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CHEMICAL AND PHARMACOLOGICAL PROPERTIES OF THE GENUS COPAIFERA IN THE TREATMENT OF INJURIES/WOUNDS: INTEGRATIVE REVIEW

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ABSTRACT

Objective: To identify chemical and pharmacological properties of *Copaifera* in the treatment of injuries and wounds. **Method:** Integrative literature review conducted in the LILACS, MEDLINE, PubMed, Taylor & Francis and Scopus databases in January 2022, using the search strategy: "Chemical Properties" AND "*Copaifera*" AND "Wounds and Injuries" and "Pharmacology" AND "*Copaifera*" AND "Wounds and Injuries." Original articles, full text, identified according to level of evidence, written in Portuguese, English or Spanish, were included. **Results:** In the primary search 261 articles were found. After systematized selection, 12 studies were selected for qualitative analysis. Species of the genus *Copaifera* have pharmacological properties favorable for wound treatment: control of inflammatory pain, reduction of inflammatory reaction, tissue reepithelialization and repair, angiogenesis, wound retraction and scar remodeling. Among the chemical properties associated with the treatment of injuries, the presence of bioactive compounds stand out: diterpenes, 3-hydroxy-copalic, sesquiterpenes, kolavic-15-methyl ester. Among the tested diterpenes, kaurenoic and copalic acids showed significant hemolytic activities. Only copalic acid and hardwickiic acid inhibited nitric oxide production in lipopolysaccharide-activated macrophages. **Conclusion:** Plants of the genus *Copaifera* have chemical and pharmacological properties favorable for the treatment of injuries and wounds.

DESCRIPTORS: Pharmacology. Wounds and injuries. Enterostomal therapy.

PROPRIEDADES QUÍMICAS E FARMACOLÓGICAS DO GÊNERO COPAIFERA NO TRATAMENTO DE LESÕES/FERIDAS: REVISÃO INTEGRATIVA

RESUMO

Objetivo: Identificar propriedades químicas e farmacológicas do gênero *Copaifera* no tratamento de lesões e feridas. **Método:** Revisão integrativa da literatura realizada nas bases de dados LILACS, MEDLINE, PubMed, Taylor & Francis e Scopus, em janeiro de 2022, por meio da estratégia de busca: "*Chemical Properties*" AND "*Copaifera*" AND "*Wounds and Injuries*" e "*Pharmacology*" AND "*Copaifera*" AND "*Wounds and Injuries*". Foram incluídos artigos originais, de texto completo, identificados de acordo nível de evidência, redigidos em português, inglês ou espanhol. **Resultados:** Na busca primária foram encontrados 261 artigos. Após a seleção sistematizada, 12 estudos foram selecionados para análise qualitativa. Espécies do gênero *Copaifera* apresentam propriedades farmacológicas

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favoráveis ao tratamento de feridas: controle da dor inflamatória, diminuição da reação inflamatória, reepitelização e reparo tecidual, angiogênese, retração da ferida e remodelagem de cicatrizes. Dentre as propriedades químicas associadas ao tratamento de lesões, destacam-se presença de compostos bioativos: diterpenos, 3-hidroxi-copálico, sesquiterpenos, éster kolavic-15-metílico. Entre os diterpenos testados, o caurenoico e os ácidos copálicos mostraram atividades hemolíticas significativas. Apenas o ácido copálico e o ácido hardwíckiico inibiram a produção de óxido nítrico em macrófagos ativados por lipopolissacarídeos. **Conclusão:** As plantas do gênero *Copaifera* apresentam propriedades químicas e farmacológicas favoráveis ao tratamento de lesões e feridas.

DESCRITORES: Farmacologia. Ferimentos e lesões. Estomaterapia.

PROPIEDADES QUÍMICAS Y FARMACOLÓGICAS DEL GÉNERO COPAIFERA EN EL TRATAMIENTO DE LESIONES/HERIDAS: REVISIÓN INTEGRADORA

RESUMEN

Objetivo: Identificar las propiedades químicas y farmacológicas del género Copaifera en el tratamiento de lesiones y heridas. **Método:** Revisión integradora de la literatura realizada en las bases de datos LILACS, MEDLINE, PubMed, Taylor & Francis y Scopus, en enero de 2022, mediante la estrategia de búsqueda: "Chemical Properties" AND "Copaifera" AND "Wounds and Injuries" e "Pharmacology" AND "Copaifera" AND "Wounds and Injuries". Se incluyeron artículos originales, a texto completo, identificados según el nivel de evidencia, escritos en portugués, inglés o español. **Resultados:** En la búsqueda primaria se encontraron 261 artículos. Tras una selección sistematizada, se seleccionaron 12 estudios para el análisis cualitativo. Las especies del género Copaifera presentan propiedades farmacológicas favorables para el tratamiento de las enfermedades: control del dolor inflamatorio, disminución de la reacción inflamatoria, reepitelización y reparación tecidual, angiogénesis, retracción de la piel y remodelación de las cicatrices. Entre las propiedades químicas asociadas al tratamiento de las lesiones, destaca la presencia de compuestos bioactivos: diterpenos, 3-hidroxicopálico, sesquiterpenos, éster kolavico-15-metilo. Entre los diterpenos probados, los ácidos kaurenoico y copálico mostraron actividades hemolíticas significativas. Sólo el ácido copálico y el ácido hardwickiico inhibieron la producción de óxido nítrico en macrófagos activados por lipopolisacáridos. **Conclusión:** Las plantas del género Copaifera presentan propiedades químicas y farmacológicas favorables para el tratamiento de lesiones y heridas.

DESCRIPTORES: Farmacología. Heridas y Lesiones. Estomaterapia.

INTRODUCTION

The fruit trees of copaibeiras, of the genus *Copaifera*, are rich in their chemical and pharmacological properties[1]. Altogether, more than 70 species of this genus can be found in Latin America and Africa. These plants have been studied by some classification systems, which, depending on the species, may be present in different families[2].

Also called *pau d'óleo* (oil wood), this plant has transparent-looking oil and its color ranges from yellow to brown and can also appear in red, as in the species *Copaifera langsdorffii*[3]. The oils of the different species belonging to the genus Copaifera have been used for years, mainly by native Latin Americans, for medicinal purposes, including treating wounds and injuries[4]. It is believed that this knowledge was acquired by observing injured animals rubbing their bodies on the copaiba trunk to extract them directly from their wounds[1].

Besides serving as an analgesic (copalic acid) and antitumor (collavenol diterpene and hardwickiic acid), Copaiba oil can also aid healing, with anti-inflammatory activity as the main since, among its compounds, hydrocarbons, sesquiterpenes are identified, but especially β-bisabolene and β-cariophilene[5].

Wounds are tissue injuries caused by intrinsic and/or extrinsic factors and can be treated differently depending on their etiology[6]. The wound healing process consists of phases: inflammatory, proliferative/granulation and maturation, where each step is fundamental for rehabilitating the injured tissue[7]. Some factors can delay the process, such as age, nutritional

status of the individual, infections, diabetes mellitus, cardiocirculatory and coagulation disorders, atherosclerosis, renal dysfunction and smoking[8].

All etiological aspects and the wound's history must be considered to design care plans[9]. Concerning the use of products in the treatment of these injuries, with technological advances and the extraction of new materials, numerous coverages have been discovered over the years, which helps professionals in decision-making regarding these types of care[6].

Therefore, the National Policy of Integrative and Complementary Practices is a way of using therapeutic resources not derived from medicines, which seeks the recognition of traditions for human care, comes to validate and include the use of medicinal plants as a form of intervention for a range of illnesses[10].

In this way, one can see the importance of exploring the benefits of using copaiba trees to treat wounds and injuries. Therefore, the objective of this article was to identify the chemical and pharmacological properties of the genus *Copaifera* in treating lesions and wounds.

METHOD

The integrative literature review was used as the method[11] to gather and synthesize evidence from research results on the chemical and pharmacological properties of the genus *Copaifera* that may interfere with the treatment of lesions/wounds.

The following steps were implemented in the carrying of this study: 1) identification of the theme and selection of the hypothesis or research question; 2) establishment of criteria for inclusion and exclusion of studies/sampling or literature search; 3) definition of information to be extracted from selected studies/categorization of studies; 4) evaluation of included studies; 5) interpretation of results; and 6) presentation of the review and synthesis of knowledge[11].

When thinking about the problematizing question, it was proposed its elaboration according to the acronym PICO[12], a concept that enables the construction of the research question in a targeted way, in which P (population/patients): individuals who have wounds/injuries; I (intervention): copaiba as therapy; C (comparison/control): not applicable; and O (outcome/outcome): interference in the healing process of lesions/wounds. Therefore, the research was developed based on the guiding question: "Which chemical and pharmacological properties of the genus Copaifera are useful in treating injuries/wounds?"

For this study, data were collected from the following databases: Latin American and Caribbean Health Sciences Literature (Literatura Latino-Americana e do Caribe em Ciências da Saúde - LILACS), Online Medical Literature Search and Analysis System (Sistema Online de Busca e Análise de Literatura Médica -MEDLINE), National Library of Medicine (PubMed), Taylor & Francis Online and Scopus.

The searches were carried out in January 2022 using a combination of controlled and uncontrolled descriptors. Terms contained in the structured vocabulary Descriptors in Health Sciences (Descritores em Ciências da Saúde-DeCS): "*Chemical Properties, Pharmacology and Wounds and Injuries*", as well as the uncontrolled descriptor: "*Copaifera*", appropriate to the research question.

For sample selection, the combination of descriptors with the Boolean AND operator was used as a search strategy: "*Chemical Properties*" AND "*Copaifera*" AND "*Wounds and Injuries*" and "*Pharmacology*" AND "*Copaifera*" AND "*Wounds and Injuries*" aiming to cover the most significant number of studies on the subject (Table 1).

Table 1. Search strategy and articles found. Crato, Ceará, Brasil. 2022.

Search strategy	LILACS	MEDLINE	PUBMED	SCOPUS	TAYLOR & FRANCIS ONLINE
Chemical Properties AND Copaifera AND Wounds and Injuries.	2	11	51	56	1
Pharmacology AND Copaifera AND Wounds and Injuries.	1	9	63	66	1
TOTAL	3	20	114	122	2

Source: Elaborated by the authors.

The articles were submitted to the reading of titles and abstracts, including original studies in full text involving preclinical and/or clinical research, without estimated publication period, written in Portuguese, English and Spanish. Studies that considered other biological activities and other reviews were excluded.

The flowchart adapted from the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) was used to describe constant information at each stage of the search and selection of studies (Fig.1).

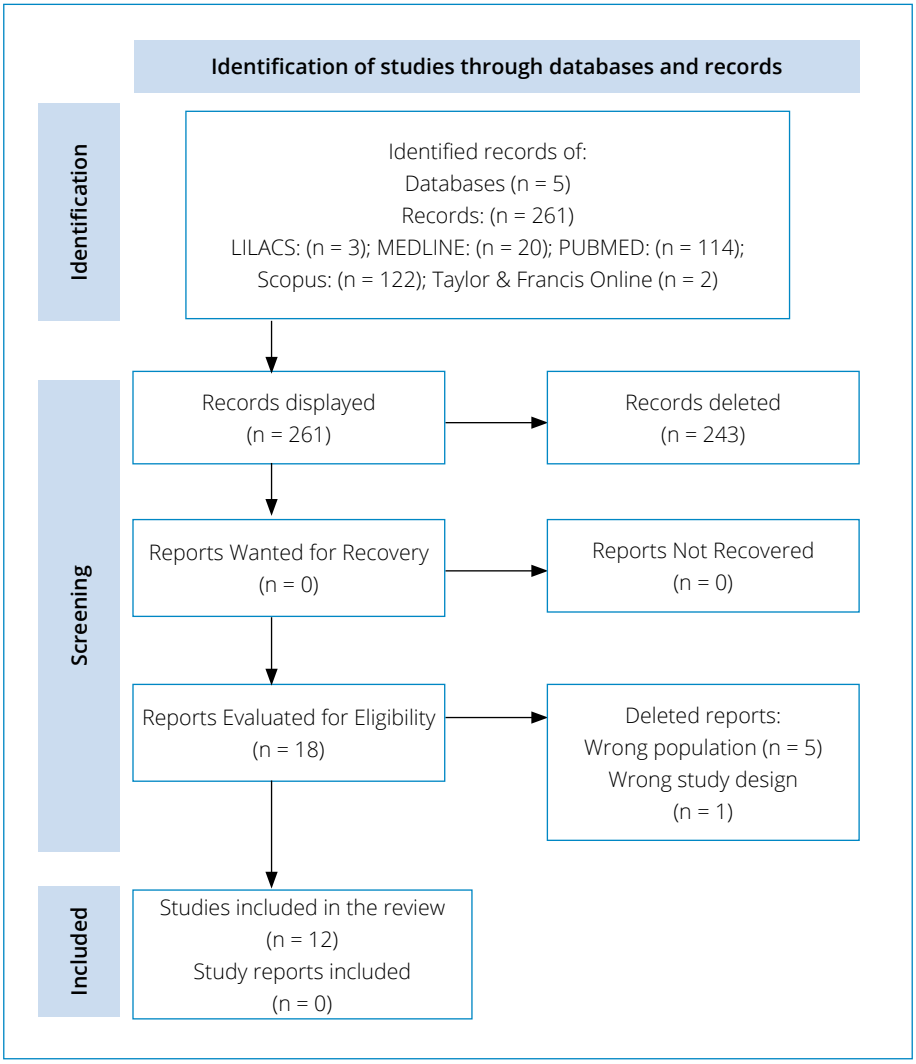

Figure 1. PRISMA flowchart demonstrating the selection of articles.

Source: Elaborated by the authors.

RESULTS

After analyzing the articles in title and abstract, 18 were selected for reading in full, from which it was found that five were repeated and 1 with methodological flaws.

The studies included in this review were classified according to their level of evidence, which is divided into six categories, which include: Level 1: controlled or randomized clinical trials; Level 2: evidence from studies with an experimental design; Level 3: evidence from a study with a quasi-experimental design; Level 4: evidence from non-experimental studies or a qualitative approach; Level 5: evidence resulting from case reports or experience; Level 6: evidence from expert opinions[13].

The data were organized into tables that contemplated the characterization of the articles concerning the identification of the studies (Table 2) and the main results of this research (Table 3).

Table 2. Characterization of the reviewed articles: author/year, base/journal, title, methodological design and level of evidence.

Reference	Author/ year	Base/journal	Title	Methodological design	Level of evidence
14	Dias-da-Silva et al. (2013)	Scopus/ J Clin Exp Dent	*A influência da administração tópica e sistêmica do óleo de copaíba na cicatrização da ferida alveolar após a extração dentária em ratos*	Randomized experimental study	Level 1
15	Vargas et al. (2015)	Scopus/ Molecules	*Atividades biológicas e citotoxicidade de diterpenos de Copaifera spp. oleorresinas*	Experimental study	Level 1
16	Gushiken et al. (2017)	Scopus/ Hindawi	*Potencial de cura de feridas de pele e mecanismos do extrato hidroalcóolico de folhas e oleorresina de Copaifera langsdorffii Desf. Kuntze em ratos*	Randomized experimental study	Level 1
17	Amorim et al. (2017)	Scopus/ Plos One	*Propriedades curativas de Copaifera paupera em ratos diabéticos*	Experimental study	Level 1
18	Teixeira et al. (2017)	Scopus/BMC Complementary and Alternative Medicine	*Oleorresina de copaiba (Copaifera reticulata Ducke) modula a inflamação em modelo de lesão da língua de ratos*	Randomized experimental study	Level 1
19	Senedese et al. (2019)	Scopus/ Biomedicine & Pharmacotherapy	*Papel quimiopreventivo da oleorresina de Copaifera reticulata Ducke na carcinogênese do cólon*	Experimental study	Level 1
20	Becker et al. (2020)	PubMed/Journal of Ethnopharmacology	*A oleorresina de copaíba tem atividade antinociceptiva tópica em modo de queimadura da pele induzida por radiação UVB.*	Study of gas chromatography	Level 2
21	Alvarenga et al. (2020)	Scopus/ Journal of Molecular Sciences	*Segurança e eficácia da oleorresina de copaíba (C. reticulata Ducke) na inflamação e reparação de tecidos de feridas orais em ratos*	Randomized experimental study	Level 1
22	Kauer et al. (2020)	Scopus/ Full Article	*Tratamento experimental de feridas cutâneas com extrato de Copaifera langsdorffii Desf Kuntze (Leguminosae) e resina de óleo em cavalos*	Randomized experimental study	Level 1
23	Waibel et al. (2021)	Scopus/ Dermatol Ther	*Prospectivo, Randomizado, Double-Blind, Placebo, Estudo controlado sobre a eficácia do óleo de copaíba em gel à base de silicone para reduzir a formação de cicatrizes*	A prospective, randomized, double-blind study	Nível 1
24	Almeida Junior et al. (2021)	Scopus/ Veterinary Sciences	*Potencial anti-inflamatório da oleorresina da árvore amazónica Copaifera reticulata com uma composição química inusitada em ratos*	Estudo experimental randomizado	Level 1
25	Paranhos et al. (2022)	Scopus/ Polymers	*Membrana quitosana contendo óleo de copaíba (Copaifera spp.) para tratamento de feridas de pele*	Estudo observacional transversal	Level 2

Table 3. Characterization of the reviewed articles: purpose of the study and main results found.

Reference	Purpose of the study	Main results found
14	To evaluate the influence of topical and systemic administration of copaiba oil on wound healing.	The results showed a high level of epithelial migration, a small number of inflammatory cells and vascular enhancement in animals conducted with copaiba oil. Rats treated with topical administration of copaiba oil showed ulcerations and many inflammatory cells.
15	To study the in vitro cytotoxicity and anti-inflammatory effects of six diterpene acids: copalic, 3-hydroxy-copalic, 3-acetoxy-copalic, hardwickiic, kolavic-15-methyl ester, and kaurenoic, isolated from oleoresins of *Copaifera* spp.	Diterpenes did not show cytotoxicity in standard cell lines, nor did they show significant changes in the viability of tumor line cells. The 3-hydroxy-copalic was able to inhibit the enzyme tyrosinase. Kolavic-15-methyl ester at 200 $\mu mol \cdot L^{-1}$ showed a high inhibition effect on lipoxygenase. Only kaurenoic and copalic acids showed significant hemolytic activities among the tested diterpenes. Furthermore, it was observed that only copalic acid and hardwickiic acid inhibited nitric oxide production in lipopolysaccharide-activated macrophages.
16	To investigate new treatments in skin repair and the mechanisms involved in the process, we used oleoresin (OR) from *C. langsdorffii* and hydroalcoholic extract of the leaves to treat wounds in the skin of rats.	The results showed that the treatments showed anti-inflammatory activity. Molecular and immunohistochemical results demonstrated the activity of *C. langsdorffii* creams on angiogenesis, re-epithelialization, wound retraction and remodeling mechanisms.
17	Evaluate the wound and healing capacity of oleoresin obtained from *C. paupera*, its mechanism of action and identify its main components.	Histological evaluations demonstrated that treatment with higher doses resulted in better resolution, wound closure, and higher levels of collagen deposition and re-epithelialization rates, even when compared to the group treated with collagenase.
18	To evaluate the anti-inflammatory and healing effect of copaiba oleoresin (*C. reticulata* Ducke) on the transfixing lesion of the tongue of rats.	The acute toxicity test showed that copal oleoresin has low toxicity. The therapy modulates the inflammatory response by decreasing the chronic inflammatory infiltration, edema and, specifically, the number of macrophages.
19	The anti-inflammatory activity of CRO and its main chemical constituent, the diterpene ent-polyaltic acid (PA), were studied to understand the mechanisms involved in this effect.	PA exerts anti-inflammatory action via the NO pathway. CRO's chemopreventive effect may be due in part to the anti-inflammatory property of its main chemical constituent, PA. Our findings indicate that CRO is a promising agent for suppressing colonic carcinogenesis.
20	To investigate the antinociceptive and anti-inflammatory effects of a topical formulation containing Copaiba oleoresin (3%) in a UVB model of skin burns induced by radiation (0.75 J/cm2) in mice.	The topical formulation containing copaiba oleoresin showed antinociceptive and anti-inflammatory effects in mice subjected to UVB radiation, and the cream formulation was stable for two months. Thus, the use of copaiba oleoresin is a promising strategy for the treatment of inflammatory pain.
21	To evaluate the effects of copaiba oleoresin on oral lesions and the safety of the proposed dosage.	Wounds treated with copaiba revealed a smaller wound area, decreased inflammatory reaction and increased re-epithelialization. Levels of kidney and liver function tests did not reveal the presence of post-treatment damage. Our findings suggest that copaiba oleoresin is a safe and effective alternative therapy for inflammation and tissue repair of oral wounds in this animal model.

continue...

Table 3. Continuation...

Reference	Purpose of the study	Main results found
22	To evaluate the curative potential of hydroalcoholic extract (HE) of *C. langsdorffii* and oleoresin creams (OR) in equine skin wounds.	Better microscopic and clinical healing activity of HE and OR was identified compared to controls. The OR group showed a better healing quality, especially after seven days of treatment. Thus, *C. langsdorffii* demonstrated its healing potential in equine skin lesions, improving macro and microscopic parameters.
23	The aim is to evaluate the effectiveness of a new silicone-based gel containing copaiba oil (Copaderm) for preventing and/or reducing the appearance of different types of abnormal scars.	Silicone-derived copaiba oil gel improved significantly in color, contour, distortion and texture for different scar types through the Manchester Scar Analysis scale. These findings contribute to reducing abnormal scar formation during the healing process.
24	Evaluate the anti-inflammatory potential of this oleoresin obtained from a national forest in the central Amazon that had an unusual chemical composition.	The anti-inflammatory potential was assessed by carrageenan-induced paw edema and air pocket assays using four concentrations of *C. reticulata* oleoresin (10, 100 and 400 mg/kg). The exudate was evaluated for nitrite concentration by the colorimetric method and for TNF-α, IL-1β and PGE2 by ELISA. Oleoresin collected from *C. reticulata* in the Amazonian summer contained six main sesquiterpene compounds (β-bisabolene, cis-eudesma-6,11-diene, trans-α-bergamotene, β-selinene, α-selinene and β-elemene) and was not toxic at a dose of 2,000 mg/kg, with low acute toxicity.
25	To investigate for the first time chitosan membranes containing different contents of copaiba oil (0.1, 0.5, 1.0 and 5.0%).	These chitosan/copaiba oil porous membranes revealed fluid absorption capacity, hydrophilic surface and humidity. In addition, the results showed that the chitosan membranes with the addition of 1.0% (v/v) of copaiba oil presented oil droplets with larger diameters, around 123.78 μm. The highest fluid absorption rates were observed in chitosan membranes containing 0.1 and 0.5% (v/v) copaiba oil. Furthermore, copaiba oil modified the crystalline structure of chitosan. Such characteristics are expected to favor the treatment of wounds.

DISCUSSION

The uses of Copaifera oil in popular medicine are many and indicate a wide variety of chemical and pharmacological properties. The primary reported activities are anti-inflammatory activities in the upper and lower pathways and wound healing. However, the oil was once considered the true panacea due to many medicinal indications. Still, its use and prescription have decreased significantly over time, mainly due to the synthesis and use of other medications for the same purposes for which the copaiba oil was indicated[26].

However, some of these previously forgotten properties have begun to be described again by researchers who have studied their use. According to Lisboa et al.[27], copaiba oil is attributed to anti-inflammatory, healing, and gastroprotective activities, which already have scientific proof from several other experimental studies. Regarding this genus, Copaifera officinalis was the first species to be described in a study on constituents of its seeds, where it was possible to observe the presence of fatty acids (hexadecanoic, 9-octadecenoic and octadecanoic); and decanoic, eicosanoic, docosanoic, tetracosanoic and hydrocarbons, these being some of the chemical compounds responsible for promoting the healing action known and attributed to some species of the copaiba genus[28].

Also, according to Lisboa et al.[27], which aimed to identify the presence of some tannin metabolites, alkaloids and flavonoid glycosides in the oil of *C. langsdorffii* Desf., it was found that tannins, alkaloids were present in the phytochemical

analysis, which led to the conclusion of the presence of sesquiterpene and diterpene constituents. These data corroborate the findings of the present study, in which the emphasis on healing activities was investigated.

When testing the effects of copaiba oil resin from the same species by topical and systemic administration, it was found that rats treated with copaiba oil systemically showed a high level of epithelial migration and a small number of inflammatory cells associated with thicker bone trabeculae. The study demonstrated that copaiba oleoresin improves the healing of sockets in rats after tooth extraction. In addition, it was also possible to verify that, when used, copaiba oleoresin leads to an increase in bone formation, not only in endogenous treatments but also in topical treatments. This study reveals that animals treated with topical copaiba oil showed reduced epithelial migration. It can be inferred that the antiseptic properties of copaiba oil resin play an essential role in the results observed in topically treated animals. In addition, these results also suggest that some components of copaiba oil, such as kaurenoic acid (the main diterpene of this oleoresin), can stop the inflammatory process and thus accelerate socket repair[14].

In their study, Gushiken et al.[16] also used oleoresin from *C. langsdorffii* in a cream formulation in the lesion model in rats. A reduction in the concentrations of pro-inflammatory cytokines TNF-α, IL-1 β, and IL-6 was observed after three days of treatment, and an increase in the anti-inflammatory cytokine IL-10, inhibiting chronic inflammation was observed after seven days of treatment, thus presenting an anti-inflammatory effect in the treatment of lesions. The anti-inflammatory effect and the reduction in the concentration of pro-inflammatory cytokines, which inhibit chronic inflammation and prevent the formation of fibrosis, were also results of the study.

In another study in which rats were used as an experimental model to test the healing efficacy of oleoresin from *Copaifera multijuga* compared to the use of nitrofurazone, it was found that the oil contributed positively to the healing of cutaneous wounds by second intention, considering the criteria of inflammation, epithelialization and neovascularization in their evaluation[19]. In a study involving the *C. reticulata* in natura, it was observed that its topical application inhibited the migration of cells to the exudate; however, it did not prevent the inhibition of exudate formation. The decrease in exudation suggests that part of the anti-inflammatory effect of copaiba oil can be attributed to the reduction in vascular permeability. With this, it can be recommended that one of the possible mechanisms involved in the removal of the inflammatory process of this species of copaiba *in natura* is the inhibition of cell migration to the inflammatory site, which may be related to the release of leukotriene B4, which is an agent chemotactic for neutrophils. This conclusion also corroborates the results found, in which a decrease in the inflammatory exudate was observed through nitrite concentration by the colorimetric method[29].

Amorim et al.[17] studied oleoresin from *C. paupera*, whose composition was determined by gas chromatography analysis coupled with mass spectrometry. It was found that the α-copaene sesquiterpene was the main component, representing 22.9%, followed by the diterpenes hardwickiic acid (8.1%) and Kaur-16-ene (6.5%), the sesquiterpenes and diterpenes identified in the oleoresin correspond to 60.2 and 25.4%, respectively. Results showed that oleoresin significantly reduced MCP-1 and TNF α production on days 7 and 10 post-excision and increased IL-10 production on both days. With ten days of treatment, it was also possible to observe the reduced cytokine quantified in the tissue. Treatment also influenced MCP-1 levels. Within seven days of treatment with *C. paupera*, elevated levels of IL-10 accumulated in wound tissues were observed. The authors suggest that the high levels of IL-10 in the groups treated with *C. paupera* improved the organization of collagen fibers, contributing positively to the wound healing process and that the reduction of TNF-α levels in the skin may justify the improvement observed in the inflammatory phase of the treated groups, which suggests that there was a decrease in this phase.

In the meantime, for developing therapies for topical or systemic use, much has been researched on medicinal plants that facilitate wound healing, provide well-being and improve the lives of individuals with some deficit in the healing process[1]. Therefore, medicinal plants can be a therapeutic resource for difficult recovery due to their active principles, which are produced during their metabolism and which grant them this therapeutic action[8].

According to the National Policy and Program of Medicinal Plants and Herbal Medicine, medicinal plants are essential for pharmacological research and drug development. Not only when their constituents are used directly as therapeutic agents but also as raw materials for synthesis or models for pharmacologically active compounds, and the potential use of medicinal plants is far from being exhausted[28].

The limitation in the number of studies that make up this review and evaluation of the level of research evidence enable an even more significant reduction in the number of studies included in the analysis that investigates the chemical and pharmacological properties of the genus *Copaifera* in treating injuries and wounds. Therefore, new studies with high power of evidence are expected to be carried out and published, with the inclusion of increasingly accurate data, to explain the mechanisms of action and interaction of the studied product in the treatment of wounds and injuries, demonstrating the mode parameters, time and several product applications.

CONCLUSION

From this integrative review, controlled or randomized clinical studies with experimental design on plants of the genus Copaifera were identified and, consequently, the potential for developing new effective drugs for treating lesions. Among the pharmacological properties, the anti-inflammatory, healing, gastroprotective, tissue modeling and reducing vascular permeability activities stand out. The study demonstrated that kaurenoic acid could stop the inflammatory process; fatty acids and decanoic, eicosanoic, docosanoic, tetracosanoic and hydrocarbons are responsible for promoting healing.

Substances with anti-inflammatory and healing activity show promise, motivating new studies in this area. However, the number of studies with levels of excellence 1 and 2 on chemical properties that may be involved in this process proved to be scarce, so it is necessary to seek perspectives for the development of studies in this area.

CONFLICT OF INTEREST

The authors declare no conflicts.

AUTHORS' CONTRIBUTION

Conceptualization: Fernandes MNM and Macedo LFR; **Methodology:** Macedo LFR; **Research:** Macedo LFR; **Writing – First version:** Macedo LFR, Rodrigues VRT, Feitosa EMS and Silva MR; **Writing – Reviewing & Editing:** Macedo LFR; Rodrigues VRT, Feitosa EMS and Silva MR; **Acquisition of Financing:** Moreira RA; **Resources:** Sampaio LRL; **Supervision:** Fernandes MNM and Sampaio LRL.

DATA AVAILABILITY STATEMENT

Data will be available upon request.

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