Review Article

Phytochemistry and Ethnopharmacology of *Jatropha gossypiifolia* L. (Euphorbiaceae): A Review and Future Direction

ABSTRACT

Background: The Plant of *Jatropha gossypiifolia* is known for their many biological activities including anticoagulant, antihypertensive, anti-inflammatory, antibacterial, antiviral, antifungal and other.
Aim: To provide update knowledge on the phytochemistry, ethnopharmacology, toxicology and some medically interesting activities *Jatropha gossypiifolia*.
Study Design: Multidisciplinary advanced bibliographic surveys and dissemination of the resulted knowledge.
Results: The literature review shows that *Jatropha gossypiifolia* has antibacterial, antiviral properties on different types of viruses. Different parts of the plant such as leaves, roots, latex, seeds, fruits and other parts have been reported to have different compounds which have interesting bioactivities and medicinal properties.
Conclusion: The present mini-review can therefore help inform future scientific research towards the development of anti-inflammatory, anti-cancer, anti-Hepatitis B virus, and anti-Covid-19 herbal drugs of relevance as well as nutraceuticals from *Jatropha curcas* for the improvement of human health and wellbeing using reverse pharmacology approach.

Keywords: Jatropha gossypiifolia, Pharmacology, Ethnopharmacology, antiviral

1. INTRODUCTION

Introduction *Jatropha gossypiifolia* is a plant with multiple uses in traditional medicine. The genus *Jatropha* has been reported in a number of reviews covering various aspects, for example, phytochemistry, pharmacology and medicinal properties [1,2], diterpenes [3], toxicity [4], nutritional, biochemical and pharmaceutical potential of proteins [5] and chemical constituents [6]. Although a few reviews have been published recently on the medicinal benefits and applications of *J. gossypiifolia* species [7,8], there is still a critical need for a comprehensive review that covers the therapeutic (antiviral) and toxicological potential of this plant species. This review attempts to bring together available information on the botany, traditional uses, phytochemistry, pharmacology, and toxicity of *J. gossypiifolia*. It is hoped that this review can provide a scientific basis for explaining the ethnopharmacological use, especially the antiviral activity of *J. gossypiifolia*.

2. METHODOLOGY

The literature review was conducted on *J. gossypiifolia* during searches on different databases such as PubMed, PubMed Central, Scielo, DOAJ, Google scholar and Science Direct. The scientific names of *J. gossypiifolia,* compounds, biological activities and toxicology of the plants of interest were used as keywords. The chemical structures of the natural compounds from *J. gossypiifolia* were drawn using ChemBioDraw Ultra 12.0 software

3. RESULTS AND DISCUSSION

3.1. TAXONOMY AND BOTANICAL DESCRIPTION

The genus *Jatropha* belongs to the *Euphorbiaceae* family. Native to tropical America, *Jatropha* species are now widespread throughout the tropical and subtropical regions of Asia and Africa, where they are traditionally used to treat several ailments. The name "Jatropha" has its roots in the Greek language and its meaning is associated with the medicinal purpose. From the Greek, "jatros" means "doctor" and "trophe" means "food". Several species of this genus have been studied for their pharmacological and chemical properties, including *Jatropha curcas, J. isabellei, J. gossypiifolia, J. integerrima* and *J. macrorhiza* [9].

Despite the importance of the *Jatropha* genus, only a few species have been chemically evaluated. The genus is known to be an important source of secondary metabolites, such as terpenes, which are fairly well known in this genus [10]. In general, studies on the chemical composition of Jatropha species have led to the identification of monoterpenes, sesquiterpenes, diterpenes, triterpenes, cyclic peptides, lignans, neolignans, sesquineolignans, flavonoids, coumarins, coumarino lignans, alkaloids, and eudesmenoic acids.

The Euphorbiaceae family, which is considered the largest group of angiosperms, has about 8,900 species in 350 genus and 6 subfamilies worldwide. These species are found specifically in climatic conditions. Among the main genera belonging to this family is *Jatropha*, which belongs to the subfamily Crotonoideae, the clan Jatropheae, and is represented by about 250 species. The current family is widely appropriate in tropical and subtropical areas of Asian and African countries. The subgenus Jatropha has by far the widest distribution, with specimens mainly in Asia, India, Southeast Asia, Sri Lanka, North America in the South Pacific and Africa. Metabolites, antioxidants, lignoids, as well as other polyphenols have been found in different foods derived from various components of the plant. Antidiabetic [11,12], antibacterial, reducing, breast cancer aiding, and bashing activities stand out among the key activities frequently read for this organism (counting different types of mixtures from various parts of the plant). These activities endorse a portion of all its common uses [13,14]. Many polyphenols have also been used as specific secondary metabolites to provide defense against harmful ultraviolet radiation from pathogens. The antioxidant properties of polyphenols play a major role in strengthening the immune system and serve to combat various diseases such as blood sugar, cardiovascular and others [15].

J. gossypiifolia, also known as False castor, Cotton-leaf medicinal, Wild medicinal or Red medicinal, is a plant of the Euphorbiaceae family with purple and yellow inflorescences.

The species appears as an erect plant that can grow up to 1.5 meters high. Its succulent stems contain a white latex

The leaves, only present at the end of the stems, have a three-lobed blade. They present glandular hairs on their margin as well as on their long petiole. The young leaves, sticky and of a deep purple, become light green with time.

The flowers are grouped in clusters at the end of the stems. They measure one centimeter in diameter and have 5 obovate purple petals.
The fruits are oblong capsules with 3 compartments that can be seen from the outside. Once reached maturity, the fruit explodes by projecting its seeds to more than 3 meters. They can thus grow not far (autochory), or be carried by the animals (zoochory). The species is very resistant because the seeds can remain viable in the ground during 10 years, and their germination can be encouraged by the fires.

Figure 1: Leaf, fruit and flowers of *Jatropha gossypiifolia* L.

3.2. ETHNOBOTANICAL

Many of the restorative properties of *J. gossypiifolia* species are taken into account in conventional medicine. Some properties identified with *J. gossypiifolia* are also regular to different types of *Jatropha* species, where human and veterinary uses are represented. Various parts of the plant are used, for example, leaves, stems, roots are used in various types of preparation (mixture, decoction and maceration, among others), by various courses and structures (oral, topical, etc.). The most frequent information mentions calming, antidiarrheal, antiophidic, painkiller, antipyretic, antimicrobial, recuperative, antianemic, antidiabetic and antihemorrhagic activities, among many different models [16,17]. Some properties are attributed to explicit parts of the plant, while others are attributed to various parts. The use of the leaves and/or aerial parts of this plant as an anti-inflammatory, analgesic, healing and anti-infective in several skin diseases is a common practice in many countries. The use of baths or dressings with this plant species is frequently reported in traditional medicine.

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3.4. MICROSCOPY STUDY

A pharmacognosy study by microscopy method, one of the simplest and cheapest methods to establish the correct identity of raw materials was carried out to determine the macro and microscopic characters of the leaf and stem of *J. gossypiifolia* Linn. Physicochemical analysis of parameters such as drying loss, total ash, water-soluble ash, acid insoluble ash, sulfated ash, and extraction values in different solvents (petroleum ether, toluene, ethyl acetate, methanol and water) was carried out. A qualitative phytochemical analysis and a fluorescence analysis were also performed. From the results found that the leaves have a cordate base, a sarmentate glandular margin, a subacute apex and both surfaces are very rough with stiff surface hairs. Internally, there are anomoctic stomata, epidermis, parenchymal tissue, secretory glands, calcium oxalate crystals in clusters, simple starch grains, glandular trichomes and simple covering trichomes, dispersed as such throughout the epidermal cells or attached to them. The majority of glandular trichomes had a uniseriate stalk with 4 or 5 cells in the petiole region [18].

3.5. PHYTOCHEMISTRY

Phytochemical analysis of the powder revealed the presence of different phytoconstituents such as alkaloids, tannins, saponins, phlobatanins, flavonoids and triterpenes were present in maximum amounts. In the physicochemical analysis, all the parameters were present within the limits. The maximum extractive value was in the polar solvent methanol and water.

The phytochemical analysis revealed the presence of alkaloids, flavonoids, proteins, tannins, steroids and/or terpenoids and sugars.

The aqueous extract of *J. gossypiifolia* leaves was prepared by decoction and phytochemical analysis revealed the presence of sugars, alkaloids, flavonoids, tannins, terpenoids and/or steroids and proteins [19].

The methanolic leaf extract contains cardiac glycosides, steroids, triterpenes, tannins and flavonoids [19].

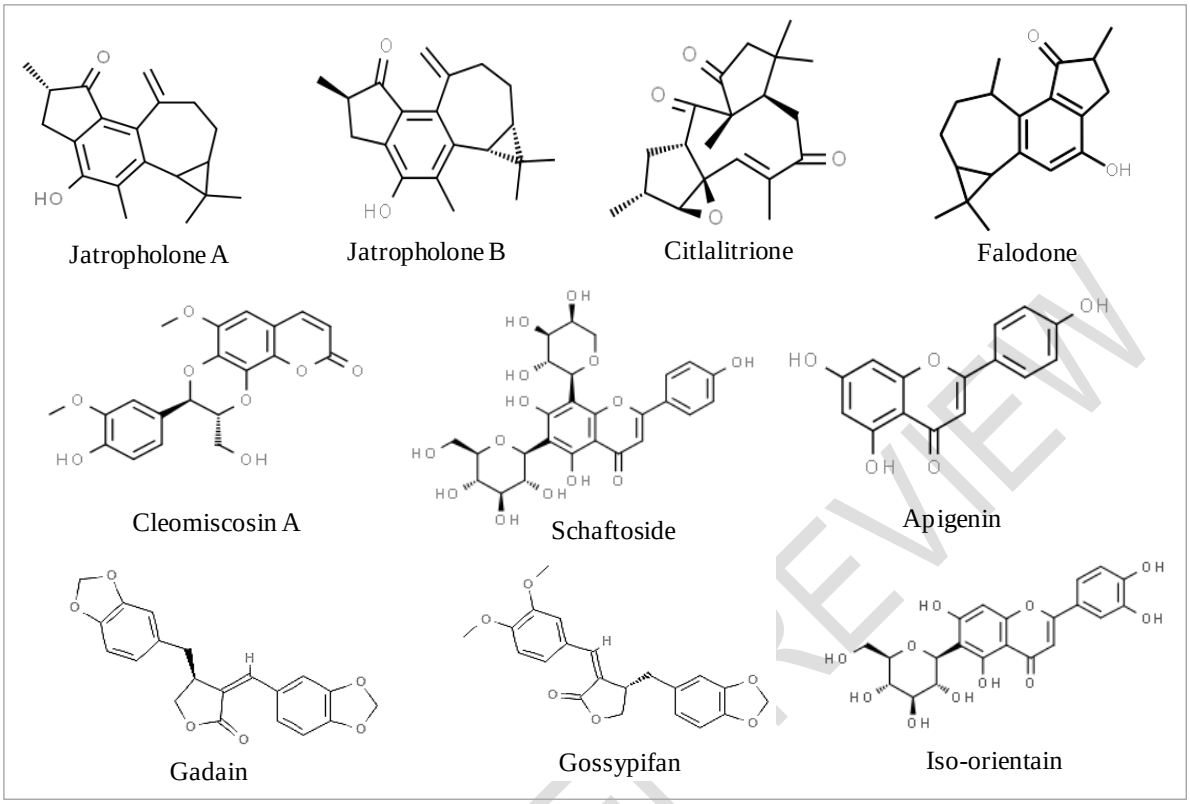

Figure 2: Some main compounds isolated in *J. gossypiifolia*

Pharmacological studies of the Jatropha genus have demonstrated correlations between secondary metabolites and several bioactivities, such as antileishmanial [20], antimicrobial [21], antihelminthic [22], cytotoxic [23], antiespasmodic [24], antitumor, antioxidant, anagelian [25] and gastroprotective activity [26].

Jatropha species, including *J. gossypiifolia* is hardly studied regarding biological properties. Studies demonstrating the natural capacity of fluid extracts are scarce until now. Among the main properties considered, there are activities such as antihypertensive, anticancer, antimicrobial, anti-inflammatory, etc.

3.7 ANTICANCER ACTIVITY

Jatrofolianes A (1) and B (2) are two highly modified lathyran diterpenoids isolated from *Jatropha gossypiifolia*. Jatrofolianes A (1) includes an unusual transannular 1,3-dioxolane moiety, forming a unique 5/6/5/8/3 ring system, while Jatrofolianes B (2) has a novel 10, 11:13,14-diseco-lathyran backbone with a 12-member macrocyclic lactone ring. Their structures were determined by spectroscopic analysis, quantum chemical calculations and single crystal X-ray diffraction. Both showed significant multidrug resistance (MDR) reversal activity to HepG2/ADR and HCT-15/5-FU cancer cells at 10 μM [27].

3.8 INSECTICIDAL ACTIVITY

Paul-André et al. [28] reported in the literature that the cassava mealybug *Phenacoccus herreni* (*Sternorryncha*: Pseudococcidae) is a pest of cassava, *Manihot esculenta* Crantz

(Euphorbiaceae), in South America. The proteins, which represent direct gene products, are prime candidates in genetic engineering manipulations for host plant resistance. *J. gossypiifolia* L. (Euphorbiaceae), a plant species known to contain insect-toxic proteins, exhibited insecticidal properties to *P. herreni*. The toxic compounds consisting of proteins of approximately 101.02 kDa appeared to be mainly localized in mature leaves. Further studies are needed to identify the proteins and ensure that they are not toxic to mammals.

The action of the stem, leaves and fruit of extracts of *J. gossypiifolia* on *Biomphalaria glabrata* showed by analyzing the survival, feeding capacity and oviposition capacity. The results obtained from the extracts showed that by macerating the parts of the plant in ethanol at 92%, which were then evaporated until obtaining a dry residue and make the phytochemical study. They studied the molluscicidal activity on *B. glabrata* using the procedures recommended by WHO (1965). The amount of food ingested and oviposition were measured in each experiment. *J. gossypiifolia* leaf extract was found to be a potent molluscicidal agent, causing 100% mortality of *B. glabrata* even at the lowest concentration tested, 25 ppm. With regard to the fruit extract, a variation in mortality was observed, depending on the concentration used (100, 75, 50 and 25 ppm) i.e. dose dependent. Snails that were in contact with the fruit extract had a significant reduction in feeding and embryo number compared to the control. The stem extract did not exhibit molluscicidal activity or influence the feeding and oviposition abilities of B. glabrata at the concentrations tested. The leaf and fruit extracts of *J. gossypiifolia* studied showed molluscicidal effect and may be sources of useful compounds for schistosomiasis control [29].

3.9 ANTICOAGULANT, ANTIOXIDANT ACTIVITIES AND TOXICITY

J. gossypiifolia L. (Euphorbiaceae) is a medicinal plant widely used in traditional medicine. The leaf teas are popular as an antithrombotic agent and the branches are frequently used as a "thick blood" agent. Considering that the anticoagulant activity associated with antioxidant properties could be beneficial for various cardiovascular diseases. The phytochemical analysis was performed by thin layer chromatography (TLC) and spectrophotometric quantification of sugars, proteins and phenolic compounds. The anticoagulant activity was evaluated by prothrombin time (PT) and activated partial thromboplastin time (aPTT) tests. The ability to act in the fibrinolytic system (fibrinolytic and fibrinogenolytic activities) was also evaluated. Antioxidant activity was assessed by total antioxidant capacity, reducing power, copper chelating activity, iron chelating activity, hydroxyl radical scavenging activity and superoxide radical scavenging activity. Potential toxicity was assessed by the hemolytic assay and the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay in HEK-293 cells. Results: EC showed significant anticoagulant activity in the aPTT assay, whereas no action was observed in the PT assay, suggesting a preferential action toward the intrinsic and/or common pathway of coagulation. No effect was observed in the fibrinolytic system. Using the aPTT assay, it was observed that the residual aqueous fraction (RA) was the most active, being twice as active as CE. RA showed a very significant antioxidant activity in all models tested, comparable or even superior to that of CE. Regarding safety, CE and RA did not produce significant cytotoxicity in both tests employed. Phytochemical analysis revealed the presence of alkaloids, flavonoids, proteins, tannins, steroids and/or terpenoids and sugars. The EC and RA possess significant anticoagulant and antioxidant activity and absence of cytotoxic

effect *in vitro*, thus showing the potential of the plant, especially of the RA fraction, as a new source of bioactive molecules for therapeutic purposes, with particular emphasis on the treatment of cardiovascular diseases [30].

The activity of cancer prevention agent by concentrates of *J. gossypiifolia* was evaluated by one of the researchers. The high phenol and flavonoid content of the leaves prompted the researchers to evaluate the anticancer activity of the leaves. DPPH free radical and nitric oxide research techniques were used to examine the potency of the cancer prevention agent in vitro of methanol, ethyl acetic acid, aqueous extracts, showing positive results. The authors attributed the antioxidant property against free radicals to flavonoids. Then, the analysis indicated that various extracts (petroleum ether, chloroform, ethyl acetic acid and n-butanol) of the whole plant of *J. gossypiifolia* had not shown cancer preventing activity in the research with DPPH assay, whole cell enhancement limit and lipid peroxidation tests. Among them, the ethyl acetic acid extract is the most reactive, which corresponds to the highest concentration of phenolics and in correlation with the different extracts [30].

3.10 ANTIHYPERTENSIVE EFFECT

The roots of *J. gossypiifolia* are known for their uses, the hypotensive and vasorelaxant impacts of the ethanolic concentrate of the pieces of the plant remained tested by Abreu et al. The analysis revealed that the concentrate, in a partially subordinate way, created a decrease in systolic pulse in conscious normotensive subjects. Such a hypotensive effect can be attributed to its vasorelaxant activity, as it created a relaxing effect subordinate to the focus in rodents whose endothelium was loaded with norepinephrine or calcium [31]. In addition, it impeded, in a punctual and noncompetitive manner, the contractile response triggered by norepinephrine in a similar plane.

3.11 HYPOTENSIVE EFFECT

A study was done to investigate the hypotensive effects of ethanolic extract (EE) of *J. gossypiifolia* L. Oral administration of EE (125 or 250 mgkgy1 day) caused a significant dose-dependent reduction in systolic blood pressure. Concentration-response curves y1 to norepinephrine (NE) or Ca^{2+} ion was shifted nonparallel by 2q to the right, and maximal contractile responses were depressed in a concentration-dependent manner by EE (0.1 or 0.5 mgyml) in the endothelium-deprived mesenteric artery. Cumulative additions of EE (0.1-30 mgyml) elicited a concentration-dependent relaxing response in the endothelium-deprived mesenteric artery precontracted with NE or Ca^{2+}. In conclusion, our results showed that EE from *J. gossypiifolia* L. can induce hypotension, orally, in conscious normotensive rats and vasorelaxant activity on rat mesenteric rings precontracted with NE or Ca^{2+} [32].

3.12 ANTI-INFLAMMATORY PROPERTIES

Many important current uses of *J. gossypiifolia* are identified with a provocative procedure. One researcher demonstrated that the methanolic concentrate of the leaves of the species used has an intense and consistently soothing melting action. The concentrate, at oral doses of 445 and 1050 mg/kg, has the potential to limit intense carrageenan-induced paw edema in rodents and, at oral doses of 55 and 105 mg/kg, prevents the incessant development of cotton ball-induced granulomas in rodents [33]. In addition, *J. gossypiifolia* leaf glue

demonstrated a critical decrease in TPA-triggered close incendiary changes in the rodent ear edema prototype. In another review, pain alleviation and relief effects in animals, particularly mice, were demonstrated by benzene and petroleum ether mixtures of *J. gossypiifolia* extracts. Only the separate bioethanol produced significant pain relief in the Eddys gas plate and dorsal fin experiments and a relaxing movement in the carrageenan-induced paw edema when administered at 240 and 230 mg/kg/day for 12 hours, depending on the primary outcome. The calming action of *J. gossypiifolia* bark was also demonstrated in carrageenan-induced paw edema in rodents. The anti-inflammatory properties of the extract of the plant *Rostachys japonicus A. Berger* (*O. japonicus*) were also studied, with the plant extracted in 95% ethanol, and the extract was then fractionated by subjecting it to a series of organic solvents, including n-hexane (hexane), dichloromethane (DCM), ethyl acetate (EtOAc), n-butanol (BuOH), and water (H_2O). The anti-inflammatory properties of the extract were then determined on RAW 264.7 cells stimulated with lipopolysaccharide. Western blotting was also performed to analyze the capacity of transcription factors and inflammatory mediators [34]. But also, the anti-inflammatory effects of *Phellinus linteus* were determined on RAW 264.7 cells stimulated by lipopolysaccharide [35]. In the literature it has been reported that using the technique of in vitro adjustment of human red platelet layer, one of the researchers showed that ethyl alcohol and water extracts of *J. gossypiifolia* leaves possess attenuating movement. According to the creators, since human red platelet films resemble segments of the lysosomal layer, the hypotonicity-induced lysis backlash of these cells could be taken as a measure to assess the attenuating activity of the mixtures. The pain-relieving property of the methanolic extract of *J. gossypiifolia* leaves was evaluated in the acid corrosion-initiated wriggling test in mice, where an exceptionally remarkable restraint was found of 68.58 and 66.15% at 200 and 405 mg/kg oral portions, individually.

The study carried out on topical anti-inflammatory activity of the aqueous extract of *J. gossypiifolia* leaves was conducted with the objective of developing a safe and effective plant gel with anti-inflammatory potential. First, the acute topical anti-inflammatory activity of *J. gossypiifolia* extract was evaluated in ear edema induced by a single application of croton oil in mice. Next, a polaxamer-based gel containing *J. gossypiifolia* extract was developed, physicochemically characterized and evaluated in the same inflammation model to assess whether incorporation of the extract into the gel would affect its anti-inflammatory potential. The best formulation was then tested in ear edema induced by multiple applications of croton oil in mice to evaluate its chronic anti-inflammatory potential. Inflammatory parameters assessed included edema, nitrite concentration, honeyoperoxidase (MPO) activity, and oxidative damage in lipids and proteins. Finally, a skin irritation/corrosion test in mice was performed to evaluate the safety of the developed gel. Phytochemical characterization of the *J. gossypiifolia* extract was performed by high performance liquid chromatography with diode array detector (HPLC-DAD). *J. gossypiifolia* showed significant acute anti-inflammatory activity in the ear edema model, and this activity was significantly increased when equivalent amounts of the extract were applied and incorporated into the developed polaxamer gels. The gels containing different amounts of the extract significantly reduced the levels of edema, nitrite and MPO enzyme in

the ears of mice, with an intensity similar to that of the standard anti-inflammatory drug dexamethasone [36].

3.13 PROPERTIES AND HEALING ACTION

In the literature it has been reported that the healing activity of the crude ethanol concentrate of *J. gossypiifolia* was evaluated in the recovery by suturing of the dorsal abdominal volume of rodents. The concentration was controlled by intralesional insertion of 410 milligrams into the pulmonary fossa, resulting in a much more remarkable seizure on the normally obvious evaluation, as well as evaluation of the more visible strain and pseudovascular. In any case, a more remarkable incendiary procedure was likewise observed, and other histological levels were similar to the reference group, showing that overall, the concentrate introduced injury recovery properties in the occasion model. Another analysis was to make the restorative activity of the unrefined hydro-ethanolic concentrate of the leaves of *J. gossypiifolia* in the procedure of recovery of the sutures performed on the bladder of rodents, and the comparative results remained introduced, although an improvement was observed in some limits. In general, it was felt that no ideal recovery impact was observed with the organization of a solitary intraperitoneal portion of *J. gossypiifolia* L. In another investigation dissecting the morphological parts of the recovery procedure occurring in open skin wounds in rodents under topical organization of the crude concentrate of *J. gossypiifolia*, the authors also observed a non-appearance of recovery activity, although some histological improvement was demonstrated [36].

However, considering the impact of *J. gossypiifolia* on the colonic anastomosis repair procedure in rodents. One researcher demonstrated that administration of a single 1 mL/kg portion of aqueous alcohol concentrate from flying portions has a significant impact on the healing procedure. Furthermore, Vale et al. reported that ethanolic extract of *J. gossypiifolia* at a single dose of 220 mg/kg intraperitoneally supported the gastrorrhaphy recovery procedure and decreased the intense inflammatory response *in vivo*.

3.14 HEMOSTATIC PROPERTY

Use of *J. gossypiifolia* latex is extended as a hemostatic component to prevent drainage dispersal. The consequences of the whole blood clotting time using Lee and White's strategy, the drainage time using Ivys' technique were completely decreased when the stem latex was presented, which leads to a pro-coagulant movement. Regarding the conceivable component of activity, as a result of the analyses that show the encouraging activity of latex on egg whites, the authors recommend that latex accelerates the thickening elements by bringing coagulation levels into close contact, and then the initiation of the coagulation course incites the age of thrombin and the development of coagulation occurs very quickly compared to the control trial, which took minutes to complete thickening. It is imperative to emphasize that, as far as we can tell, this is the main analysis performed on human models [36].

3.15 ANTICHOLINESTERASE PROPERTY

Acetylcholinesterase inhibitors are commonly used to combat Alzheimer's disease, due to the cholinergic hypothesis. *J. gossypiifolia* had a significant antitumor effect, with an IC_{50} of

0.08 mg/mL in a methanolic extract of leaves [37]. Another study revealed that solubilized plant rubber has the ability to suppress tissue tentatively sensitive to butyrylcholinesterase complex in Dhal marulius, a species of water plane tree.

3.16 CONTRACEPTIVE ACTIVITY

J. gossypiifolia has been evaluated for its anti-fertility activity, as an option in contrast to oral prophylactic compounds [38]. The extract of the leaves of *J. gossypiifolia* changed the significant hormones associated with the main pathway of the estrous cycle, demonstrating its anti-fertility impact on mice. By evaluating at different levels (estrogenic and early abortifacient property), the anti-fertility impact of the extract was again demonstrated.

3.17 TOCOLYTIC ACTIVITY

In view of the ethnopharmacological use of plants as a tocolytic cure, the consequences on calcium-induced uterine smooth muscle contraction of ethanolic extracts were evaluated. The crude extract and, to an advanced degree, the chloroformic division decreased the calcium-induced uterine smooth muscle contractile response, advancing the rightward shift of the total calcium curves, just to decrease the largest withdrawals [39].

In Brazil, a study was done on ethanolic extract and fractions of the aerial parts of *J. gossypiifolia* L. were tested for their effects on calcium-induced contraction of uterine smooth muscle. Strips of rat uterus were incubated with the ethanolic extract (0.1, 0.5, and 1.0 mg/mL), the chloroform fraction (0.25; 0.5 mg/mL), or the aqueous fraction (0.25; 0.5 mg/mL). Ethanolic extract promoted a rightward shift in cumulative calcium curves, and reduced maximal contractions by 27.3% and 80.3% (0.5 and 1.0 mg/mL, respectively). The chloroform fraction inhibited uterine muscle reactivity to calcium, resulting in a reduction in maximal contractile response in 27.4% and 45.1%, respectively. In contrast, these parameters were only slightly reduced in the presence of the aqueous fraction. Overall these results suggest that the ethanolic extract and fractions of *J. gossypiifolia* reduce the calcium-induced contractile response of uterine smooth muscle, corroborating its ethnopharmacological application as a tocolytic remedy [40].

3.18 ANTINEOPLASTIC ACTIVITY

The most remarkable pharmacological properties of *J. gossypiifolia* include antineoplastic activity that is often related to the substance as of lignose and terpenoids. Researchers have reported in the literature that when the ethanolic extract of the roots containing the diterpene jatrophone, showed great restrictive activity *in vitro* against cells obtained from human nasopharyngeal cancer cells and lymphocytic leukemia and *in vivo* against standard, e.g., sarcoma 180 and intramuscular carcinosarcoma Walker 259 [32]. Subsequently, triple naive antitumor activities of jatrophone were isolated via petroleum ether extract removals from *J. gossypiifolia*. Later, two different diterpenes with intense antineoplastic activity were released from *J. gossypiifolia* [40].

3.19 ANTI-PROTOZOAL, ANTIMICROBIAL AND ANALGESIC ACTIVITIES

Extracts of *J. gossypiifolia* L. (Euphorbiaceae) have been used in ethnomedicine for the treatment of various ailments. The biological activity of jatrophone, a macrocyclic

diterpenoid isolated from the roots of *J. gossypiifolia*. Phytochemical studies followed by chromatographic separation of the root bark extract with methanol led to the isolation of a macrocyclic diterpenoid, identified as jatrophone on the basis of mass spectral and NMR data and by comparison with the literature. The isolated compound, jatrophone, was evaluated for its anti-protozoal activity against *Plasmodium falciparum* [D6 (chloroquine-sensitive) and W2 (chloroquine-resistant)], *Leishmania donovani* and *Trypanosoma brucei* strains. Antimicrobial activity was evaluated against selected fungal and bacterial type cultures. Analgesic activity was studied using the acetic acid-induced torsion model and the hot plate model in mice. Cytotoxicity was evaluated against the VERO (monkey kidney fibroblasts) cell line using the neural red uptake method. Jatrophone showed significant antiplasmodial and antileishmanial activities with IC_{50}s of 0.55, 0.52, and <0.4 µg/mL for *P. falciparum* (strain D6), *P. falciparum* (strain W2), and *L. donovani* respectively. Compound 1 was highly cytotoxic to the VERO cell line with an IC_{50} of 0.43 µg/mL. Jatrophone demonstrated a significant analgesic effect with a percentage reduction in acetic acid-induced wrinkles of 54.03% and 66.35% at 5 and 10 mg/kg, respectively. No significant antimicrobial activity was observed against the test organisms [41].

3.20 ANTIVENOM ACTIVITY

Snakebite is a serious public health problem because of its high morbidity and mortality. The main specific treatment available is antivenom serum, which has some disadvantages, such as poor neutralization of local effects, risk of immunological reactions, high cost and difficult access in some areas. In this context, the search for alternative therapies is relevant. Therefore, the objective of this study was to evaluate the antiophidic properties of *J. gossypiifolia*, a medicinal plant used in folk medicine to treat snakebite. The aqueous extract of *J. gossypiifolia* leaves was prepared by decoction and phytochemical analysis revealed the presence of sugars, alkaloids, flavonoids, tannins, terpenes and/or steroids and proteins. The extract was able to inhibit enzymatic and biological activities induced by the venom of the snake *Bothrops jararaca in vitro* and *in vivo*. Blood incoagulability was effectively inhibited by the extract orally. Local hemorrhagic and edematogenic effects were also inhibited, the former up to 56% and the latter up to 100%, in animals treated with the extract orally and intraperitoneally, respectively. The inhibition of the myotoxic action of *B. jararaca* reached almost 100%. From the enzymatic tests performed, it is possible to suggest that the antiophidic activity may be due to an inhibitory action on snake venom metalloproteinases (SVMPs) and/or serine proteinases (SVSPs), including fibrinogenolytic enzymes, coagulation factor activators and thrombin-like enzymes (SVTLEs), as well as on catalytically inactive phospholipases A2 (Lys49 PLA2). The anti-inflammatory activity, at least partially, could also be related to the inhibition of local effects. In addition, protein precipitation and antioxidation activities may also be important features contributing to the presented activity [19].

3.21 ANTICONVULSANT EFFECT

J. gossypiifolia leaves have been widely used for the treatment of epilepsy and infantile convulsions in the ethnomedical practice of northern Nigeria. In this study, researchers examined the anticonvulsant properties of this plant part using established scientific

protocols. Phytochemical screening and acute toxicity assessment of methanolic leaf extract was performed while maximal electroshock induced seizure models in roosters (MEST), pentylenetetrazole (PTZ), strychnine (STN) and 4-aminopyridine (4-AP) were used in mice. The methanolic leaf extract contains cardiac glycosides, steroids, triterpenes, tannins, and flavonoids, while the median lethal dose of the extract was estimated to be 1131 mg/kg. In the anticonvulsant studies, the extract at all doses tested (75, 150, and 300 mg/kg) did not delay the recovery time of convulsed roosters in the MEST model or the mean onset of convulsions in the PTZ and 4-AP models in mice compared to controls. In contrast, the 150 mg/kg extract significantly ($p \leq 0.05$) delayed the mean onset of seizures in mice in the STN model compared with control treatments [42].

3.22 CERCARICIDAL EFFECT

New treatment strategies for schistosomiasis need to be evaluated, as strains resistant to the only available drug, Praziquantel, have already been described. Thus, researchers demonstrated the antiparasitic effects of ethanolic extracts of *J. gossypiifolia* and *Piper arboreum* on cercariae and adult worms of *Schistosoma mansoni*. Bioassays were performed at a concentration of 0-10,000 µg/mL for 0-72 hours. Adult worms were stained with carmine to assess external and internal damage. Chemical screening was performed by high-performance liquid chromatography. *P. arboreum* showed the best cercaricidal effect, with a 100% reduction in viability in only 60 min. *J. gossypiifolia* extract was more effective against adult worms, with a 100% reduction in viability of male and female worms after 12 and 24 h, respectively. *P. arboreum* and *J. gossypiifolia* were equally effective in inhibiting oviposition of *S. mansoni* (93% reduction) and in damaging the internal and external structures of adult worms. Flavonoids were identified in both extracts and phenolic compounds and amides only in *P. arboreum*. Thus, for the first time, ethanolic extracts of *P. arboreum* and *J. gossypiifolia* leaves were shown to be biologically active against cercariae and adult *S. mansoni* worms *in vitro* [43].

3.23 ANTIULCER EFFECT

To evaluate the methanolic extract of *J. gossypiifolia* L. (MEJG) for its gastro-protective activity on Wistar rats. The anti-ulcer activity of MEJG (100 and 200 mg/kg, b.w.) was evaluated using aspirin (200 mg/kg, p.o.) plus pylorus ligation ulcer model and the parameters studied were ulcer index (UI), gastric juice volume, pH, total acidity and total acid production. The same extract was studied by the ethanol-induced ulcer model (80%, 5 mL/kg, intragastrically), and the UI and biochemical parameters were studied. Oral administration of MEJG (100 and 200 mg/kg) significantly ($P < 0.001$) attenuated the ulcer score and anti-secretory parameters (such as gastric content volume, free acidity, total acidity, and total acid production) in rats undergoing pyloric ligation with aspirin. The extract also significantly ($P < 0.001$) attenuated the ulcer score in the ethanol-induced ulcer model and the level of lipid peroxidation and significantly increased the level of glutathione peroxides, catalase and superoxide dismutase activity. MEJG may possess active constituents such as alkaloids, glycosides, flavonoids and terpenes, which may play a major role in the gastroprotective effect in Wistar rats. The present study provides scientific support for the anti-ulcer activities of the extracts of this plant and also affirms the

antioxidant potential of the extracts. However, it corroborates the traditional claims for the use of this drug in the treatment of gastric ulcer [44].

3.24 ANTIDIURETIC AND ANTI-HYPERGLYCEMIC ACTIVITIES

A study was conducted on the antidiuretic and anti-hyperglycemic activities of *J. gossypiifolia* leaf extract on streptozotocin-induced diabetic rats. Methods: Leaves were shade-dried, pulverized and prepared as an extract. 30, 50 and 100 mg/kg of *J. gossypiifolia* leaf extracts were subjected to diuretic and hyperglycemic properties using the established protocol of diuresis and diabetes test on the bladders of emptied rats by gentle compression in the pelvic region and gentle pulling on their tails. 0.5 mL/kg of normal saline, reference drug and test were administered with a single dose of the different drugs, and streptozotocin (STZ) was freshly prepared in 0.1 M citrate buffer with pH 4.5 before induction, the animals were fasted for 24 hours, and a single dose of 45 mg STZ per kg body weight was administered intraperitoneally. Urine and blood samples were isolated from the rats and centrifuged for determination of the renal function test. Diuretic and antidiabetic indices were evaluated according to the adopted method. Results: This study showed that the gradual doses of the extract significantly increased the diuretic effect, especially at 100 mg/kg, the diuretic index increased by 4.29 and urine volume by 5.06 and 10 mg/kg Hydrochlorothiazide by 6.23 mL compared with the untreated group (1.18 mL) ($p < 0.0001$). It also regulated renal function in a homeostatic state. Progressive doses (30, 50, and 100 mg/kg) of the extract significantly reduced the streptozotocin-induced increase in blood glucose level at day 14 (84.00, 60.67, and 42.00 IU/mL) compared with glibenclamide 20 mg/kg and diabetic control (81.67 and 463.00 IU/mL) ($p > 0.05$). In addition, the extract maintained normal body mass index, biochemical and anatomical structure [45].

3.25 ANTIVIRAL ACTIVITIES

The antiviral activities of *J. gossypiifolia* have been reported in several studies (46-47). Different parts of the plant have been exhibiting antiviral activities. Seeds and fruits are reported to have anti Influenza (H1N1) properties. It has also been reported anti-Herpes simplex virus Type-2 (HSV-2) and Para 3 virus activities. The Para 3 virus is a Human Parainfluenza Virus (HPV) that most of the time associated with bronchiolitis, bronchitis, and pneumonia.

3.26 TOXICITY, CYTOTOXIC, GENOTOXIC AND MUTAGENIC EFFECTS

The species of the genus *Jatropha* are well known for their high toxicity. This toxin is mainly caused by the latex or the plants. An electrical wound causes the extraction of latex from the aerial components, which is very corrosive and painful to the mucosa. Toxalbumins, which cause erythropoiesis, phagocytosis and hemolytic anemia, as well as damage to other cell types, are abundant in plants, which also include a matrix of compounds that can cause psoriasis. In particular, somatic symptoms include digestive problems. Initial treatment may also result in heart, cognitive or kidney problems. Some toxicity tests have found *J. gossypiifolia* to be toxic, while others have found it to be non-toxic. To make the correct assumptions about toxicity, one must examine the models used,

the amounts administered, and the types of extraction used (liquid extract and plant extract), among other things. In a laboratory examination of toxicity in cattle, it was found that even a high injection of 40 g/kg of fresh leaf tissue was lethal. Gastrointestinal, respiratory, and disruptive technologies, as well as mild and socially destructive improvements in kidney histology, characterized the pathological picture of the entire laboratory sheep. Adolf et *al*. conducted a study related to the detection of the acute toxicity of *Jatropha* in a sequential manner. The monounsaturated ester of the nuisance 12-deoxy-16-hydroxylphorbol was extracted from the ether of *J. gossypiifolia* by parallel flow spectrometry using a bifold genomic gate. After 24 hours of processing percentages and secondary metabolites, skin irritation behavior in the rodent ear was observed. The methanol extract showed low efficacy in an *in vivo* pharmacokinetic assay using *Artemia salina* larvae. The liquid and diethyl ether fractions of methanol extracts from the aerial parts of *J. gossypiifolia* did not induce exposure in the same species in a previous analysis. Because of the common use of latex as a chemotherapeutic agent for neurological symptoms, the property of collagen from the stem of *J. gossypiifolia* was studied in Wistar rats by applying various doses of synthetic silicone to the incised skin daily for two weeks. According to the authors, rubber application did not generate major differences in metabolic and hematological outcomes [45].

Ethanolic and aqueous leaf extracts of *J. gossypiifolia* were evaluated using the *Allium cepa* test system. In addition, the phytochemical profile of the extracts was also obtained. *A. cepa* bulbs were subjected to different concentrations of the two extracts (0.001, 0.01, 0.1, 1, and 10 mg/mL). Distilled water was used for the negative control and methyl methanesulfonate (4 x 10-4 M) and trifluralin (0.84 ppm) for the positive controls. Mitotic index values at all concentrations of ethanolic extract and at 0.1, 1, and 10 mg/mL of aqueous extract showed a significant decrease. Alterations, such as chromosome adhesion, C-metaphases, chromosome bridges, nuclear buds and micronuclei were verified in both extracts, but loss of chromosomes indicating genotoxic activity was observed only in the ethanolic extract. The presence of micronuclei upon administration of the extracts also indicates mutagenic action at the chromosome level. In the ethanolic extract, aneugenicity appeared to be the main activity, probably due to the activity of terpenes and/or flavonoids, whereas in the aqueous extract, clastogenic activity appeared to be the main activity, probably due to the effect of flavonoids and/or saponins. Thus, it was suggested that extracts of this species should be used with great caution for medicinal purposes [48].

The effect of oral administration of ethanolic extract of *J. gossypiifolia* root and Prednisolone on kidney histology and renal function of albino rats was studied to evaluate the safety and toxicity of this plant as an herbal remedy. The rats used in this study were divided into four groups: I, II, III and IV. Group I served as a control and received only food and water. Groups II, III, and IV were further divided into groups IIa, IIb, IIIa, IIIb, IVa, and IVb. Groups IIa, IIIa, and IVa received 10 mg/kg, 20 mg/kg, and 30 mg/kg body weight of the extract, whereas groups IIb, IIIb, and IVb received 10 mg/kg, 20 mg/kg, and 30 mg/kg body weight of the extract and more than 10 mg/kg body weight of Prednisolone per day, respectively. The animals were sacrificed on days 7, 10, and 14, and their kidneys were collected and processed for histological studies. Their blood was also collected for measurement of serum urea. Photomicrographs of histological sections from rats in groups II, III, and IV revealed changes from the control group, and serum urea levels were

significantly higher in these groups. The histologic changes observed were consistent with glomerulonephritis and included increased urinary space (Bowman), narrowing and distortion of the glomerular tuft, and scarring of the glomeruli. The changes appeared to be both dose and time-dependent, and the administration of Prednisolone as an adjuvant had no ameliorative effect. They concluded that ethanolic extract of *J. gossypiifolia* root is toxic to the kidney and causes increased retention of urea in the blood [49].

4. CONCLUSION

The literature review showed that *J. gossypiifolia* Linn. presents an important potential for drug development based on popular uses and biological studies. When considering the large spectrum of biological activities and medicinal properties, we can realize the role that it can play a role against viruses, bacteria or different cancers. As a candidate plant for disease control, it is therefore imperative to evaluate the biological activity of this plant and to set up a research program for the development of new bioactive compounds.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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