

Scientific evidence on the biological activities of a native plant in the Brazilian Northeast - the purple top

Evidências científicas acerca das atividades biológicas de uma planta nativa do Nordeste brasileiro – o pião roxo

Maria Lysete de Assis Bastos¹

RESUMO

Objetivo: identificar evidências científicas acerca das atividades biológicas da *J. gossypifolia* (pião roxo). **Métodos:** revisão integrativa nas bases de dados Literatura Latino-Americana e do Caribe em Ciências da Saúde, Medical Literature Analysis and Retrieval System Online, SCOPUS, Biblioteca Virtual de Saúde e Scientific Electronic Library Online. Foram selecionados 16 artigos, após a aplicação dos critérios de inclusão e exclusão. **Resultados:** a maioria dos estudos é de origem nacional, publicados em português e oriundo do nordeste. Quanto ao período de publicação, mais de 30% foram publicados em 2006. Nas atividades biológicas, referem-se à tóxica (43,7%), cicatrizante (31,2%), anti-inflamatória (12,5%), cicatrizante/anti-inflamatória, cicatrizante/tóxica e anticoagulante, antioxidante e tóxica (6,2%) para cada uma, respectivamente. **Conclusão:** Os estudos assinalam para a continuação de pesquisas referentes ao uso popular do pião roxo, principalmente para tratar feridas, dor e inflamação, visando a promoção da saúde na Atenção Básica, conforme a Política Nacional de Práticas Integrativas e Complementares no SUS.

Descritores: Cicatrização de feridas; Medicina tradicional; Toxicidade.

ABSTRACT

Objective: to identify the scientific evidence about the biological activities of *J. gossypifolia* (purple top). **Methods:** Integrative review in Latin American and Caribbean Literature in Health Sciences, Medical Literature Analysis and Retrieval System Online, SCOPUS, Virtual Health Library and Scientific Electronic Library Online. We selected 16 articles, after applying the inclusion and exclusion criteria. **Results:** most of the studies are of national origin, published in Portuguese and coming from the northeast of Brazil. As for the publication period, more than 30% were published in 2006. In biological activities, they refer to the toxic (43.7%), healing (31.2%), anti-inflammatory (12.5%), healing / anti-inflammatory, healing / toxic and anticoagulant, antioxidant and toxic (6.2%) for each, respectively. **Conclusion:** The studies indicate the continuation of researches related to the popular use of the purple top, mainly to treat wounds, pain and inflammation, aiming at health promotion in Primary Care, according to the National Policy of Integrative and Complementary Practices in SUS.

Descriptors: Wound Healing; Medicine Traditional; Toxicity.

NOTA

INTRODUCTION

The use of natural resources has shown an increasing tendency in healthcare, due to economic advantages, less possibility of side effects to the organism and greater access to the population, gaining relevant space in a complementary way to allopathic drug therapies.

There are reports of the use of plants as an alternative treatment for health recovery that coincide with the existence of the human species, dating up to 3000 years BC ⁽¹⁾. In this way, human kind has acquired empirical knowledge that has been passed on to other generations, showing remarkable evolution in the use of this natural resource over the years, from the simplest forms of local treatment to sophisticated forms of industrial manufacturing used by modern man ⁽²⁾.

Given that a large part of the population is constantly living in precarious conditions and that in many places in Brazil, health and sanitary care is inaccessible, it is presumed that the consequences of these conditions favor the population or the community for the search of medicinal plants due to how much easier it is to acquire it.

Because of this, science has been demonstrating that medicinal plants have great influence in maintaining the health conditions of people. This is due to the increase of studies about them, which lead to the scientific evidence of the therapeutic action of several popularly known plant species, but, above all, the fact that the treatment with the mentioned plants is part of the popular culture, being used and widespread for many generations ⁽³⁾.

The discovery of bioactive compounds comes mainly from the various chemical studies carried out from medicinal plants and their applications, which have been disseminated for the development of new drugs ⁽¹⁾. It is estimated that there are 25,000 to 75,000 plant species used in traditional medicine in the world. However, only 1% was validated by scientific studies and investigated under its phytochemical aspect ⁽⁴⁾, which justifies the growing interest of professionals in the field, in the study of isolation processes and in the development of methods for the synthesis of such compounds.

It is in this context that the role of nurses in the search for new therapeutic options is evidenced, through the use of medicinal plants as an inherent part of the caring exercise, strengthening the autonomy and integrality of the actions in their care practice, since the universe of health transcends the walls of hospital institutions and even of the basic network ⁽⁵⁾.

In 2005, Brazil formulated the National Policy on Integrative and Complementary Practices (PNPIC) in order to standardize and harmonize the practice of traditional medicine in the Brazilian population and to comply with the recommendation of the World Health Organization (WHO), bringing the guidelines and actions for inser-

tion of services and products related to traditional Chinese medicine - acupuncture, homeopathy and medicinal plants and phytotherapy under the Unified Health System (SUS) ⁽⁶⁾.

In this perspective, studies based on the biological properties of medicinal plants are being developed, among them are the researches with the use of *Jatropha gossypifolia* L., a species widely distributed in tropical countries and semi-arid regions of Africa and the Americas, which is included in the National List of Medicinal Plants of Interest to SUS (RENISUS) ⁽⁷⁾.

J. gossypifolia, known as the purple top or purple pinion, belongs to the Euphorbiaceae family; genus *Jatropha*; *gossypifolia* species, presents itself as a tree with large alternating leaves, purple flowers, small and capsular fruits. This plant species is notable for its analgesic and anti-inflammatory potential, as well as for its use in the treatment of skin diseases, wound healing, dysentery, leprosy, arthritis, otitis, alopecia, venereal diseases, stomach cramps, abdominal tract, rheumatism and bite of venomous animals, becoming pertinent in the practice of folk medicine based on the specific knowledge of this plant ⁽⁸⁾.

However, *J. gossypifolia* has been reported by common sense as one of the main toxic plants known in Brazil ⁽⁹⁾. This information indicates the need for a survey of the production of studies related to this plant species. Thus, research can contribute as a source of knowledge for the development of experimental studies, aiding in the complex evaluation of the risk / benefit ratio of the use of this plant. Thus, the objective was to identify the scientific evidence about the biological activities of *J. gossypifolia* (purple top).

MÉTODOS

It is an integrative review of the literature, which is configured as a research modality that aims to gather and synthesize the studies carried out on a given topic in order to come to a conclusion, based on the results evidenced in each study ⁽¹⁰⁾. It represents yet another resource for the construction of knowledge in health and given its nature, can subsidize the development and accuracy of clinical practice and consequent interventions that result in patient safety.

For the development of the integrative review, six stages were covered: 1) establishment of the guiding question; 2) sampling or searching in the literature; 3) categorization of studies; 4) evaluation of studies included in the review; 5) interpretation of results; 6) synthesis of the knowledge or presentation of the review, in order to guarantee the methodological accuracy of the study and ensure that the guiding question is answered ⁽¹⁰⁾. Thus, the following guiding question was asked: what biological activities does the plant species *J. gossypifolia* present?

Data collection was carried out between January and April 2016, through a cross-over of the literature of the following databases: Latin American and Caribbean Literature in Health Sciences (LILACS), Medical Literature Analysis and Retrieval System Online (MEDLINE), SCOPUS, Virtual Health Library (VHL) and Scientific Electronic Library Online (SciELO).

National and international publications published in the Portuguese, English and Spanish languages of the last 10 years, published between the period 2006 to 2016, available online in full and free of charge in the databases that presented considerations on the biological activities of *Jatropha gossypifolia* in their discussion were used as inclusion criteria. We opted to exclude studies that corresponded to editorials, conference summaries, annals, reviews, comments and articles repeated in more than one database.

From the keywords, the primary descriptor *Jatropha gossypifolia* L. was used with the following secondary descriptors: cicatrização deferidas/wound healing/cicatrización de heridas, toxicidade/toxicity/toxicidad, medicina popular/folk medicine/medicina popular. As a search strategy, the research was performed from the intersection of only English descriptors separated by the Boolean operator AND.

In all, 152 articles were found, of which 99 (65.1%) were previously excluded by repetition in the databases and 37 (24.3%) because they did not meet the inclusion criteria. Thus, the sample obtained for the review was constituted by 16 (10.5%) studies.

The content of the studies was analyzed by the reading and re-reading of their results, which allowed to identify relevant characteristics that were repeated or stood out, allowing the organization of the data into categories by action activity. Categorization is considered as an operation to classify constituent elements of a set⁽¹¹⁾.

After reading in full, and in order to make a synthesis, a collection instrument was elaborated, including information: title / period, type of study / level of evidence, country, language, year of publication, objectives, activity biological and sample.

The selected articles were classified according to the level of evidence, considering the design used for the development of the study, using the classification system composed of seven levels: level I - evidence from systematic reviews or meta-analysis of relevant clinical trials; level II - evidence derived from at least one well-delineated randomized controlled trial; level III - well-delineated clinical trials without randomization; level IV - well-delineated cohort and case-control studies; level V - systematic review of descriptive and qualitative studies; level VI - evidence derived from a single descriptive or qualitative study and level VII - opinion of authorities or report of

expert committees. The evidences belonging to levels I and II are considered strong, from III to V moderate evidence and VI and VII weak evidence⁽¹²⁾.

As for the biological activities of *J. gossypifolia* L., they were allocated in six thematic categories. Thus, for the analysis processing, the results were organized in two tables. The first one shows the characterization of the studies, containing in this item the data referring to the title / period, type of study / level of evidence, country and year of publication. While the objectives, biological activities and sample (n) are arranged in the second table. For better understanding, the biological activity was distributed in the following categories: 1) cicatrizant activity, 2) toxic, 3) anti-inflammatory, 4) healing / anti-inflammatory, 5) healing / toxic, and 6) anticoagulant, antioxidant and toxic.

RESULTS

a) Characterization of the studies

According to Table 1, the majority (62.5%) was published in Portuguese and 6 (37.5%) in English. Despite this, only one study (6.3%) was Indian and 15 (93.7%) were Brazilian, six from the state of Maranhão, followed by four from Rio Grande do Norte, three from Paraíba, one from Piauí and another one of Pernambuco. As to the period of publication of the articles, five (31.2%) were published in 2006, and the most recent and only publication in 2016 represents 6.2% of the sample. Articles are listed alphabetically

Regarding the type of study / corresponding level of evidence (Table 1), 13 (81.2%) of the articles are experimental with level of evidence VI and three (18.7%) are reviews with level of evidence V.

b) Thematic categories, according to biological activity

The details of the objectives of the selected studies are presented in Table 2. It is also observed that seven (43.7%) of the studies refer to the thematic category, toxic activity, five (31.2%) to the cicatrizant, two (12.5%) to anti-inflammatory, one (6.2%) to healing / anti-inflammatory, one (6.2%) cicatrizant / toxic and one (6.2%) to anticoagulant, antioxidant and toxic.

DISCUSSION

Of the 16 articles in the study, most are written in Portuguese, national origin and come from the northeast region. These data corroborate with a study, which describes *J. gossypifolia* as a medicinal plant known in Latin America and India, with widespread distribution in the Brazilian northeast, for its compatibility with high temperatures. It belongs to the family Euphorbiaceae, considered the third with the greatest number of plant species

TABLE 1 – Distribution of studies according to author (s), according to title / journal, type of study / level of evidence, place and year of publication. Maceió-AI, 2017, n = 16

No	Title/ Journal	Type of study / level of evidence	Country	Year
1.	Action of the extract of <i>J. gossypifolia</i> L. (purple top) on the healing of colonic anastomosis: experimental study in rats. <i>Acta Cir Bras.</i>	Experimental/VI	Brazil	2006
2.	Anti-inflammatory activity of <i>J. gossypifolia</i> L. leaves in albino rats and Wistar rats. <i>JSIR</i>	Experimental/VI	India	2011
3.	Evaluation of the use of crude extract of <i>J. gossypifolia</i> L. in the healing of cutaneous wounds in rats. <i>Acta Cir Bras.</i>	Experimental/VI	Brasil	2006
4.	Phytomedication of <i>J. gossypifolia</i> L. on healing of sutures in the ventral abdominal wall of rats. <i>Acta Cir Bras.</i>	Experimental/VI	Brasil	2006
5.	Histopathological evaluation in rats after acute treatment with the ethanolic extract of aerial parts of <i>J. gossypifolia</i> . <i>Rev. bras. farmacogn.</i>	Experimental/VI	Brasil	2008
6.	Chronic toxicologic study of the ethanolic extract of the aerial parts of <i>J. gossypifolia</i> in rats. <i>Rev. bras. farmacogn.</i>	Experimental/VI	Brazil	2012
7.	Comparative study of gastrorrhaphy healing with and without the use of the extract of <i>J. gossypifolia</i> L. (purple top) in rats. <i>Acta Cir Bras.</i>	Experimental/VI	Brazil	2006
8.	Study of the healing of sutures in the urinary bladder of rats with and without the use of crude extract of <i>J. gossypifolia</i> L. intraperitoneal. <i>Acta Cir Bras.</i>	Experimental/VI	Brazil	2006
9.	Acute toxicological study of the ethanolic extract of aerial parts of <i>J. gossypifolia</i> L. in rats. <i>Rev. bras. farmacogn.</i>	Experimental/VI	Brazil	2008
10.	Phytochemistry and biological activities of the genus <i>Jatropha</i> : mini-review. <i>Visão Acadêmica</i>	Review /V	Brazil	2010
11.	Genotoxic potential of leaf extracts of <i>J. gossypifolia</i> L. <i>Genet Mol Res</i>	Experimental/VI	Brazil	2016
12.	Genotoxic potential of the latex from cotton-leaf physicnut (<i>J. gossypifolia</i> L.). <i>Genet Mol Biol.</i>	Experimental/VI	Brazil	2015
13.	In vitro anticoagulant and antioxidant activities of <i>J. gossypifolia</i> L. (Euphorbiaceae) leaves aiming therapeutical applications. <i>eCAM.</i>	Experimental/VI	Brazil	2014
14.	<i>J. gossypifolia</i> L. (Euphorbiaceae): A review of traditional uses, phytochemistry, pharmacology and toxicology of this medicinal plant. <i>eCAM</i>	Review /V	Brazil	2014
15.	Therapeutic possibilities and toxicological risk of <i>J. gossypifolia</i> L.: a narrative review. <i>Rev. bras. farmacogn.</i>	Review/V	Brazil	2010
16.	Systemic and local anti-inflammatory activity of aqueous leaf extract from <i>J. gossypifolia</i> L. (Euphorbiaceae). <i>Int J Pharm Pharm Sci</i>	Experimental/VI	Brazil	2014

TABLE 2 – Distribution of studies according to author (s), according to objective, biological activity and sample of evidence. Maceió-AI, 2017, n = 16

No.	Objective	Biological activity	Sample (rats)
1.	To analyze the action of <i>J. gossypifolia</i> L. (purple top) on the healing of colonic anastomosis in rats.	Cicatrizant and Anti-inflammatory	40
2.	Evaluation of the local and systemic anti-inflammatory activity of <i>J. gossypifolia</i> L. using animal models.	Anti-inflammatory	6
3.	To evaluate the morphological aspects of the cicatricial process of open cutaneous wounds of rats using the crude extract of <i>J. gossypifolia</i> L.	Cicatrizant	60
4.	To assess the influence of the intraperitoneal administration of <i>J. gossypifolia</i> L. on the healing of ventral abdominal wall sutures of rats, observing macroscopic, tensiometric and microscopic aspects.	Cicatrizant	40
5.	Search for histopathological changes in viscera of rats under acute treatment with the Ethanol Extract (EE) of <i>J. gossypifolia</i> L.	toxic	24
6.	To evaluate the chronic toxicity of the Ethanol Extract (EE) of <i>J. gossypifolia</i> L., Euphorbiaceae, in rats, in order to generate data to analyze the risk / benefit relationship of a possible therapeutic use of this species.	toxic	40
7.	To evaluate the use of the crude extract of <i>J. gossypifolia</i> L. in the cicatrization of gastrorrhifias in rats.	Cicatrizant	40
8.	To compare the macroscopic and histological alterations provided by the use of the crude extract of <i>J. gossypifolia</i> L. intraperitoneal in the healing of sutures performed in the urinary bladder of rats.	Cicatrizant	24
9.	Evaluation of the acute toxicity of Ethanol Extract (EE) from aerial parts of <i>J. gossypifolia</i> L.	toxic	ND
10.	Emphasize the importance of this genus and stimulate new lines of research in the investigation of bioactive compounds.	Cicatrizant	NA
11.	To evaluate the cytotoxic, genotoxic and mutagenic effects of ethanolic and aqueous extracts of leaves of <i>J. gossypifolia</i> , using the <i>Allium cepa</i> test system.	toxic	NA
12.	To analyze the toxic, cytotoxic and genotoxic effects of latex of <i>J. gossypifolia</i> by means of the test system of <i>Allium cepa</i> .	toxic	NA
13.	The evaluation of the anticoagulant and antioxidant activity of the leaves of <i>J. gossypifolia</i> , seeking new therapeutic uses for this plant.	Anticoagulant, antioxidant and toxic	ND
14.	To provide an update on the general overview of traditional uses, as well as the phytochemistry, pharmacology and toxicity data of the species <i>J. gossypifolia</i> L.	toxic	ND
15.	To present an up-to-date source of information to those interested in developing research that helps in the complex evaluation of the risk / benefit relationship of the therapeutic use of <i>J. gossypifolia</i> and, consequently, the promotion of rational use of this plant (and derivatives) in folk medicine	Cicatrizant and toxic	20
16.	To evaluate the anti-inflammatory activity of the aqueous extract of the leaf of <i>J. gossypifolia</i> and to characterize its phytochemical constituent.	Anti-inflammatory	24

ND - Not defined; NA - Not applicable, because it refers to an in vitro study.

in the caatinga, agricultural potential in the production of biofuel, animal food and medicinal use ⁽¹³⁾.

The caatinga biome is unique in its heterogeneity, with native communities of low purchasing power, which hold a wide popular pharmacopoeia. In this aspect, it was identified in a study that the families Fabaceae, Anacardiaceae and Euphorbiaceae of this region exhibit great potential for bioactive compounds. Researchers in this study have suggested ethnopharmacological investigations with these families in the search for new phytotherapies as a strategy for the sustainable use of natural resources and to boost the region's economy through local productive arrangements (APL) for the cultivation of medicinal plants ⁽¹⁴⁾.

Thus, it can be inferred from the literature that, since the Northeast is a region that still lacks proper health-care and is a geographic space in which *J. gossypifolia* proliferates easily, most studies have been carried out by researchers from the northeast of Brazil.

As for the period of publication of articles, the highest percentage (31.2%) occurred in 2006, decreasing in the following years, until 2016. Thus, it is observed that there is a significant deficit in the quantitative of scientific productions on the biological activities of the purple top, as *J. gossypifolia* is known in Brazil. It can be inferred that the scarcity of publications on the subject is due to the low expressiveness of the caatinga, in the national productive sector. However, it is necessary to stimulate the continuation of studies to obtain their biological properties with low or no toxicity ⁽¹⁵⁾.

J. gossypifolia has been popularly used to treat various conditions such as rheumatism, ulcers, hydrops, hypertension, wound healing, gingival infections, stomach pain, eczema, diarrhea, hemorrhage, diabetes, cancer and fever. Comparative study with and without the use of extract of this species in the healing of gastrorrhafias in rats demonstrated that the extract contributed to the favoring of the cicatricial process, increasing its resistance to the test of resistance to atmospheric air insufflation. On the third day of postoperative and in its microscopic analysis, it was observed that it favored cicatrization, increasing the coaptation of the borders and reducing the acute inflammation on the seventh day of observation ⁽¹⁷⁾.

Another study that evaluated the action of the crude extract on open cutaneous wounds of rats showed a comparative improvement in the healing of the lesions treated with the extracts. The healing properties of *J. gossypifolia* were also investigated by the topical application of the crude extract to cutaneous wounds of rats, with positive results for this biological activity ⁽¹⁸⁾.

The mouse is routinely used as an experimental model for the study of healing and testing of plant extracts and drugs on the skin, since it has already been standardized by many studies, which corroborates with the

findings of this work, since in the experimental studies that constituted significant part of the sample, the rat is predominantly the most commonly used animal model, due mainly to small size, easy acquisition and standardization regarding age, weight, sex, housing, feeding, cleaning care and experimental manipulation ⁽¹⁹⁾.

An experimental study with rats showed the action of the extract of *J. gossypifolia* on the healing of colonic anastomosis, concluding that there was a positive influence on the strength of the anastomosis on the third postoperative day and the occurrence of small favor in the cicatricial process ⁽²⁰⁾. However, a study evaluating the healing of sutures in the bladder of rats did not identify the healing effect of said extract, applied intraperitoneally ⁽²¹⁾. Similarly, another study that evaluated the phytotherapeutic action of this plant did not show a significant improvement in the cicatricial process of suture in the abdominal wall of rats at the concentration of 100 mg / mL, being administered the dose of 100 mg / kg of weight ⁽²²⁾.

Healing is a complex biological process that involves cellular, physiological and biochemical events, covering distinct phases, such as inflammation, chemotaxis, cell proliferation, differentiation and remodeling, and is essential to maintain the integrity of the organism ⁽²³⁾.

The anti-inflammatory activity of *J. gossypifolia* was confirmed against TPA-induced edema (12-Otetradecanoylphorbol-13-acetate) in rat ears and against the response of carrageenan-induced paw edema ⁽²⁴⁾. Research on the systemic and local anti-inflammatory activity of the aqueous extracts of *J. gossypifolia* described the presence of flavonoids and phenolic compounds in this plant. Such metabolites have several pharmacological activities, mainly anti-inflammatory. The action of flavonoids is relevant because they are an alternative option for the treatment of inflammatory processes ⁽²⁵⁾.

A cytotoxic study, related to the ethanolic extract of this plant species, identified signs of neurological, gastrointestinal and pulmonary damage in animals treated with oral doses, confirming that these data are mainly associated with the high percentage of lethality at doses close to the therapeutic levels indicated chronic toxicity ⁽⁹⁾. On the other hand, another research on the acute toxicity of *J. gossypifolia* showed that the acute treatment of Wistar rats with the ethanolic extract of aerial parts of this plant promoted minor histopathological changes in liver and lung of animals treated with the highest experimental dose (5 g / kg), confirming that the product has relatively low acute oral toxicity ⁽²⁶⁾.

However, the absence of in vitro cytotoxicity against human cells was demonstrated when it demonstrated a relatively low acute toxicity, proving to be a good source of antioxidant compounds, being this free radical scavenging capacity attributed to the presence of flavonoids ⁽²⁷⁾.

The limitation of this study is the low occurrence of ethnopharmacological and preclinical studies that explore the biological activities of *J. gossypifolia* more extensively in the field of folk medicine.

CONCLUSION

Publications on biological activities of the purple top on wound treatment have been tenuous, however, the results presented in this review demonstrate the widespread use of the plant species *J. gossypifolia* in folk medicine and suggest potential for the development of new drugs and / or biotechnological products. However, as regards its biological activities, additional studies with a chemical, pharmacological and clinical approach are

necessary on this plant, to better elucidate the mechanisms of action of its bioactive compounds. It was also observed that the investigations evidenced the anti-inflammatory action of the purple top, however, its healing and cytotoxic potentials were not fully elucidated, since there were divergent results between studies with similar approaches.

These data provide subsidies for the continuation of studies regarding the popular use of the purple top, mainly in the treatment of wounds, pain and inflammation, so that it can be used safely for the purpose of promoting the health of users in Primary Care, according to the National Policy of Integrative and Complementary Practices in SUS.

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