abaxial part has multicellular non-glandular trichome (1–7 cells), these trichomes are the essential characteristics for taxonomic identification.[37] The shape of the epidermal cells, the nature of the anticline walls, the types of stomata and the number of stomata per microscopic field are shown in Table 3.

Secondary metabolites in plants are strongly affected by different biotic and abiotic stresses. Environmental factors produce stress conditions, on which leaf morphology mainly depends and affect the chemical composition of leaves, secondary metabolites or active ingredients, and other compounds that plants produce, which are generally the basis of their medicinal activity.[38]

With the closure of the stomata, there is a decrease in the diffusion of CO_2 to the leaf mesophile, thus causing a reduction in the photosynthetic rate, affecting the accumulation of photoassimilates, which can reduce crop productivity and activate secondary metabolism as a way of protecting against stress.

Stomata are closed due to hybrid stress, as a consequence the CO_2 adsorption significantly decreases, as a consequence, the consumption of reducing equivalents (NADPH) for CO_2 fixation, through the Calvin cycle decreases considerably, generating a large excess of reducing

Table 1: Ethnopharmacological uses of *S. obtusifolia* in traditional communities.

Disease / Uses	Geographical area	References
Chagas disease and ulcers	Amazon, Brazil	[23]
Antifungal	Marajoara-PA, Brazil	[24]
Laxatives, impetiginous diseases and asthma control	Argentina	[23]
Antimalarial, problems with male sexual organs, stomach and menstrual cramps.	Mali	[22]
Skin diseases, ringworm and eczema, constipation.	Dantewada tribal people, Chhattisgarh, India.	[25]
Itches	Bangladesh.	[26]
Diseases of the digestive system	Takkad people of Kaduna state, Nigeria.	[27]
Diabetes	Kano Metropolis, northern Nigeria	[28]
Control hypertension	Ouémé in Bénin	[29]
Abscess, constipation and rheumatism	Senegal	[30]
Treatment of male infertility	Indigenous peoples of Badagry from Lagos state, Nigeria	[31]
Treatment of scorpion bites, gingivitis, dysentery and diarrhea	Nigeria	[32]
Control cough, pneumonia, fever and conjunctivitis	Nigeria	[33]

Table 2: Important anatomical characteristics on the abaxial surface of *S. obtusifolia* (in cm).

Leaflet length	4.20±1.1930
Leaflet width	2.20±0.6856
Blade length	4.96±0.1746
Petiole length	2.86±0.4690
Number of leaflets	3.00±0.0000
Leaf length	29.7±9.3963
Petal length	1.56±0.2345
Pedicel length	2.00±0.6519

Source: Soladoye *et al*. (2010).

Table 3: Stomatal and leaf trichotic variation of *S. obtusifolia*.

	Adaxial	Abaxial
Epidermal cell	Polygonal	Polygonal
Anticline wall	Straight	Straight
Stoma type	Paracitic	Paracitic, Anisocytic
Number of stomas/microscopic field	32	37
Unicellular glandular trichome	Negative	Negative
Multicellular glandular trichome	Negative	Negative
Unicellular non-glandular trichome	Positive	Negative
Multicellular non-glandular trichome	Negative	Positive (1-7 cells)

Source: Begum *et al*. (2014)

equivalents. As an effect, metabolic processes are directed towards the synthesis of highly reduced compounds, such as, for example, phenols or alkaloids.[39]

In the epidermis, subepidermis, hair, cuticle and epicuticular material, flavonoids are found and are responsible for absorbing ultraviolet radiation, there is a direct relationship between the intensity of solar radiation and the production of phenolic compounds, such as flavonoids, tannins and anthocyanins; it also influences the concentration and/or composition of terpenoids, cyanogenic glycosides and alkaloids.[40] This is due to the fact that these metabolites absorb and/or dissipate solar energy, preventing damage to internal tissues by ultraviolet radiation.

Chemical study of *S. obtusifolia* extracts

Phytochemical study of S. obtusifolia

The phytochemical study of *S. obtusifolia* leaf plant extracts is important, because it identifies secondary metabolites and their possible applications in therapeutic treatments such as antitumor, antioxidants, anti-inflammatory, anticancer, antimicrobial, and antifungal.

In order to obtain the highest secondary metabolite in vegetables, it will depend a lot on the type of solvent used in the extraction process. A good solvent in plant extractions must have low toxicity, ease of evaporation at low temperature, promoting rapid physiological absorption of the extract, preservative action, among other factors. Factors affecting the choice of solvent are amounts of phytochemicals to be extracted, extraction rate, diversity of different compounds extracted, diversity of inhibitory compounds extracted, ease of subsequent handling of the extracts, toxicity of the solvent in the bioassay process, potential health hazard extractors.[41]

That is why studies carried out on different extracts such as acetate, ethanolic, methanolic, aqueous, benzine show the presence of secondary metabolites such as alkaloids, anthraquinones, steroids, triterpenoids, alkaloids, flavonoids, saponins, tannins and coumarin glycosides and others, such as shown in Table 4.

According to Table 4, it could say that the leaves of *S. obtusifolia* are rich in alkaloids, flavonoids, saponins, since they are extracted in three or more extracts.

According to Tiwari (2011), water is a universal solvent, used to extract plant products with antimicrobial and antioxidant activity, according to Table 4 it is observed that the aqueous extract of *S. obtusifolia*, the presence of tannins (antimicrobial) was observed, saponins (antioxidant), terpenoids (antimicrobial), steroids (antimicrobial), flavonoids (antimicrobial), flobatanins, alkaloids, glycosides, glycosides. Flavonoids were not found in the ethanolic extract, but it indicates positive for the aqueous extract and benzine extract, this indicates that the ethanol solvent does not extract to the flavonoids. The same is true for the alkaloid that cannot be extracted by the benzine solvent.

Sudi *et al*. (2011) in their phytochemical study of the flavonoid of the leaves of *S. obtusifolia* in aqueous extract obtained a positive result (Table 4), although Silva *et al*. (2010) obtain a negative result (Table 4), according to the literature, there are several factors that influence the extraction, such as the part of the plant material used, its origin, the degree of processing, the particle size, the solvent used, the extraction time, temperature, polarity and solvent concentration.[44]

The ethanolic extract has greater activity in the extraction of metabolites in relation to the aqueous extract that can be attributed to the presence of greater amounts of polyphenols. This means that they are more

Table 4: Class of secondary metabolites of acetane extract, ethanolic extracts, methanolic extract, aqueous extract and benzine extracts from *S. obtusifolia* leaves.

Secondary metabolites	EAE	EE	ME	AE	BEPE
Phenols				- [1]	
Tannins			+ [42]	+ [32]	
Pyrogelic tannins				- [1]	
Tannins phobafenics	+ [32]			+ [1]	
Anthocyanin and anthocyanidin				-	
Saponin	+ [32]	+ [42]	+ [42]	+ [1]	+ [43]
Terpenoids			+ [32]	+ [32]	
Steroids				+[1]	
Triterpenoids				-[1]	
Flavonoids	+ [32]		+ [32]	+ [32], - [1]	- [43]
Flavones, flavonols and xanthones				- [1]	
Flavonols, flavanones, flavonols and xanthones				- [1]	
Flavanones				- [1]	
Flobataninos			+ [32]	+ [32]	
Leucoantocyanidins				- [1]	
Chalcones and auronas				- [1]	
Alkaloids	+ [32]		+ [42]	+ [32]	- [43]
Cardiac Glycosides			+[42]		
Glycosides					+[43]
Anthraquinone glycosides			+[42]		

Legend: (Em branco) = unrealized. Ethyl acetate extract (EAE). Ethanol extract (EE). Methanolic extract (ME). Aqueous extract (AE). Benzene extract or petroleum ether (BEPE) efficient in the degradation of leaf cell walls, which have a non-polar character, which is why polyphenols are released from leaf cells. It can also be explained the decrease in the activity of the aqueous extract to the enzyme polyphenol oxidase, which degrades polyphenols in aqueous extracts, while in methanol and ethanol they are inactive. In addition, ethanol penetrates the cell membrane more easily to extract intracellular ingredients from plant material. Methanol is more polar than ethanol, but due to its cytotoxic nature, it is not suitable for extraction in certain types of studies, as it can lead to incorrect results. Petroleum ether is a non-polar solvent used to extract lipophilic metabolites, such as saponin, glycosides.[44]

Studies by Mishra *et al*. (2017) (Table 4), the ethanolic extract has secondary metabolites such as: anthraquinones, steroids and Triterpenoids, Alkaloids and others. And there are Flavonoids with only the methanolic extract. The presence of alkaloids that have detoxifying and antihypertensive properties, the presence of saponins showing anti-hypercholesterolemic and antifungal activities.

Studies of Biological Activities

Due to the wide use of the plant leaves of *S. obtusifolia* in popular medicine in different parts of the world, it is important to study their biological activity and consequently introduce them into therapeutic treatments. Some biological activities are attributed to their classes of compounds (Table 5).

Table 5: Main compounds and some of the biological activities attributed to *S. obtusifolia.*

Secondary metabolite	Biological activity
Chromenes	Antifungal, Trypanocidal, Antioxidant,[45] Antiparasitic Analgesic, Relaxers, Antibacterial, Antitumor, Antidepressant.Antiretroviral, Anti-inflammatory.[46]
Euxanthone	Antitumor.[47] Anti-inflammatory.[48]
Isogentisin	Antimicrobials.[49]
Terpenes	Insect repellents.[50] Inflammatory.[51] Antimicrobial and Antioxidant.[52]
Terpenoids	Antiparasitic.[53] Allelopathic, antifungal.[50] Antidiarrheals and Antimicrobials.[41] Sedative, anxiolytic, antinociceptive, anticonvulsant, pro-convulsive, hallucinogenic.[54]
Flavonoids	Antifungal.[42] Anti-inflammatory.[51] Antispasmodic, Antiallergic, Antiulcerogenic, Antiviral.[55] Antidiarrheals, Antimicrobials.[41] Larvicide.[56]
Crisofanol	Antitumor.[57,58]
Phenolic compounds	Antioxidants.[59]
Lupeol	Anti-inflammatory.[60] Anti-phallic, hematoprotective, cardioprotective, antitumor.[61]
Tannins	Anticancerigen.[55] Antidiarrheals and Antimicrobials.[41]
Alkaloids	Antifungal.[42] Antidiarrheals and Antimicrobials.[41] Larvicide.[62] Antibacterial.[63]
Saponins	Anti-inflammatory.[51] Antifungal.[42] Anticancer antigens.[41] Analgesics, antiulcerogenic and sedative.[64] Larvicide.[65]
Emodina	Laxative.[5]
Steroids	Antimicrobial.[66]

According to Table 5, it is possible to observe the different secondary metabolites found in *S. obtusifolia*, of which the main biological activities that the secondary metabolites have are, antifungal, anti-inflammatory, antimicrobial, larvicide, antidiarrheal, antitumor. Having an important relevance in the anti-inflammatory and antitumor activity, since they are found in almost all the secondary matabolites of the leaf extracts of *S. obtusifolia* (Table 5), due to these secondary metabolites it makes *S. obtusifolia* a very important medicinal plant in pharmacological world.

Toxic activity

Plants of the genus *Senna sp*. they are described as toxic to ruminants, mainly because they cause a disease characterized by myopathy and degenerative cardiomyopathy.[67]

According to Souza (2015), in his study entitled: "Toxic diseases of cattle in Mato Grosso do Sul" determined that *S. obtusifolia* is toxic. The ingestion of green leaves and pods by grazing cattle produces indigestion.[68,69] They are also described as toxic to cattle, causing muscle necrosis.[70]

The main clinical signs that cattle show in poisoning by *Senna* plants are muscle weakness and morbidity coefficients, where lethality is 52.7% and 100%, respectively. Spontaneous poisoning by *Senna obtusifolia* in cattle produces an accumulation of proteins inside the cells, known as hyaline degeneration and segmental flocular necrosis of the skeletal muscles. The administration of vitamin E, and selenium was not effective in the treatment as occurs in other *Senna* species.[70]

The toxic activity of *S. obtusifolia* extracts is mainly attributed to the presence of alkaloids, a toxic albumin, a hepatotoxin, anthraquinones and possibly other components.[70]

Studies carried out on *Senna* can induce significant toxic effects in rats. *S. obtusifolia*, produces acute intestinal and hepatorrenal damage in rats. The ethanol extract of *S. obtusifolia* increases the activity of Glutamate-PyruvateTransamines. Previous studies on the toxicity of *S. obtusifolia* in rats.[71] have shown an increase in Glutamate-PyruvateTransamines, also increasing the level of serum creatinine where it clearly reflects toxic damage. In total mainly due to the increase in the level of globulin.[72] In conclusion, *S. obtusifolia* has toxicity activity and as a potential drug it is important to eliminate or decrease its toxicity, for this it is necessary to carry out new studies regarding the toxicity of the extract of *S. obtusifolia*.

Antioxidant activity

Antioxidants are compounds that act as blockers of the oxide-reductive processes triggered by free radicals. The antioxidant activity of plant extracts is mainly attributed to the presence of phenolic compounds, such as flavonoids and anthraquinones.[73] *S. obtusifolia* presents anthraquinone metabolites as Fisciona.[5]

S. obtusifolia leaves are a source of biologically active compounds with antioxidant properties.[74] In the literature it shows some important results on the antioxidant and antifungal activity of the methanolic extract of the stem of *S. obtusifolia*.[22]

Arya (2010) studied the correlation between antioxidant activity and the total phenolic content of *S. obtusifolia* suggesting that there was a significant and positive correlation between antioxidant activities and total phenolic content. The antioxidant effect of several polyphenols that act as inhibitors of hydroxyl radical formation has been correlated with iron chelating properties.

Rodrigues *et al*. (2013), for the antioxidant activity of leaf extracts and stem of *S. obtusifolia* with a concentration of 500 mg/mL found that the highest percentage of the antioxidant activity of the ethanolic leaf extract was 73.46% and its IC_{50} was 1.65 μg/mL, is greater compared to the ethanol extract of stem with a maximum value of 17.91% and its IC_{50}

of 10.44 μg/mL both by the method of sequestration of the 2,2-diphenyl-1-picryl-hydrazyl radical (DPPH). The DPPH method must necessarily complement with the Ferric Thiocyanate (FTC) test, since the DPPH method does not detect pro-oxidant substances.

It can be concluded that the leaf ethanol extract of *S. obtusifolia* has the antioxidant property, with the leaf extract being larger compared to the stem extract. And this may be due to the fact that the leaf extract has a greater amount of flavonoids than the stem extract.

Allelopathic activity

The term allelopathy was coined by the German researcher Hans Molisch in 1937, used as the harmful and/or beneficial effect between plants through biochemical interactions, including microorganisms.[75]

Among the substances with allelopathic activities, tannins, cyanogenic glycosides, alkaloids, sesquiterpenes, flavonoids, phenolic acids and others stand out. However, their concentrations in tissues depend on several factors, such as nutritional characteristics of the soil, temperature and rainfall. The production of metabolites is of fundamental importance with regard to the self-defense provided by the release of allelochemicals by different routes (volatilization, root exudation, leaching and decomposition of residues).[75] The literature indicates that the reduction of nitrogen, in legumes and grasses, makes the plant sensitive to inhibition by allelopathy. This was demonstrated by the effect of Agropyron.[76]

S. obtusifolia has allelopathic potential in different extracts as shown in Table 6 (aqueous, ethanolic hydroalcoholic), hydroalcoholic extract, has the highest percentage of leaf inhibition (*Paspalum maritimum*) up to 46.3%, this is due to the possibility of extracting polar compounds as nonpolar.[77]

S. obtusifolia has allelochemicals such as flavonoids, tannins, terpenoids, alkaloids that can suppress and/or inhibit the germination and growth of vegetable plants, therefore, they have the potential to be used as a herbicide.

The leaves of *S. obtusifolia* have allelopathic potential, which can be explained by the chemical nature of the secondary metabolites that it presents as phenolic compounds, in the literature such compounds are cited as responsible for the allelopathic activity of plant species. It can be concluded then that *S. obtusifolia* is a potential source of allelopathic compounds that can be used in research for alternative herbicides, more bioselective, less harmful to human health and the environment.

Table 6: Aleopathic effect of *S. obtusifolia* from different extracts of *S. obtusifolia* applied to different plants.

Extract	Plant	Percentage of leaf inhibition	References
Ethanol	*Lactuca sativa*	28,1	[78]
	Allium cepa	11,7	
Aqueous	*Vigna unguiculataZea mays*	7,02±0,4	[79]
		12,0±0,8	[1]
	Lycopersicum esculentum	30,0	
Hydroalcoholic	*Paspalum maritimum*	46,3±1,5	[80]
	Brachiaria brizantha	26,0±2,0	
	Brachiaria humidicola	16,7±1,5	
	Brachiaria decumbens	24,3±1,5	

Antimicrobial activity

Scientific studies prove that species of the genus *Senna* can act as an antimicrobial agente.[21] The leaves of *S. obtusifolia* are a source of biologically active compounds with antimicrobial properties.[63,74,81]

According to Rodrigues *et al.* (2013), found that the ethanolic extract of *S. obtusifólia* (leaf) has antibacterial activity inhibiting 30% of the bacteria of the species of *Staphylococcus aureus*, from the concentration of 50 mg/mL. Even though they find that it does not inhibit the bacteria of the *Escherichia coli* species at the different concentrations studied.

The aqueous extracts of acetone, hexane, dichloromethane, methanol of *S. obtusifolia* have a broad spectrum of activity against bacteria such as *Neisseria gonorrheae*, *Salmonella sp*, *Pseudomonas aeruginosa*, *Proteus vulgari*s, *Staphylococcus aureus*, *Escherichia coli*, *Salmonella typhi*, *Streptococcus pneumoniae*, *Aspergillus niger*, *Aspergillus tamari*, *Candida albicans*, *Klebsiella pneumoniae*, *Fusarium oxysporum* and *Streptococcus pneumonia*. The broad spectrum antibacterial activities of the plant extract, possibly due to the alkaloids and flavonoids identified.[63,81]

The antimicrobial action of flavonoids is probably related to the ability to complex extracellular and soluble proteins, as well as cell wall structures. More lipophilic flavonoids can act by causing the rupture of microbial membranes.[82]

Secondary antimicrobial metabolites isolated from *S. obtusifolia* can act as regulators of intermediate metabolism, activating or blocking enzymatic reactions, directly affecting protein synthesis at the nuclear or ribosomal level, or even altering membrane structures.[52]

It can be concluded that the different leaf extracts of *S. obtusifolia* have antibacterial properties where its use in folk medicine is justified, the *S. obtusifolia* extract can be a source of strong antibiotics that can be used as raw material for drug synthesis effective antibacterials in the pharmaceutical industries and thus obtain medicines for the treatment of various bacterial infections/diseases in our society.

Anti-hyperglycemic activity

The methanolic extract of aerial parts of *S. obtusifolia* can act synergistically with glibenclamide to reduce blood glucose in glucose-loaded mice.[7] The methanolic extract of whole *S. obtusifolia* plants can effectively decrease high blood glucose levels, which at the highest dose tested, which was 400 mg of *S. obtusifolia* methyl extract per kg of body weight in mice, was just as effective regarding glibenclamide.[84]

Khanom *et al*. (2017) administered the methanolic extract of *S. obtusofolia* at a dose of 400 mg/kg to mice loaded with glucose significantly reduced the blood glucose level by 22.3%. By comparison, with a standard anti-hyperglycemic drug, glibenclamide, when administered at a dose of 10 mg/kg of body weight, reduced the blood glucose level by 38.3%. A combination of 10 mg/kg of glibenclamide plus 100, 200 and 400 mg of the extract decreased blood glucose levels, respectively, by 39.0, 42.3 and 44.0%. The results suggest that the administration of the foliar methanol extract of *S. obtusifolia* may decrease the dependence on glibenclamide to lower blood glucose.

Khanom *et al*. (2017) suggest researching whether the plant can have its anti-hyperglycemic properties after cooking and whether the cooked plant is edible, since *S. obtusifolia* is easy to obtain because it is considered a weed by farmers.

Different groups of phytochemicals such as anthraquinones, phytosterols, triterpenoids and flavonoids have been reported from the plant. These phytochemicals may be responsible for the anti-hyperglycemic effects.[85]

It can be concluded that *S. obtusifolia* leaf methanolic extract can be considered a potential source of anti-hyperglycemic compounds and can also act synergistically with anti-hyperglycemic drugs such as glibenclamide.

Fungicidal activity

The literature shows that *S. obtusifolia* has antifungal properties,[22,84] studies carried out reveal that the extracts of petroleum ether, chloroform and ethanol and methanolic from the leaves of *S. obtusifolia* have properties antifungal agents, acting effectively against fungi, *Aspergillus niger*, *Aspergillus tamari*, *Candida albicans*, *Fusarium oxysporum*, *Aspergillus fumigatus* and *Candida albicans* where the ethanolic extract of *S. obtusifolia* leaves showed greater sensitivity against *Aspergillus fumigatus* with a minimum inhibitory concentration of 0,3116 mg/mL.[84,85] *S. obtusifolia* has better antifungal efficacy compared to its close relative *S. tora* in all investigated fungal pathogens.[85] The methanolic extract contains antifungal compounds that act synergistically, inhibiting fungal growth and reproduction.[84,85] The methanolic extract extracts a greater amount of secondary metabolites than other extracts such as aqueous, acetone, ethyl and others, which are responsible for the fungicidal activity such as, saponin, alkaloids, flavonoids and terpenoids.

It can be concluded that the leaf extract of *S. obtusifolia* can be considered a potential source of anti-fungal compounds since, according to the literature, it can fight a great variety of fungi.

Anti-inflammatory activity

The nuclear factor-kappa B (NF-κB) is a type of multifunctional nuclear transcription factor involved in the regulation of gene transcription to influence the pathological evolution of inflammatory diseases and plays an important role in the development and progression of malignant cancers.[86] According to Kim *et al*. (2011) the NF-κB pathway plays an essential role in the pathogenic development of ulcerative colitis which is a chronic inflammatory bowel disease and, until now, therapeutic agents for ulcerative colitis, including aminosalicylates, corticosteroids and immune inhibitors, still cannot have satisfactory effects on patients.[87]

The study found that treatment with *S. obtusifolia* (1 g/kg) in colitis induced by sodium dextran sulfate reduces body weight loss and shortening of the colon in mice, also significantly suppresses levels of interleukin (IL)-6 and expression of cyclooxygenase-2 in colon tissues treated with sodium dextran sulfate.[88]

Its therapeutic mechanism is associated with the reduction of NF-κBp65 activation in colon tissues.[87]

According to Table 5, saponins, lupeol, flavonoids, euxanthone have anti-inflammatory properties and are one of the phytochemical constituents present in the methanolic extract of the leaves of *S. obtusifolia*.

The anti-inflammatory activity of saponin possibly happens due to various mechanisms such as inhibition of the degradation of corticosteroids, corticomimetic activity, which interferes with the metabolism of inflammatory mediators, acting on the complement system.[64]

Lupeol is a secondary metabolite of the leaf extract of *S. obtusifolia* and has an anti-inflammatory property, where it significantly reduced the edema produced by 12-O-tetradecanoyl-formolacetate in the ear edema model. It also significantly decreases the levels of myeloperoxidase (a specific marker of neutrophil activity), causing a reduction in the filtration of cells in inflamed tissues of chamandungos.[64]

Flavonoids, which have a series of pharmacological properties, highlighting the anti-inflammatory activity, due to their ability to regulate the activity of enzymes and the synthesis of substances involved in this process such as cytokines, chemokines and adhesion molecules, and thus minimizes the inflammatory process.[89]

Euxantone exerts anti-inflammatory effects by inhibiting the production of tumor necrosis factor-α (TNF-α), interleukins (IL-1β and IL-6) in neonatal mice induced by sevoflurane and also euxantone has neuroprotective activities that have been associated with decreased of cell death due to apoptosis induced by sevoflurane and neuroinflammation, in addition euxantone confers neuroprotection by positively regulating the expression of erythroid nuclear factor 2 (Nrf2).[91]

According to the literature, it can be concluded that *S. obtusifolia* has a great potential in the biological activity (anti-inflammatory) of secondary metabolites (saponins, lupeol, flavonoids, euxantone) and can serve as a source of future pharmacological studies specifically against chronic inflammatory bowel disease that does not yet have satisfactory drugs for sick people.

Larvicidal Activity

S. obtusifolia has the property of larvicide, as shown in Table 7,[91,92] where they work with different types of larvae (*Anopheles stephensi* and *Culex quinquefasciatus*) and obtain optimum results of up to 100% mortality (*Culex quinquefasciatus*).

According to Table 7, the ethanolic extract caused significant mortality (up to 100%) that could effectively be used to control the spread of mosquitoes (*Culex quinquefasciatus*). According to the literature, the secondary metabolites alkaloids, flavonoids and triterpenoids have been associated with insecticidal activity[56] and the presence of saponins, tannins and alkaloids,[62] which act by interrupting the larval development and absorption of food, in addition to other harmful actions.The larvicidal and preventive effect of the oviposition of *S. obtusifolia* against *Anopheles stephensi* and *Culex quinquefasciatus* make the ethanolic extract of *S. obtusifolia* an alternative to the synthetic insecticide in mosquito control programs.

Table 7: Larvicidal activity of the ethanolic extract of the leaves of *S. obtusifolia*.

Larva	Stage	Concentration (mg/L)	Mortality (%)	Reference
Anopheles stephensi.	3º	0.4	92.5	[91]
Culex quinquefasciatus	4º	75	100	[92]

CONCLUSION

According to the literature, there is current evidence, which indicates that the secondary metabolites containing the different extracts of *S. obtusifolia* have biological activity such as toxic, aleopathic, antimicrobial, antifungal, antioxidant, antihyperglycemic, allelopathic, anti-inflammatory, larvicidal, having an important current development of extracts of anti-inflammatory pharmacological activity against chronic inflammatory bowel disease that still cannot have satisfactory effects on patients, also provides for breast cancer, prostate cancer still little explored, arthritis, diabetes, heart disease , renal toxicity and liver toxicity. The detailed information in the literature on *S. obtusifolia* reveals that this species has a widespread use in many regions of the world and has a wide pharmacological action proven in scientific research. It is concluded that the extract of *S. obtusifolia* has a high pharmaceutical value, especially in its anti-inflammatory activity.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

CAPES: Coordination for the Improvement of Higher Education Personnel; **ITIS:** Integrated Taxonomic Information System; **mm:** millimeters; **cm:** centimeters; **μm:** micrometers; **g:** grams; **μg:** microgram; **mL:** milliliters; **mg:** milligrams; **kg:** kilograms; **HS:** Howard Samuel; **Cassia L:** Cassia Lindheimeriana; **Subg:** subgênero; ***C. obtusifolia* L:** *Cassia obtusifolia* Lindheimeriana; ***C. tora* L:** *Cassia tora* Lindheimeriana; ***S. obtusifolia* (L.):** *Senna obtusifolia* (Lindheimeriana); **USA:** United States of América; **CO2:** Carbon dioxide; **NADPH:** Dihydronicotinamide-Adenine Dinucleotide Phosphate; **EAE:** Ethyl acetate extract; **EE:** Ethanol Extract; **ME:** Methanolic Extract; **AE:** Extract Aqueous; **BEPE:** Benzene Extract or Petroleum Ether; ***et al*.:** e other; **IC_{50}:** Half Maximal Inhibitory Concentration; **DPPH:** 2,2-Diphenyl-1-Picryl-Hydrazyl Radical; **NF-κB:** Nuclear Factor-Kappa Beta; **NF-κBp65:** Nuclear Factor Kappa B p65 subunit; **TNF-α:** Tumor Necrosis factor-alpha; **Nrf2:** Erythroid Nuclear Factor 2; **PA:** Pará; **sp:** Species; **FTC:** Ferric Thiocyanate; **IL-6:** Interleukin 6; **IL-1β:** interleukin 1 beta; **CNPq:** National Council for Scientific and Technological Development; **UNIFAP:** Federal University of Amapá.

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