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REVIEW ARTICLE

Use of Medicinal Plants in the Treatment of Erysipelas: A Review

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ABSTRACT

Erysipelas infection is caused by Gram-positive bacteria, in particular, β-hemolytic *Streptococcus pyogenes* streptococci (B, C, and G). Typically treated with benzathine penicillin, the bacterial resistance and entry points in the skin favor disease recurrence. The use of herbs is a widespread traditional practice in the general population as an alternative method for curing diseases and symptoms with subsequent improvement in quality of life. It represents a more affordable treatment for the lower-class population. This article reviews the use of medicinal plants in the treatment of erysipelas. A review was conducted identifying medicinal plants that can be used for the treatment of erysipelas. The search was conducted from publications from 1980 to 2016 by combining the search terms "medicinal plant" and "erysipelas." The databases used in the research were PubMed, Web of Science, Google Scholar, Medical Literature Analysis and Retrieval System Online, Latin American and Caribbean Health Sciences, Cochrane Library, Scopus, and ScienceDirect. Data from the included articles are summarized in two tables with ethnopharmacological and pharmacological information. In this review, 30 articles were included. The selected plants have different popular indications of use, for example, to combat fever, inflammatory processes, and skin problems. The pharmacological studies evaluate the anti-inflammatory, antimicrobial, antioxidant, toxicological, immunomodulatory, and antiprotozoal properties of plants using *in vitro* and *in vivo* methods. The plants mentioned in this study are reported as viable possibilities for the treatment of erysipelas. Future research may be carried out to elucidate the active principles, mechanisms of action, and pharmacodynamic aspects and thus propose a new treatment.

Key words: Erysipelas, ethnopharmacology, medicinal plants, treatment

INTRODUCTION

Erysipelas is an infection that involves the superficial layers of the skin caused by Gram-positive bacteria, such as group A streptococcus: *Streptococcus pyogenes*, β-hemolytic streptococci (B, C, and G), and *S. aureus*, and the Gram-negative *Pseudomonas aeruginosa*.[1] Popularly known as Fire-of-Santo-Antônio, it was considered as a bacterial infection of high mortality in the preantibiotic era.[2] It is a frequent disease in clinical practice, which presents a high rate of recurrence of approximately 23%–29% of the cases treated.[3] Although it is considered a common disease, the etiology is still not well established, and it presents a differential diagnosis with Wells Syndrome, contact dermatitis, and deep venous thrombosis.[1] In most cases, it is related to the presence of *S. pyogenes*. The virulence of such microorganisms is based on the secretion of surface proteins, particularly protein M, and on structures that directly or indirectly prevent phagocytosis involved in adhesion and carbohydrate metabolism or induce the release of pro-inflammatory cytokines.[4]

The disease usually affects lower limbs and the face. It shows the following clinical symptoms: fever, pain, located redness, and swelling. However, the disease may worsen forming vesicles and/or blisters with a serous content, bleeding involving lymph vessels, acute glomerulonephritis, sepsis, septic arthritis, and endocarditis. The acute complications of disease are abscess and/or necrosis. The complications of a general nature are toxidermia and bacteremia/septicemia. Recurrences represent the late complication more frequent, being responsible for the high morbidity rate.[1] It may cause death.[5]

The treatment is performed using injectable antibiotics, such as benzathine penicillin, erythromycin, or clindamycin. However, many microorganisms are resistant to this treatment, making the therapy more difficult. In addition, the use of the isolated antibiotic does not promote wound healing, thereby enabling a gateway into the diseased skin and consequently the appearance of opportunistic infections.[6]

The search for medicinal plants as an alternative treatment for skin diseases is an ancient practice, especially when related to diseases with difficult healing.[7] Normally, the potential of drugs made from medicinal plants is associated with the promotion of angiogenesis. The formation of new vessels is important during the healing process since it ensures the supply of nutrients to sustain cell metabolism, as well as facilitate the elimination of toxic substances through circulation.[8]

The use of medicinal plants in tissue reconstruction has evolved over the years from simple applications using herbs on the site to an improvement of sophisticated technologies in pharmaceutical industrial production.[9] Were identified countries that take an interest in developing research investigating the wound healing potential of medicinal plants. Among these countries, Brazil had the largest number of publications,

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followed by India, United States, Cuba, Turkey, China, Peru, Japan, and Thailand.[10]

Scientific studies report the need for the discovery of new drugs for the treatment of erysipelas. Currently, the clinical approach is made using penicillin, empirically.[11] Considering the difficulties related to the treatment and the convenience of discovering new herbal or plant drugs that are safe for patients and that are effective in treatment, thereby reducing recurrence, this study aims to investigate the literature on the use of medicinal plants for the treatment of erysipelas.

MATERIALS AND METHODS

A review was performed identifying medicinal plants used for the treatment of erysipelas. This type of research allows for the analysis and inference by a researcher on the issues of interest.[12]

The search was conducted from publications combining the search terms "medicinal plant" and "wrysipelas" with Boolean operators "and." The databases used in the research were PubMed, Web of Science, Google Scholar, Medical Literature Analysis and Retrieval System Online, Latin American and Caribbean Health Sciences, Cochrane Library, Scopus, and ScienceDirect. Inclusion criteria were original papers published between 1986 and 2016, written in English, Portuguese, or Spanish, which presented medicinal plants with indication for the treatment of erysipelas. Exclusion criteria were articles that present treatment with nonherbal materials, book chapters, short communication, review articles, historical articles, and papers without available full-text.

Data from the included articles are summarized in two tables with ethnopharmacological and pharmacological information. The species are organized in alphabetical order. The site The Plant List (www.theplantlist.org) was used to validate the scientific names and synonyms of the botanical taxa. In addition, plants that obtained more than one citation had their characteristics described.

RESULTS AND DISCUSSION

In this review, 30 articles on ethnopharmacology and pharmacology were included. Table 1 shows 18 ethnopharmacological articles selected. In these papers, 54 species were cited belonging to 37 different botanical families. Leaves were the part of the plant that was most cited for use, followed by flowers.

These works present the species that are also used for the treatment of erysipelas. However, no work that aimed to investigate medicinal plants popularly used only for erysipelas treatment was verified among the studies evaluated. The authors cite the ethnopharmacological use of the species and among the indications is the treatment of erysipelas.

The selected plants have different popular indications of use, for example, to combat fever, inflammatory processes, skin problems, or scarring was seen in ethnopharmacological articles. However, erysipelas is an infectious disease that causes pain, edema, fever, and skin wounds. The population chooses the plant species that have the capacity to decrease the symptoms of the disease.

Biodiversity, especially in developing countries, needs to be explored since the use of medicinal plants is a strategy that has a lower cost when compared with treatments with synthetic drugs. The investment in researches with medicinal plants can help the countries that have an ethnopharmacological potential.[31] Brazil and India are the countries with the highest number of publications among the selected manuscripts.

Brazil has a wide biodiversity and many classes of active compounds have been isolated from Brazilian medicinal plants. Moreover, the tradition of the use of medicinal plants has called the attention of Brazilian researchers and has accelerated the interest in natural products, both from academia and pharmaceutical companies.[32] India has the Council of Medical Research on medicinal plants that encourages the development of quality standards for pharmacopeial bodies and the drug industry with the intention of generating high-quality traditional or herbal drugs, a fact that would increase the country's scientific production.[33]

The researches on pharmacological properties of medicinal plants with indication of use for the treatment of erysipelas are compiled. Twelve pharmacological articles were selected. In these papers, 16 species were cited belonging to 10 different botanical families [Table 2]. These studies evaluate anti-inflammatory, antimicrobial, antioxidant, toxicological, immunomodulatory, and antiprotozoal properties of plants using *in vitro* and *in vivo* methods. Brazil and India appear with the highest numbers of publications, followed by China. The rich diversity of medicinal plants in China provides an important source of medicinal raw materials, both for traditional medicine systems and for the pharmaceutical industry.[34]

The absence of articles aimed at the treatment of erysipelas, of ethnopharmacological or pharmacological origin, suggests that the subject is not well explored in the academic environment and reveals the need for further studies. Academic and pharmaceutical investment in research is required for the development of herbal formulations that can be used as an alternative treatment. The use of herbal preparations in replacing benzathine penicillin will mean quality of life for patients and the possibility of a different clinical management of the disease.

The antimicrobial evaluation of the ethanolic extract of *Portulaca quadrifolia* L. through the disc diffusion technique revealed that the extract has activity against the species *Shigella dysenteriae* with inhibitory growth between 10 and 20 mm. This study was conducted to evaluate Indian plants used in traditional medicine. The aim of this work was to identify the ability of the alcoholic extracts from 45 species for inhibiting bacterial and fungal growth. In addition, the authors did a phytochemical study of the species. *P. quadrifolia* is the only species among the selected ones that has been used for erysipelas. However, the extract tested only inhibited the growth of a bacterial strain and showed no secondary compounds in its chemical constitution.[44]

The antimicrobial activity of the ethanolic extract the strains *Portulaca pilosa* L. obtaining inhibition of the growth of *P. aeruginosa* and *S. aureus*. Minimal inhibitory concentration (MIC) by the broth microdilution method showed that the crude ethanolic extract of *Peperomia pellucida* against *S. aureus* and *P. aeruginosa* had a MIC of 62.5 mg/mL.[43] The resin glycosides from *Ipomoea wolcottiana* Rose increased the effect of the antibiotics against multidrug-resistant strains. However, the assay was performed only against of *Escherichia coli*, *Salmonella enterica* serovar Typhi, and *Shigella flexneri*.[40]

Amazon Waiapi Indians treat malaria with an inhalation of vapor obtained from leaves of *Virola surinamensis*. The bark resin from the species is used in folk medicine for the treatment of erysipelas.[45] The presence of sesquiterpene nerolidol is related to the antimalarial activity of the plant. The treatment, *in vitro*, of *Plasmodium falciparum* with 100 mg/mL of nerolidol over 48 h caused 100% inhibition in the development of young trophozoite.[45] The antiulcerogenic activity of the resin extract of this species was also verified, through different models of lesion in mice. Besides, the authors report that the species is used as a natural form of treatment for different gastritis, inflammation, and erysipelas.[46]

The increase of antioxidant substances in the healing process is important because in granulation tissues these antioxidants hasten the process of wound healing by destroying the free radicals.[47] Free radicals can alter the functioning of many molecular complexes, leading to loss of form and function. Antioxidants can protect against the damage induced by free radicals acting at various levels.[48] The inflammatory phase of the healing period generates a situation known as oxidative burst, caused by the cells involved in the inflammatory process. This

Table 1: Ethnopharmacological medicinal plants used for the treatment of erysipelas

Botanical taxa	Family	Common name	Part of the plant used	Other traditional uses	Country	Reference
Achillea millefolium L.	Compositae	---	Flowers	Diarrhea	Lithuania	[13]
Adenocalymma alliaceum (Lam.) Miers	Bignoniaceae	Cipó-d'alho	Leaves	Rheumatism	Brazil	[14]
Adiantum philippense L.	Pteridaceae	---	Leaves	---	India	[15]
Aloe vera (L.) Burm. f.	Xanthorrhoeaceae	Babosa	Leaves	Ulcer and swelling, skin inflammations, burns, eczemas	Brazil	[14]
		Aloe vera	---		Brazil	[16]
Amygdalus communis L.	Rosaceae	---	Seeds	Migraine, eye treatment, fever	Egypt	[17]
Ballota hirsuta Benth.	Lamiaceae	---	Flowery plant	Hypercholesterolemia	Spain	[18]
Bellis perennis L.	Compositae	---	---	Ringworm	Ireland	[19]
Bidens pilosa L.	Compositae	Beggartick	---	Diabetes, wounds, dysentery, gonorrhea, malaria, cough, gases	Brazil	[16]
Callaeum antifebrile (Ruiz ex Griseb) D.M. Johnson	Malpighiaceae	Caabi, pajezinho	Leaves	Ulcer and swelling	Brazil	[14]
Callitris quadrivalvis Rich and A. Rich.	Cupressaceae	---	---	Diarrhea and hemorrhage.	Egypt	[17]
Cannabis sativa L.	Cannabaceae	---	Flowers	Diarrhea	Lithuania	[13]
Carapa guianensis Aubl.	Meliaceae	Andiroba	Seeds	Rheumatism	Brazil	[14]
		Cedro	Wood	Stomach ache, diarrhea, vomiting		
Cassia fistula L.	Leguminosae	Sarakkondri	Leaves	Malaria, ulcers, rheumatism	India	[20]
Cassia hirsuta L.	Leguminosae	Senna	---	Diabetes, wounds, dysentery, gonorrhea, malaria, cough, gases	Brazil	[16]
Castanea sativa Mill.	Fagaceae	---	Fruits	Odontalgy and haemorrhoids	Spain	[18]
Cecropia leucocoma Miq.	Urticaceae	Imbaúba branca	Leaves	Rheumatism, legs and verms, gastritis, cancer, flu, ulcer, swelling	Brazil	[14]
Chenopodium ambrosioides L.	Amaranthaceae	Mastruz	Leaves	Verms, gastritis, cancer, flu, ulcer, swelling	Brazil	[14]
Cichorium intybus L.	Compositae	---	Seeds and root	Fever and cancer	Egypt	[17]
Ficus carica L.	Moraceae	Fig	Fruit	Dermatitis and carbuncles	Israel	[21]
Ficus sycomorus L.	Moraceae	Sycomore	Ashes from wood	Ulcers, tumors, inflammation	Israel	[21]
Glaucium grandiflorum Boiss. A. and Huet	Papaveraceae	Tarla guulu	Root	---	Turkey	[22]
Hibiscus sabdariffa L.	Malvaceae	Vinagreira roxa	Leaves	Rheumatism	Brazil	[14]
Himatanthus articulatus (Vahl.) Woodson	Apocynaceae	Sucuúba do campo	Latex and bark	Genitourinary infections and abortion	Brazil	[14]
Humulus lupulus L.	Cannabaceae	---	Flowers	Insomnia and anxiety	Lithuania	[13]
Juglans regia L.	Juglandaceae	Ceviz	Bark	---	Turkey	[22]
Justicia pectoralis Jacq.	Acanthaceae	Japana do sertão	Leaves	Rheumatism, legs and arm pain, headache, stroke	Brazil	[14]
Kalanchoe pinnata (Lam.) Pers.	Crassulaceae	Pirarucú	Leaves	Ulcer and swelling	Brazil	[14]
Luffa cylindrica L. M. Roem.	Cucurbitaceae	Bucha	Leaves	Erysipelas	Brazil	[14]
Lycopersicon esculentum Mill	Solanaceae	Tomate	Whole plant	Swollen legs	Brazil	[14]
Marrubium vulgare L.	Lamiaceae	---	Aerial part	Hypercholesterolemia	Spain	[18]
Mentha spicata L.	Lamiaceae	---	---	---	Greece	[23]
Mentha suaveolens Ehrh	Lamiaceae	---	Leaves	Herpes	Spain	[18]
Mentha X *piperita* L.	Lamiaceae	---	---	---	Greece	[23]
Momordica charantia L.	Cucurbitaceae	Melão São Caetano	Flowers	Skin lesions and itchiness.	Brazil	[24]
Olea europaea L.	Oleaceae	---	Fruit oil	Psoriasis and burns	Spain	[18]
Petiveria alliacea L.	Phytolaccaceae	Mucura-caá	Leaves	Rheumatism, skin ailments	Brazil	[14]
Philodendron acutatum Schott.	Araceae	Cipó-tracuá	Leaves	Abscess	Brazil	[14]
		Cipó-imbé	---	Back pain	Brazil	[25]
Phragmites communis Trin.	Poaceae	---	---	Diuretic, alopecia, bites, skin diseases	Egypt	[17]
Polyscias scutellaria (Burm. F.) Fosberg	Araliaceae	Cuia-de-pajé	Leaves	Magic use	Brazil	[14]
Portulaca oleracea L.	Portulacaceae	---	Leaves, Stem and Flowers	Swelling and elephantiasis	Egypt	[17]
Punica granatum L.	Lythraceae	---	Flower and seeds	Fevers, cancer, soft and hard inflammatory swellings	Egypt	[17]
Ruta graveolens L.	Rutaceae	Arrruda	---	Calmative and uterine problem	Brazil	[25]

Contd...

Table 1: Contd...

Botanical taxa	Family	Common name	Part of the plant used	Other traditional uses	Country	Reference
Sambucus nigra L.	Adoxaceae	Sabuc --- Astunpa, intsusa, sabuko, saúco	Bark and flowers Leaves ---	Wounds, furuncles, boils, pimples, eczemas, burns, hard skin, herpes, seborrhea, dermatitis, for respiratory problems Insect bites, gout asthma --- Wounds, furuncles, boils, pimples, burns, eczemas, hard skin, herpes, seborrhea dermatitis	Iberian Peninsula Spain Spain	[26] [18] [27]
Scrophularia nodosa L.	Scrophulariaceae	---	---	Swellings, burns, wounds	Ireland	[19]
Stachytarpheta cayennensis (Rich.) Vahl	Verbenaceae	Rinchão	Leaves	Anemia	Brazil	[14]
Urera baccifera L Gaudich. ex Wedd.	Urticaceae	Urtiga-brava	Root	---	Brazil	[28]
Viola odorata L.	Violaceae	---	---	Cancer, inflammatory swellings, elephantiasis	Egypt	[17]
Virola surinamensis (Rol. ex Rottb.) Warb	Myristicaceae	Mucuíba	Bark	---	Brazil	[28]
Withania somnifera (L.) Dunal	Solanaceae	Poison gooseberry	Leaves	Intestinal pain, gonorrhea, to treat pain in muscles	Somalia	[29]
Woodfordia fruticosa (L.) Kurz	Lythraceae	Fire flame	Flowers	Bowel disorders, dysentery, leprosy, blood diseases, leucorrhoea, menorrhagia, toothache	India	[30]

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stress increases the consumption of oxygen, resulting in the production of reactive oxygen and nitrogen derivatives. Antioxidant compounds, in this way, have an important role in promoting healing.[49] The effect of antioxidant prevents cell damage and increases collagen fibrillary endurance. Evaluating the antioxidant effect of plants is important when investigating their potential for healing.[47] The antioxidant potential of the species: *Castanea seguinii* Dode, *Castanea mollissima* Blume, *Podophyllum hexandrum* Royle, *Forsythia suspensa* (Thunb.) Vahl., and *Acacia leucophloea* (Roxb.) Willd. was verified in the pharmacological studies, by *in vitro* and *in vivo* tests.

The antioxidant power of methanolic extracts of plants used in Chinese medicine was also evaluated.[38] The authors identified the concentration required to eliminate 50% of 2,2-diphenyl-1-picrylhydrazyl (DPPH). *C. mollissima* Blume (IC_{50} 0.319 ± 0.018) and *C. seguinii* Dode (IC_{50} 0.345 ± 0.022)[39] used the same methodology, to verify the antioxidant capacity of the oil isolated from *F. suspensa* (Thunb.) Vahl. leaves. In addition to DPPH, the β-carotene bleaching test was also evaluated. The authors had results of IC_{50} of 22.35 and 29.51 mg/mL, respectively. The authors relate the antioxidant capacity of plants to chemical composition, due to the presence of phenolic compounds. The antioxidant capacity of the acetone extract from stem bark of *A. leucophloea* was determined by the gene expression of antioxidant enzymes. The study demonstrated that *A. leucophloea* extract inhibited H_2O_2-mediated oxidative stress by regulating the expression of enzymes/manganese, catalase, and glutathione peroxidase. The activity was dose dependent (25, 50, and 75 μg/mL); the authors suggest future studies to relate mechanisms of action and chemical components.[35]

These pharmacological assays are not sufficient to establish a relationship between the plants and the treatment of erysipelas. The plant species are cited as a possibility for the treatment of erysipelas, but there is no concrete scientific evidence to assure this use. Antimicrobial activities are important; however, they need to ensure that plant present activities against the microorganisms found in the lesions of patients with erysipelas. Antioxidant assay needs to be associated with anti-inflammatory and healing, through *in vivo* and *in vitro* evaluations. Identification of the antimicrobial profile, evaluations of immunomodulatory, anti-inflammatory, and healing activities, cytotoxicity models *in vitro* and *in vivo* are necessary to correctly establish the use of these species for the treatment of erysipelas.

CHARACTERISTICS OF THE MOST CITED PLANTS FOR USE IN TREATMENT OF ERYSIPELAS

The most cited plants in ethnopharmacological and pharmacological articles were briefly described their characteristics although no work with these species directly related to the treatment of erysipelas was found. The species were: *Aloe vera* (L.) Burm. *f.*; *Sambucus nigra* L; *Stachytarpheta cayennensis* (Rich.) Vahl., and *Virola surinamensis* (Rol. ex Rottb.) Warb.

Aloe vera (L.) Burm. f.

A. vera (*Xanthorrhoeaceae*) is an herbaceous, succulent plant, which grows up to 1 m high, and is probably of African origin. It has thick, succulent leaves attached to a short stem.[9] It is a medicinal plant with different properties, being ascribed to the inner colorless gel and to the exudates from the outer layers. *A. vera* is a natural cleaner that has the power to penetrate in the tissues. The species has strong antibiotic, virucidal, fungicidal, and anti-inflammatory properties, presenting an absorption by the skin greater than the water and chemical constituents with an action on the immune system.[50]

In vitro studies indicated that *A. vera* leaf gel can inhibit the growth of bacteria strains: *S. aureus, Enterococcus faecalis,*[51] *Bacillus cereus* (MTCC 1272), *E. coli* (MTCC 1687), *P. aeruginosa* (MTCC 1688), *Salmonella typhi* (MTCC 531), *Klebsiella pneumoniae* (MTCC 530), *S. flexneri* and *S. pyogenes.*[52] A study exploited the usage of *A. vera* plant extract as a reducing agent to synthesize silver nanoparticles (AgNP) to evaluate its efficiency in antimicrobial activity. The results showed that the

Table 2: Pharmacological activities of medicinal plants used to treat erysipelas

Botanical taxa	Family	Part of the plant used	Activity-(model)	Extract/ compound-Dose	Control	Compound group	Country	Reference
Acacia leucophloea (Roxb.) Willd.	Leguminosae	Bark	Antioxidant (*in vitro*)	Acetone extract 25, 50 and 75 µg/mL	Untreated control	Flavonoids, terpenes, tannins, amines, alkaloids	India	[35]
Andrographis paniculata (Burm. f.)	Acanthaceae	EtOAc fractions	Anti-inflammatory (*in vitro*)	Ethanolic 10 µg/ml	Untreated	---	China	[36]
Cassia occidentalis L.	Leguminosaeae	Stem and Leaves	Toxicity (*in vivo*)	Hydroalcoholic 0.625; 1.25; 2.5 and 5 g/kg	Distilled water	Flavonoids, anthraquinones, triterpenes, saponins	Brazil	[37]
Castanea mollissima Blume *Castanea seguinii* Dode	Fagaceae Fagaceae	Leaves	Antioxidant (*in vitro*)	Methanolic 0.319±0.018 0.345±0.022	Ascorbic acid	Casuarinin, chestannin Tannins	China	[38]
Forsythia suspensa (Thunb.) Vahl	*Oleaceae*	Seeds	Antioxidant (*in vitro*)	Oil of seeds 22.35 mg/mL	DPPH-β-carotene/ linoleic acid	Volatile oils, phenolic compounds	China	[39]
Ipomoea wolcottiana Rose	Convolvulaceae	Flowers	Antibacterial (*in vitro*)	Resin glycosides 512 µg/mL	Tetracycline kanamycin, chloramphenicol	Glycolipids	Mexico	[40]
Piper aduncum L.	Piperaceae	Leaves	Antileishmanial and Antifungal (*in vitro*)	Methanolic	Amphotericin B	Alkaloids, sterols, tannins, flavonoids, anthraquinones	Brazil	[41]
Podophyllum hexandrum Royle	Berberidaceae	Rhizome	Antioxidant (*in vivo*)	Methanolic 5, 10 and 15 mg%	Watter α-tocopherol	Lignan	India	[42]
Polygonum hydropiperoides Michx	Polygonaceae	Leaves Flowers	Antileishmanial and Antifungal (*in vitro*)	Methanolic	Amphotericin B	Alkaloids, triterpenoids, tannins, sterols flavonoids Triterpenoids, coumarins, flavonoids	Brazil	[41]
Portulaca pilosa L.	Portulacaceae	Leaves	Antimicrobial (*in vitro*)	Ethanolic 500 µg/mL	---	Phenols, tannins, steroids, triterpenoids, cardiac glycosides, carotenoids	Brazil	[43]
Portulaca quadrifida L.	Portulacaceae	Stem and Leaves	Antimicrobial (*in vitro*)	Ethanolic 150 mg/ml	Antifungal and standard antibiotics	Alkaloids, flavonoids	India	[44]
Pothomorphe umbellata (L.) Miq.	Piperaceae	Leaves	Antileishmanial and antifungal (*in vitro*)	Methanolic	Amphotericin B	Alkaloids, Sterols, Tannins, Flavonoids	Brazil	[41]
Stachytarpheta cayennensis (Rich.) Vahl.	Verbenaceae	Leaves	Antileishmanial and Antifungal (*in vitro*)	Methanolic	Amphotericin B	Alkaloids, triterpenoids, coumarins, flavonoids	Brazil	[41]
Virola surinamensis (Rol. ex Rottb.) Warb.	Myristicaceae	Leaves	Antimalarial (*in vitro*) Antiulcerogenic (*in vivo*)	Nerolidol (100 mg/ mL) Ethanolic (500 mg/ Kg)	Methionine Lansoprazole (30 mg/kg) Cimetidine (100 mg/kg)	Lignans, monoterpenes, arylpropanoids, propyophenones, flavonoids	Brazil	[45] [46]

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enhanced and synergetic activity of the plant extract was obtained when it combined with AgNP. The inhibition of growth was verified in the following strains*: S. aureus, B. cereus, Micrococcus luteus, E. coli,* and *K. pneumoniae*.[53]

Studies have shown that treatment with *A. vera* gel extracts resulted in faster healing of wounds. Polysaccharides from the plant promote both the proliferation of fibroblasts and the production of hyaluronic acid, and hydroxyproline in the fibroblasts acts on the healing process.[54] Besides polysaccharides, there are in the chemical constitution antioxidant substances, including α-tocopherol (Vitamin E), carotenoids, ascorbic acid (Vitamin C), flavonoids, and tannins.[55] The presence of anthraquinones, which is a structural analog of tetracycline, as an active compound, is related to the antibacterial activity from the species. The anthraquinones act like tetracycline which inhibits bacterial protein synthesis by blocking the ribosome.[56]

An *in vitro* study demonstrated that *A. vera* ethanolic extract showed cytotoxic activity against fibroblasts at the concentration of 50 µg/mL, according to the MTT test. However, fibroblast migration analysis at this concentration demonstrated that after 72 h of treatment, there was an improvement in cell proliferation and migration. The authors suggest that stimulating cell proliferation and migration may cause the extract to aid in the healing process.[57]

The acute toxicity of the hydroalcoholic extracts of *A. vera* leaves was tested in chicks using concentrations (40–1.280 mg/kg). The results showed that it can be considered safe since they caused neither lethality nor adverse changes in their general behavior.[58] An *in vitro* study showed that toxicity of the gel and the whole leaf materials from *A. vera* are safe to use on skin tissue.[59] Toxicological tests are important for guiding research that aims to develop drugs because they guarantee the safety of use, corroborating with ethnopharmacological knowledge.

Sambucus nigra L.

S. nigra (*Adoxaceae*) is large shrub or tree of 3–4 m in height and presents an irregular and many-branched canopy, with tortuous trunk and fissured bark, native of South America.[9] Phytochemical studies of the aerial parts of the plant showed compounds, such as glycosides, flavonoids (rutin and quercetin), tannins, essential oils, triterpene acids, and reducing sugars.[60]

Pharmacological studies have shown evidence of the following properties for *S. nigra*: anti-inflammatory,[61] anti-*Helicobacter pylori*,[22] and antioxidant.[62]

The presence of these chemical compounds imparts anti-inflammatory, antioxidant, and expectorant properties in the species.[63] Studies showed the power of the fruits of *S. nigra* L. in lower of the inflammatory response. This action is related to the presence of immune modulating components, including anthocyanins, flavonols, and phenolic acids.[64]

In vitro anti-inflammatory assay of aqueous extract of *S. nigra* L. fruit in co-cultured intestinal epithelial cells and lipopolysaccharide (LPS)-stimulated macrophages showed that in concentration (1 mg/mL) the extract has the ability to inhibit proinflammatory pathway in LPS-stimulated macrophages by downregulating the expression of proinflammatory genes.[65]

A study with *S. nigra* extracts evaluated its ability against bacterial and viral strains. There was a reduction in the growth of microorganisms of human clinical importance, at concentrations of 5%, 10%, 15%, and 20%. Furthermore, the authors suggest that the concentrations tested were not toxic to cells by the MTT assay.[66]

The anti-inflammatory, antiseptic, and healing properties of *S. nigra* were assessed in experimental model of thermal skin burns, in Wistar rats. 1% silver sulfadiazine cream and cold-cream group were compared with cold-cream containing 10% vegetal extract. Rats treated with cold-cream containing 10% *S. nigra* extract of leaves showed a good epithelization, the wound healing being almost complete for 21 days. The inflammatory reaction and edema were smaller. The authors suggest that the presence of flavonoids and tannins compounds of the cold-cream with 10% extract is responsible for accelerating the repair of rat skin.[67]

Another study evaluated the healing effect of different leaf extracts of *Sambucus ebulus* L. on rats and mice using incision and excision model of healing. The extracts were incorporated into a 1% concentration ointment base. The positive control was done with Madecassol® ointment. The methanolic extract of *S. ebulus* leaves was found to be remarkably active on *in vivo* wound models. The compound quercetin 3-O-glucoside was isolated from the methanolic extract as one of the active wound-healing ingredients. However, the extract presented a better action than the isolated compound, which suggests that the activity is related to the synergism of the compounds present in the crude extract.[68]

An *in vitro* study evaluated the cytotoxic potential of aqueous extracts of the fruits of *S. nigra.* The authors concluded that in concentration (1 mg/ml), there was no cytotoxic, genotoxic, and mutagenic activity. Therefore, the use of fruits as functional food components could be postulated; however, further *in vivo* studies should also be conducted to confirm the health benefits of aqueous extract.[69]

Stachytarpheta cayennensis (Rich.) Vahl

S. cayennensis (*Verbenaceae*) is an annual or perennial subbush, erect, branched, grows to 70–100 cm high, has few flowers, blue in color, and is a plant native to Brazil.[70] Phytochemical screenings reveal that plants of the genus *Stachytarpheta* contain terpenes, flavonoids, arylpropanoids, iridoids, carbohydrates, glycosides, saponins, alkaloids, terpenoids, and steroids.[71]

Stachytarpheta jamaicensis is widely known for its high medicinal importance in traditional and folk medicinal systems in various countries. This plant has been reported to possess pharmacological effects due to the presence of various bioactive phytochemicals.[72] It demonstrates analgesic, antimalarial, and anti-inflammatory effects. *S. cayennensis* is used popularly in antiallergic, bronchodilatory, digestion stimulating, antacid and antidiarrheal, anti-inflammatory, antioxidant, and antimicrobial treatments.[73]

An *in vitro* study evaluated the antimicrobial activity of organic extracts of roots of the species. It showed activity against *Bacillus subtilis, Staphylococcus saprophyticus, Staphylococcus epidermidis, S. aureus*, and *S. pyogenes*.[74] The methanol extract of the leaves of *S. cayennensis* can have potent immunomodulatory effect on both humoral-mediated and cell-mediated immune responses. The authors emphasized that the presence of flavonoids increases the helper T-cells, interleukin 2, interferon, and macrophages; it is thus useful against several diseases of immune dysfunction.[73] Pharmacological studies showed evidence of the anti-inflammatory, antinociceptive, antiparasitic, and antioxidant capacity of the species. In addition, low toxicity provides safe therapeutic use.[73,75,76]

Virola surinamensis (Rol. ex Rottb.) Warb

V. surinamensis (Myristicaceae) is a tree with a pyramidal shape, 25–35 m high, has a cylindrical trunk, simple leaves, and small yellow flowers. It is native of alagadic forests of the Amazon region.[9] Phytochemical research demonstrates the presence of steroids, flavonoids, lignans, and polyketides.[77] There are studies in the literature mentioning several activities of this species, such as larvicide, antinociceptive, anti-inflammatory, antitumor, gastroprotective, and trypanocidal activities.[77-79]

A study *in vivo* with mice showed that the ethanolic extract (500 mg/kg) demonstrated gastroprotective activity. The authors have evidenced the action of epicatechin present in its composition, which activated the defense mechanism of the gastric mucosa against aggressive factors, but its use demands great care because toxicological symptoms are mentioned by the population.[46]

A study carried out with lignan (grandisin) associated the antinociceptive and anti-inflammatory effects of the species with the presence of this composition, corroborating the use in popular medicine of plants rich in grandisin for the treatment of symptoms caused by the inflammatory process, such as pain and edema. Besides this, the authors suggested that the mechanism of action of the molecule involves inhibition of the prostaglandin formation and/or activity through mechanisms of inhibition of cyclooxygenase activity or prostaglandin receptor antagonist action.[79] The use of this species for the treatment of erysipelas may be related to the presence of lignin, a molecule that has anti-inflammatory action, which reduces symptoms such as edema, pain, heat, and flushing at the lesion site.[77]

CONCLUSION

Erysipelas is a disease with clinical importance, especially when considering the consequences of its acute and late complications. However, it is poorly studied. It is thus not possible to clarify the disease mechanisms and develop new drugs, especially from medicinal plants. The usual treatment is conducted through an intramuscular administration of benzathine penicillin. Research involving the search for alternative treatments is scarce.

Popular use of plants without scientific evidence should be carefully evaluated as this can lead to complications to the health of the individual. This use must be validated through scientific research to be recognized as a possibility of treatment. Ethnopharmacological articles only cite the different uses of species, among which is the treatment of erysipelas.

It was not possible to find any ethnopharmacological articles that approached integrally the popular plants for the treatment of erysipelas.

Articles with pharmacological activities evaluate antimicrobial, antioxidant, anti-inflammatory, and immunomodulatory capacities of the plant species, most of them being *in vitro*. This shows, therefore, the need for research that evaluates healing, immunomodulatory and antibacterial activities. *In vitro* and *in vivo* preclinical tests, involving disease causing pathogens, identification of active principles to combat these microorganisms, cytotoxic assays, should be performed.

The plants mentioned in this study are reported as viable possibilities for the treatment of erysipelas. Future research may be carried out to elucidate the active principles, mechanisms of action, and pharmacodynamic aspects and thus propose a new treatment with changes in the clinical management of the disease.

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Conflicts of interest

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REFERENCES

1. Caetano M, Amorim I. Erisipela. Acta Med Port 2005;18:385-94.
2. Okajima RM, de Freitas TH, Zaitz C. Erysipelas: a clinical study of 35 pacients hospitalized at the São Paulo Central Hospital of Irmandade da Santa Casa de Misericórdia. Ann Bras Dermatol 2004;79:295-303.
3. Alcantara C, Alcantara VC. Healing process of wounds caused by erysipelas in a patient suffering from diabetes mellitus. Com Ciências Saúde 2009;20:173-84.
4. Steer AC, Carapetis JR, Dale JB, Fraser JD, Good MF, Guilherme L, *et al*. Status of research and development of vaccines for *Streptococcus pyogenes*. Vaccine 2016;34:2953-8.
5. Modesto Dos Santos V, de Carvalho Santos S, Robério de Melo Nogueira P, Mendonça Ferreira Borges N. Erysipelas in the elderly: Are the concerns and economic burden increasing? Apropos of a case. Acta Dermatovenerol Alp Pannonica Adriat 2011;20:63-6.
6. Inghammar M, Rasmussen M, Linder A. Recurrent erysipelas – Risk factors and clinical presentation. BMC Infect Dis 2014;14:270.
7. Parente LM, Silva MS, Brito LA, Lino-Júnior RS, Paula JR, Trevenzol LM, *et al*. Efeito cicatrizante e atividade antibacteriana da *Calendula officinalis* L. cultivada no Brasil. Rev Bras Plantas Med 2009;11:383-91.
8. Majewska I, Gendaszewska-Darmach E. Proangiogenic activity of plant extracts in accelerating wound healing – A new face of old phytomedicines. Acta Biochim Pol 2011;58:449-60.
9. Lorenzi HE. Plantas Medicinais No Brasil/Nativas e Exóticas. Nova Odessa: Instituto Plantarum; 2002.
10. Piriz MA, Lima CA, Jardim VM, Mesquita MK, Souza AD, Heck RM. Medicinal plants in the wound healing process: a literature review. Rev Bras Planta Med 2014;16:628-36.
11. Bläckberg A, Trell K, Rasmussen M. Erysipelas, a large retrospective study of aetiology and clinical presentation. BMC Infect Dis 2015;15:402.
12. Whittemore R, Knafl K. The integrative review: Updated methodology. J Adv Nurs 2005;52:546-53.
13. Petkeviciute Z, Savickiene N, Savickas A, Jurga B, Simaitiene Z, Kalveniene Z, *et al*. Urban ethnobotany study in Samogitia region, Lithuania. J Med Plants Res 2010;4:64-71.
14. Coelho-Ferreira M. Medicinal knowledge and plant utilization in an Amazonian coastal community of Marudá, Pará state (Brazil). J Ethnopharmacol 2009;126:159-75.
15. Jain A, Katewa SS, Galav PK, Sharma P. Medicinal plant diversity of Sitamata wildlife sanctuary, Rajasthan, India. J Ethnopharmacol 2005;102:143-57.
16. Pereira ZV, Mussury RM, de Almeida AB, Sangalli A. Medicinal plants used by Ponta Porã community, Mato Grosso do Sul State. Acta Sci Biol Sci 2009;31:293-9.
17. Lev E, Amar Z. "Fossils" of practical medical knowledge from medieval Cairo. J Ethnopharmacol 2008;119:24-40.
18. Benítez G, González-Tejero MR, Molero-Mesa J. Pharmaceutical ethnobotany in the Western part of Granada province (Southern Spain): Ethnopharmacological synthesis. J Ethnopharmacol 2010;129:87-105.
19. Coady Y, Boylan F. Ethnopharmacology in Ireland: An overview. Rev Bras Farmacogn 2014;24:197-205.
20. Ranganathan R, Vijayalakshmi R, Parameswari P. Ethnomedicinal survey of Jawadhu hills in Tamil Nadu. Asian J Pharm Clin Res 2012;5:45-9.
21. Lansky EP, Paavilainen HM, Pawlus AD, Newman RA. *Ficus* spp. (fig): Ethnobotany and potential as anticancer and anti-inflammatory agents. J Ethnopharmacol 2008;119:195-213.
22. Sezik E, Yeşilada E, Honda G, Takaishi Y, Takeda Y, Tanaka T, *et al*. Traditional medicine in Turkey X. Folk medicine in central Anatolia. J Ethnopharmacol 2001;75:95-115.
23. Karousou R, Balta M, Hanlidou E, Kokkini S. "Mints", smells and traditional uses in Thessaloniki (Greece) and other Mediterranean countries. J Ethnopharmacol 2007;109:248-57.
24. Pereira CO, Lima EO, Oliveira RA, Toledo MS, Azevedo AK, Guerra MF. Abordagem etnobotânica de plantas medicinais utilizadas em dermatologia na cidade de João Pessoa-Paraíba, Brasil. Rev Bras Planta Med 2005;7:9-17.
25. Bieski IG, Leonti M, Arnason JT, Ferrier J, Rapinski M, Violante IM, *et al*. Ethnobotanical study of medicinal plants by population of Valley of Juruena region, Legal Amazon, Mato Grosso, Brazil. J Ethnopharmacol 2015;173:383-423.
26. Rigat M, Bonet MA, Garcia S, Garnatje T, Vallès J. Studies on pharmaceutical ethnobotany in the high river ter valley (Pyrenees, Catalonia, Iberian Peninsula). J Ethnopharmacol 2007;113:267-77.
27. Cavero RY, Akerreta S, Calvo MI. Pharmaceutical ethnobotany in Northern Navarra (Iberian Peninsula). J Ethnopharmacol 2011;133:138-46.
28. Davis EW, Yost JA. The ethnomedicine of the waorani of Amazonian Ecuador. J Ethnopharmacol 1983;9:273-97.
29. Samuelsson G, Farah MH, Claeson P, Hagos M, Thulin M, Hedberg O, *et al*. Inventory of plants used in traditional medicine in Somalia. IV. Plants of the families passifloraceae-zygophyllaceae. J Ethnopharmacol 1993;38:1-29.
30. Das PK, Goswami S, Chinniah A, Panda N, Banerjee S, Sahu NP, *et al*. *Woodfordia fruticosa*: Traditional uses and recent findings. J Ethnopharmacol 2007;110:189-99.
31. Sofowora A, Ogunbodede E, Onayade A. The role and place of medicinal plants in the strategies for disease prevention. Afr J Tradit Complement Altern Med 2013;10:210-29.
32. Dutra RC, Campos MM, Santos AR, Calixto JB. Medicinal plants in Brazil: Pharmacological studies, drug discovery, challenges and perspectives. Pharmacol Res 2016;112:4-29.
33. Tandon N, Yadav SS. Contributions of Indian Council of Medical Research (ICMR) in the area of medicinal plants/traditional medicine. J Ethnopharmacol 2017;197:39-45.
34. Pant S. Pant V. Status and conservation management strategies for threatened plants of Jammu and Kashmir. J Phytol 2011;3:50-6.
35. Sowndhararajan K, Hong S, Jhoo JW, Kim S, Chin NL. Effect of acetone extract from stem bark of *Acacia* species (*A. dealbata*, *A. ferruginea* and *A. leucophloea*) on antioxidant enzymes status in hydrogen peroxide-induced HepG2 cells. Saudi J Biol Sci 2015;22:685-91.
36. Chao WW, Kuo YH, Li WC, Lin BF. The production of nitric oxide and prostaglandin E2 in peritoneal macrophages is inhibited by *Andrographis paniculata*, *Angelica sinensis* and *Morus alba* ethyl acetate fractions. J Ethnopharmacol 2009;122:68-75.
37. Silva MG, Aragão TP, Vasconcelos CF, Ferreira PA, Andrade BA, Costa IM, *et al*. Acute and subacute toxicity of *Cassia occidentalis* L. stem and leaf in wistar rats. J Ethnopharmacol 2011;136:341-6.
38. Hu F, Lu R, Huang B, Liang M. Free radical scavenging activity of extracts prepared from fresh leaves of selected Chinese medicinal plants. Fitoterapia 2004;75:14-23.
39. Gai QY, Jiao J, Wei FY, Luo M, Wang W, Zu YG, *et al*. Enzyme-assisted aqueous extraction of oil from *Forsythia suspense* seed and its physicochemical property and antioxidant activity. Ind Crops Prod 2013;51:274-8.
40. Corona-Castañeda B, Rosas-Ramírez D, Castañeda-Gómez J, Aparicio-Cuevas MA, Fragoso-Serrano M, Figueroa-González G, *et al*. Resin glycosides from ipomoea wolcottiana as modulators of the multidrug resistance phenotype *in vitro*. Phytochemistry 2016;123:48-57.
41. Braga FG, Bouzada ML, Fabri RL, de O Matos M, Moreira FO, Scio E, *et al*. Antileishmanial and antifungal activity of plants used in traditional medicine in Brazil. J Ethnopharmacol 2007;111:396-402.
42. Ganie SA, Zargar BA, Masood A, Zargar MA. Effect of long dose exposure of *Podophyllum* hexandrum methanol extract on antioxidant defense system and body and organ weight

changes of albino rats. Asian Pac J Trop Biomed 2012;2:S1600-5.

43. Mendes LP, Maciel KM, Vieira AB, Mendonça LC, Silva RM, Rolim Neto PJ, *et al.* Atividade antimicrobiana de extratos etanólicos de *Peperomia pellucida* e *Portulaca pilosa*. Rev Ciênc Farm Básica Apl 2011;32:121-5.
44. Ahmad I, Beg AZ. Antimicrobial and phytochemical studies on 45 Indian medicinal plants against multi-drug resistant human pathogens. J Ethnopharmacol 2001;74:113-23.
45. Lopes NP, Kato MJ, Andrade EH, Maia JG, Yoshida M, Planchart AR, *et al.* Antimalarial use of volatile oil from leaves of *Virola surinamensis* (Rol.) warb. By Waiãpi Amazon Indians. J Ethnopharmacol 1999;67:313-9.
46. Hiruma-Lima CA, Batista LM, de Almeida AB, de Pietro Magri L, dos Santos LC, Vilegas W, *et al.* Antiulcerogenic action of ethanolic extract of the resin from *Virola surinamensis* warb. (Myristicaceae). J Ethnopharmacol 2009;122:406-9.
47. Shetty S, Udupa S, Udupa L. Evaluation of antioxidant and wound healing effects of alcoholic and aqueous extract of *Ocimum sanctum* linn in rats. Evid Based Complement Alternat Med 2008;5:95-101.
48. Capasso A. Antioxidant action and therapeutic efficacy of *Allium sativum* L. Molecules 2013;18:690-700.
49. Tümen İ, Akkol EK, Taştan H, Süntar I, Kurtca M. Research on the antioxidant, wound healing, and anti-inflammatory activities and the phytochemical composition of maritime pine (*Pinus pinaster* ait). J Ethnopharmacol 2018;211:235-46.
50. Lawrence R, Tripathi P, Jeyakumar E. Isolation, purification and evaluation of antibacterial agents from *Aloe vera*. Braz J Microbiol 2009;40:906-15.
51. Reynolds T, Dweck AC. *Aloe vera* leaf gel: A review update. J Ethnopharmacol 1999;68:3-7.
52. Nejatzadeh-Barandozi F. Antibacterial activities and antioxidant capacity of *Aloe vera*. Org Med Chem Lett 2013;3:5.
53. Logaranjan K, Raiza AJ, Gopinath SC, Chen Y, Pandian K. Shape- and size-controlled synthesis of silver nanoparticles using *Aloe vera* plant extract and their antimicrobial activity. Nanoscale Res Lett 2016;11:520.
54. Chantarawaratit P, Sangvanich P, Banlunara W, Soontornvipart K, Thunyakitpisal P. Acemannan sponges stimulate alveolar bone, cementum and periodontal ligament regeneration in a canine class II furcation defect model. J Periodontal Res 2014;49:164-78.
55. Hamman JH. Composition and applications of *Aloe vera* leaf gel. Molecules 2008;13:1599-616.
56. Habeeb F, Shakir E, Bradbury F, Cameron P, Taravati MR, Drummond AJ, *et al.* Screening methods used to determine the anti-microbial properties of *Aloe vera* inner gel. Methods 2007;42:315-20.
57. Negahdari S, Galehdari H, Kesmati M, Rezaie A, Shariati G. Wound healing activity of extracts and formulations of *Aloe vera*, henna, *Adiantum capillus-veneris*, and myrrh on mouse dermal fibroblast cells. Int J Prev Med 2017;8:18.
58. Nghonjuyi NW, Tiambo CK, Taïwe GS, Toukala JP, Lisita F, Juliano RS, *et al.* Acute and sub-chronic toxicity studies of three plants used in cameroonian ethnoveterinary medicine: *Aloe vera* (L.) burm. F. (Xanthorrhoeaceae) leaves, *Carica papaya* L. (Caricaceae) seeds or leaves, and *Mimosa pudica* L. (Fabaceae) leaves in Kabir chicks. J Ethnopharmacol 2016;178:40-9.
59. Fox LT, Mazumder A, Dwivedi A, Gerber M, du Plessis J, Hamman JH, *et al. In vitro* wound healing and cytotoxic activity of the gel and whole-leaf materials from selected aloe species. J Ethnopharmacol 2017;200:1-7.
60. Matte AK, Deak AR, Mata PTG. Triagem fitoquímica e avaliação da atividade antibacteriana de extratos das flores de *Sambucus nigra* L. (Caprifoliaceae). Rev Bras Plantas Med 2015;17 4 Suppl 3:1049-54.
61. Ebrahimzadeh MA, Mahmoudi M, Salimi E. Antiinflammatory activity of *Sambucus ebulus* hexane extracts. Fitoterapia 2006;77:146-8.
62. Dawidowicz AL, Wianowska D, Baraniak B. The antioxidant properties of alcoholic extracts from *Sambucus nigra* L. (antioxidant properties of extracts). LWT Food Sci Technol 2006;39:308-15.
63. Laffita OC, Castillo AA. Caracterización fármaco-toxicológica de la planta medicinal *Sambucus nigra* subsp. Canadensis (L). R Bolli. Rev Cuba Farm 2011;45:586-96.
64. Duymuş HG, Göger F, Başer KH. *In vitro* antioxidant properties and anthocyanin compositions of elderberry extracts. Food Chem 2014;155:112-9.
65. Olejnik A, Kowalska K, Olkowicz M, Rychlik J, Juzwa W, Myszka K, *et al.* Anti-inflammatory effects of gastrointestinal digested *Sambucus nigra* L. fruit extract analysed in co-cultured intestinal epithelial cells and lipopolysaccharide-stimulated macrophages. Funct Foods 2015;19:649-60.
66. Krawitz C, Mraheil MA, Stein M, Imirzalioglu C, Domann E, Pleschka S, *et al.* Inhibitory activity of a standardized elderberry liquid extract against clinically-relevant human respiratory bacterial pathogens and influenza A and B viruses. BMC Complement Altern Med 2011;11:16.
67. Mogoşanu GD, Popescu FC, Busuioc CJ, Pop OT, Mogoantă L, Pârvănescu H, *et al.* Effects of a topical preparation containing *Sambuci folium* extract in experimental model of thermal skin burns on rats. Farmacia 2014;62:693-703.
68. Süntar IP, Akkol EK, Yalçin FN, Koca U, Keleş H, Yesilada E, *et al.* Wound healing potential of *Sambucus ebulus* L. Leaves and isolation of an active component, quercetin 3-O-glucoside. J Ethnopharmacol 2010;129:106-14.
69. Olejnik A, Olkowicz M, Kowalska K, Rychlik J, Dembczyński R, Myszka K, *et al.* Gastrointestinal digested *Sambucus nigra* L. fruit extract protects *in vitro* cultured human colon cells against oxidative stress. Food Chem 2016;197:648-57.
70. Lorenzi H, Lacerda MT, Bacher L. Frutas no Brasil: nativas e exóticas (de consumo in natura). São Paulo: Instituto Plantarum de Estudos da Flora; 2015. p. 768.
71. Penido C, Costa KA, Futuro DO, Paiva SR, Kaplan MA, Figueiredo MR, *et al.* Anti-inflammatory and anti-ulcerogenic properties of *Stachytarpheta cayennensis* (L.C. Rich) vahl. J Ethnopharmacol 2006;104:225-33.
72. Liew PM, Yong YK. *Stachytarpheta jamaicensis* (L.) vahl: From traditional usage to pharmacological evidence. Evid Based Complement Alternat Med 2016;2016:7842340.
73. Okoye TC, Akah PA, Ezike AC, Uzor PF, Odoh UE, Igboeme SO, *et al.* Immunomodulatory effects of *Stachytarpheta cayennensis* leaf extract and its synergistic effect with artesunate. BMC Complement Altern Med 2014;14:376.
74. De Souza PA, Silva CG, Machado BR, de Lucas NC, Leitão GG, Eleutherio EC, *et al.* Evaluation of antimicrobial, antioxidant and phototoxic activities of extracts and isolated compounds from *Stachytarpheta cayennensis* (Rich.) Vahl, Verbenaceae. Rev Bras Farmacogn 2010;20:922-8.
75. Moreira RC, Costa GC, Lopes TC, Bezerra JL, Guerra RN, Rebêlo JM, *et al.* Efeito leishmanicida *in vitro* de *Stachytarpheta cayennensis* (Rich.) Vahl (Verbenaceae). Rev Bras Farmacogn 2007;17:59-63.
76. de Souza PA, Rodrigues C, Santiago AP, de Lucas NC, Leitao GG, Galina Filho A. Antioxidant activity of natural compounds of *Stachytarpheta cayennensis* (Rich.) Vahl, Verbenaceae, by scavenger of mitochondrial reactive oxygen species. Rev Bras Farmacogn 2011;21:420-6.
77. Stecanella LA, Taveira SF, Marreto RN, Valadares MC, Vieira M de S, Kato MJ, *et al.* Development and characterization of PLGA nanocapsules of grandisin isolated from *Virola surinamensis*: *In vitro* release and cytotoxicity studies. Rev Bras Farmacogn 2013;23:153-9.
78. Lopes NP, Santos PA, Kato MJ, Yoshida M. New butenolides in plantlets of *Virola surinamensis* (Myristicaceae). Chem Pharm Bull (Tokyo) 2004;52:1255-7.
79. Carvalho AA, Galdino PM, Nascimento MV, Kato MJ, Valadares MC, Cunha LC, *et al.* Antinociceptive and antiinflammatory activities of grandisin extracted from *Virola surinamensis*. Phytother Res 2010;24:113-8.