Review article / Artykuł przeglądowy

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Application of copaiba oleoresin in cosmetology and aromatherapy. A narrative review

Zastosowanie oleożywicy copaiba w kosmetologii i aromaterapii. Przegląd narracyjny

ABSTRACT

Introduction: Oleoresin obtained from trees of the genus *Copaifera* (copaiba oleoresin) has been used for centuries in traditional medicine and the treatment of infectious diseases.
Aim: The article aimed to summarize current data regarding the chemical composition, biological properties, safety profile, and potential applications of copaiba oleoresin, with particular emphasis on its significance in cosmetology and aromatherapy.
Methods: PubMed and Google Scholar database searches were conducted in June 2026. Publications from 2021-2026 were included in the analysis. Original research articles, case reports, and reviews published in English or Polish were considered.
Results: Available data indicate that copaiba oleoresin exhibits significant anti-inflammatory, antioxidant, antimicrobial, and analgesic properties, as well as wound-healing effects, primarily attributed to the presence of β-caryophyllene and diterpenes. Although the number of clinical studies remains limited, results from recent randomized trials show promising effects regarding wound healing, oral health improvement, and anxiety reduction.
Conclusions: Copaiba oleoresin is a promising, multifunctional natural ingredient with potential applications in cosmetology, aromatherapy, and complementary medicine. However, further well-designed clinical studies and the development of standardized formulations are necessary to confirm its efficacy.

Keywords: *Copaifera*, copaiba oleoresin, β-caryophyllene, aromatherapy, wound healing, complementary medicine.

STRESZCZENIE

Wstęp: Oleożywica pozyskiwana z drzew z rodzaju *Copaifera* spp. (oleożywica copaiba) jest od wieków wykorzystywana w medycynie tradycyjnej oraz w terapii chorób zakaźnych.
Cel: Celem przeglądu było podsumowanie aktualnych danych dotyczących składu chemicznego, właściwości biologicznych, profilu bezpieczeństwa oraz potencjalnych zastosowań oleożywicy copaiba, ze szczególnym uwzględnieniem jej znaczenia w kosmetologii i aromaterapii.
Metody: Przeszukiwanie baz danych PubMed oraz Google Scholar przeprowadzono w czerwcu 2026 roku. Do analizy włączono publikacje z lat 2021-2026. Uwzględniono oryginalne prace badawcze, opisy przypadków oraz artykuły przeglądowe opublikowane w języku angielskim lub polskim.
Wyniki: Dostępne dane wskazują, że oleożywica copaiba wykazuje istotne właściwości przeciwzapalne, przeciwutleniające, przeciwdrobnoustrojowe, przeciwbólowe oraz wspomagające gojenie ran, przypisywane głównie obecności β-kariofilenu oraz diterpenów. Chociaż liczba badań klinicznych jest nadal ograniczona, wyniki najnowszych randomizowanych badań wskazują na obiecujące efekty w zakresie gojenia ran, poprawy zdrowia jamy ustnej oraz redukcji lęku.
Wnioski: Oleożywica copaiba stanowi obiecujący, wielofunkcyjny naturalny składnik o potencjalnym zastosowaniu w kosmetologii, aromaterapii oraz medycynie komplementarnej. Niezbędne są jednak dalsze, dobrze zaprojektowane badania kliniczne oraz opracowanie standaryzowanych formulacji, aby potwierdzić jej skuteczność.

Słowa kluczowe: *Copaifera*, oleożywica copaiba, β-kariofilen, aromaterapia, gojenie ran, medycyna komplementarna.

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INTRODUCTION

Therapies currently classified as complementary medicine often derive from ancient healing practices or have their roots in traditional folk medicine [1]. Aromatherapy, a major complementary therapy, incorporates essential oils and other plant-based materials, including hydrosols and resins, into practices aimed at improving physical and mental well-being. Aromatic plants are an important source of numerous biologically active compounds and natural raw materials used in pharmaceutical products and cosmetic preparations [2].

Although copaiba oleoresin is not among the most widely used plant-based raw materials, it has been attracting increasing interest from the scientific community in recent years. Numerous studies have demonstrated its anti-inflammatory, wound-healing, antiseptic, and anticancer properties, making it a promising ingredient in cosmetic and dermatological formulations [3]. Preparations derived from the oleoresin or bark of trees in the genus *Copaifera* have long been used in traditional medicine as anti-inflammatory agents to treat respiratory diseases, such as bronchitis, as well as infectious diseases, including syphilis. Topical application of these preparations has also been associated with accelerated wound healing and improved tissue regeneration [4].

In traditional manual therapy methods, including massage, copaiba oleoresin and its derivatives were applied to the scalp to alleviate neurological symptoms such as pain, convulsions, or paralysis. Topical preparations were also recommended to treat various skin conditions, including tumours, ulcers, and hives. Decoctions made from the bark were used to treat infected wounds, including those resulting from animal bites, and to alleviate rheumatic ailments. Furthermore, the raw material, traditionally called copaiba balm, was commonly included in medicinal plasters applied directly to wounds and chronic ulcers [4].

The traditional terminology used to describe products derived from copaiba can be misleading under modern pharmacognostic nomenclature. Essential oil is defined as a natural, volatile mixture of organic compounds extracted from plants, most commonly by steam distillation or cold pressing. Resin, by contrast, is a thick, usually sticky substance secreted by certain plants, especially conifers, that hardens upon contact with air and protects the plant from pathogens and mechanical damage. Oleoresin is a natural mixture of resin and essential oil that combines the physicochemical and biological properties of both fractions. It occurs in many aromatic and spice plants and, after exudation, retains both its viscous consistency and characteristic aroma. Balsam, however, is a specific plant secretion containing resins, essential oils, and often benzoic acid, cinnamic acid, or their derivatives. Due to their thick consistency, pleasant scent, and protective properties, balsams have been used for centuries in both medicine and perfumery.

Copaiba oleoresin (also known as balsam) comes from species in the genus *Copaifera* (commonly called copaiba trees) in the legume family (*Fabaceae*) [5]. These trees are found primarily in the Amazon rainforest, where they grow along river and lake banks. Species of the genus *Copaifera* are also widespread in Central America and Africa [6], while in other regions they occur as introduced species (Fig. 1).

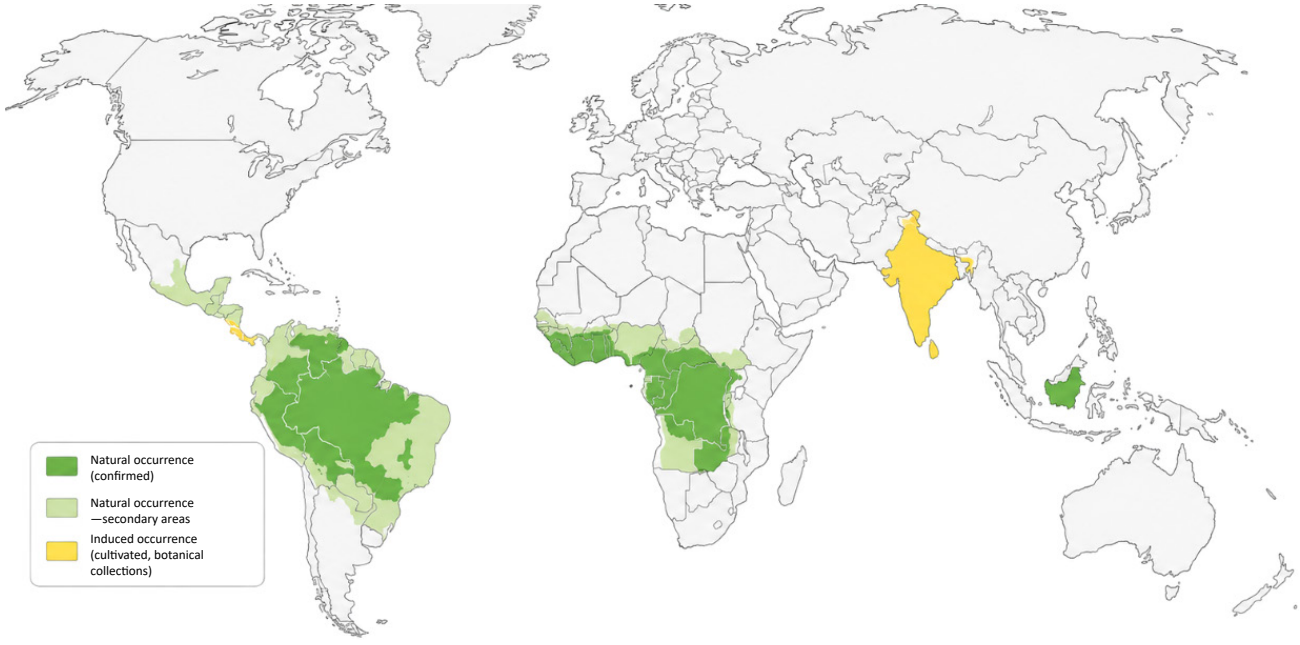


Fig. 1. Occurrence of the copaiba tree. **Source:** Author's own work based on [7, 8].

Trees of the genus *Copaifera* can reach heights of up to 40 m and trunk circumferences of about 4 m (Fig. 2). Their trunks are covered with rough, aromatic bark [6], and individual trees can live up to 400 years [9].

The species most commonly used for commercial oleoresin harvesting include *Copaifera reticulata, C. multijuga, C. langsdorffii, C. officinalis*, and *C. paupera*. Oleoresin is harvested by tapping, a method similar to collecting maple syrup. A 25 cm diameter hole is drilled into the trunk of a mature tree at 11.5 m above ground level. Once the natural resin channels within the trunk are reached, the oleoresin flows out on its own and is collected in sterile containers. After harvesting, the hole is sealed with a wooden peg or other suitable sealing material, allowing the tree to regenerate and enabling oleoresin to be harvested again after several months or years. Depending on the species, the tree's age, and environmental conditions, a single tree can yield anywhere from several hundred milliliters to several liters of oleoresin during a single harvesting cycle.



Fig. 2. The copaiba tree. **Source:** [10].

Brazil has long been the world's largest producer and exporter of copaiba oleoresin, accounting for most global production. Peru, Colombia, Venezuela, Bolivia, and Guyana

Tab. 1. Chemical composition of copaiba balm. **Source:** [3, 14].

Fraction	Compound	Chemical type	Typical content/significance
Sesquiterpenes (volatile fraction)	β-Caryophyllene	Bicyclic sesquiterpene	20-60% of the total volatile fraction
	α-Humulene	Sesquiterpene	110%
	β-Bisabolene	Sesquiterpene	The predominant component in certain species
	trans-α-bergamotene	Sesquiterpene	One of the main chemical markers
	α-Kopaene	Sesquiterpene	Minor component
	β-Elemen	Sesquiterpene	Trace component
	δ-Kadinen	Sesquiterpene	Trace component
	α-Cadinol	Sesquiterpene alcohol	Trace component
	Germacrene D	Sesquiterpene	Subtle woody-herbal fragrance notes
	α- and β-selinene	Sesquiterpenes	Variable content
	Caryophyllene oxide	Oxidized sesquiterpene	Oxidation product of β-caryophyllene (increases over time storage)
	α-Cubebene	Sesquiterpene	Excipient
	Copalic acid	Labdane diterpene	One of the most important markers of authenticity
	Hardwickic acid	Diterpene	Commonly found
	Kolavenic acid	Clerodanic diterpene	Trace component
	Polyalthic acid	Diterpene	Common resin component
Diterpenes (resin fraction)	Kaurenoic acid	Cauranic diterpene	Anti-inflammatory and antimicrobial activity
	Entagathic acid	Diterpene	Minor component
	Ozic acid	Diterpene	Present in some species (rarely reported)
	Labdane derivatives	Diterpenes	Trace component
	Clerodane derivatives	Diterpenes	Trace component
	Caurane derivatives	Diterpenes	Trace component

also harvest smaller quantities of the raw material. In recent years, growing demand for natural pharmaceutical, cosmetic, and aromatherapy products has driven rapid growth in international trade in copaiba oleoresin and products derived from this raw material. The main customers are the pharmaceutical and cosmetics industries, as well as dietary supplement manufacturers, while the most important export destinations include the United States, the European Union, Japan, and China.

The chemical composition of copaiba balm is highly variable and depends primarily on the *Copaifera* species, as well as on soil properties, climatic conditions, and anthropogenic factors, including fertilization practices [11]. The biological properties of copaiba balsam result from its two main fractions - the volatile and resinous fractions - and depend largely on the content of secondary plant metabolites, especially sesquiterpenes and diterpenes [12]. The most important sesquiterpenes identified in copaiba oleoresin include β-caryophyllene (BCP), α-humulene, and α-copaene. The diterpene fraction, found mainly in the resinous portion of the oleoresin, consists primarily of caurenic acid, alepterolic acid, copalic acid, and polialtic acid [13]. Table 1 presents the main chemical constituents of copaiba balsam.

AIM

The review aimed to summarize the latest scientific reports on copaiba oleoresin and to present its biological properties and potential applications in cosmetology and aromatherapy.

REVIEW METHODOLOGY

A search of the PubMed and Google Scholar databases was conducted in June 2026. Publications from 2021 to 2026 were included in the analysis. Original research studies, case reports, and review articles published in English or Polish were considered. The search strategy was based on the following keywords and their combinations: copaiba, copaiba tree, chemical composition, benefits of use, problematic skin, and use in cosmetology.

RESULTS

Anti-inflammatory effects

Copaiba balm has long been used in traditional medicine to treat inflammation, and modern research provides increasing evidence supporting these applications. Its anti-inflammatory properties are primarily attributed to its high sesquiterpene content, especially β-caryophyllene, considered one of the main biologically active compounds responsible for its therapeutic effects. It is precisely this anti-inflammatory activity is one of the most important mechanisms justifying the potential use of copaiba oleoresin in cosmetology and aromatherapy.

This effect was confirmed in *in vitro* studies using the J774 mouse macrophage line, in which stimulation with lipopolysaccharide (LPS) led to strong cell activation, accompanied by increased production of pro-inflammatory cytokines and reactive oxygen species (ROS). Both pure copaiba essential oil and its nanoencapsulated form, based on poly(ε-caprolactone) nanoparticles, significantly reduced the secretion of tumour necrosis factor alpha (TNF-α) and intracellular ROS levels compared to the control groups. Importantly, the nanoparticle-based formulation exhibited approximately three times stronger inhibition of TNF-α production than the non-encapsulated raw material, suggesting that nanoencapsulation enhances the bioavailability and biological activity of the active ingredients. These results indicate the potential of copaiba-derived products as ingredients in cosmetic formulations that reduce skin inflammation and oxidative stress, as well as promising anti-inflammatory agents used in aromatherapy. They also support the development of modern delivery systems for active ingredients to enhance the therapeutic efficacy of this plant-based raw material [15].

One of the best-known therapeutic applications of copaiba oleoresin is dentistry, particularly periodontology. In a study conducted by Nazário et al. [16], an experimental model of periapical inflammation in rats was used to evaluate the biological effects of copaiba oleoresin. Exposure of the dental pulp allowed bacteria to colonize the root canal, leading to chronic inflammation of the periapical tissues. This process was characterized by the activation of an immune response, an influx of inflammatory cells, and progressive resorption of the alveolar bone. This model reflects many pathophysiological mechanisms of chronic inflammatory diseases, including increased production of pro-inflammatory cytokines such as TNF-α, interleukin-1 beta (IL-1β), and interleukin-6 (IL-6), macrophage activation, and stimulation of osteoclasts responsible for bone resorption. The degree of bone loss can therefore serve as a biological marker of inflammatory severity.

Treatment with copaiba oleoresin significantly limited the development of osteolytic lesions and reduced tissue damage, suggesting that its beneficial effects extend beyond antimicrobial activity and also include the modulation of inflammatory pathways responsible for tissue degradation. According to the authors, this effect is primarily associated with the presence of β-caryophyllene and diterpenes, which inhibit the production of inflammatory mediators and osteoclast activity.

Another area of research focused on the effects of copaiba oleoresin on obesity-associated inflammation. In an experimental study in rats, oral administration of the oleoresin limited weight gain, reduced visceral adipose tissue and inflammatory severity, and improved redox homeostasis

in adipose tissue from animals with obesity induced by a high-sugar diet [17]. The authors also showed a significant reduction in markers of inflammation and oxidative stress in adipocytes, further confirming the oleoresin's systemic anti-inflammatory effect.

Experimental studies have further shown that copaiba oleoresin reduces tissue oedema and the number of leukocytes present in inflammatory exudate. This effect was accompanied by reduced concentrations of key inflammatory mediators, such as TNF-α, IL-1β, prostaglandin E_2 (PGE_2), and nitric oxide metabolites. These results suggest that copaiba oleoresin limits the recruitment of inflammatory cells to the site of tissue damage and modulates the signalling pathways that initiate and sustain the inflammatory response. Similar observations were reported in both acute inflammation models and experimental models of pneumonia, indicating to the broad spectrum of anti-inflammatory activity of the studied raw material [18].

Unlike most studies on copaiba oleoresin, which were based primarily on *in vitro* experiments or animal models, the study conducted by Cardinelli et al. [19] was a randomized controlled trial (RCT), thereby providing significantly stronger clinical evidence. The authors evaluated the efficacy of a polymer hydrogel containing *Copaifera multijuga* oleoresin for treating traumatic skin wounds, comparing its effects with standard wound care. Patients treated with the hydrogel containing copaiba oleoresin showed faster wound healing and better tissue regeneration than those receiving conventional treatment. Because proper healing depends on a well-controlled inflammatory response, these results indirectly support copaiba oleoresin's ability to modulate inflammatory processes in damaged skin. Furthermore, the therapy was well tolerated and was not associated with any significant adverse effects. As in previous studies, β-caryophyllene, copalic acid, and kaureneic acid were primarily responsible for the observed therapeutic benefits. Taken together, these results constitute some of the strongest clinical evidence currently available confirming the anti-inflammatory and regenerative potential of preparations containing copaiba oleoresin [19].

Antioxidant activity

The antioxidant activity of copaiba oleoresin has been confirmed in several animal models of both metabolic and cardiovascular diseases. Telles et al. [17] demonstrated that oral administration of copaiba oleoresin to rats fed a high-sugar diet significantly reduced the severity of oxidative stress and improved redox homeostasis. The treatment reduced oxidative stress biomarkers and improved parameters related to adipose tissue function, suggesting that copaiba oleoresin may counteract pathological processes associated with obesity and chronic low-grade inflammation [17].

Campos et al. [20] obtained similar results when they investigated the effect of copaiba oleoresin in a rat model of *cor pulmonale*. Treatment with copaiba oleoresin significantly reduced oxidative stress, as confirmed by changes in peripheral biochemical markers. The authors showed reduced free-radical-induced damage and restored the balance between reactive oxygen species production and endogenous antioxidant activity [20].

The antioxidant properties of copaiba oleoresin are primarily attributed to β-caryophyllene, α-humulene, and diterpenes such as copalic acid and kaureneic acid. These compounds have been shown to inhibit the activation of pro-inflammatory signalling pathways, reduce ROS formation, and increase the activity of endogenous antioxidant enzymes. As a result, copaiba oleoresin can simultaneously reduce oxidative stress and inflammation - two closely related processes that play a key role in the pathogenesis of many chronic diseases [21].

In most experimental studies, copaiba oleoresin was administered orally at doses of approximately 100–400 mg/kg body weight per day, although the exact dosage varied depending on the *Copaifera* species and the research model used. Despite promising results, there is still a lack of well-designed clinical trials evaluating the efficacy and optimal dosage of preparations containing copaiba oleoresin to achieve an antioxidant effect in humans. For this reason, the available data should be considered encouraging but still preliminary. Further, well-designed clinical trials are necessary to confirm the observations to date and to develop dosage recommendations.

Antibacterial and antifungal activity

Copaiba oleoresin exhibits antibacterial and antifungal properties, as confirmed in numerous laboratory studies (Tab. 2). In a study conducted by de Mello et al. [22], the *in vitro* bactericidal activity of *Copaifera duckei* oleoresin against *Streptococcus agalactiae* and *Flavobacterium columnare* was evaluated using the serial dilution method, and its efficacy was subsequently verified *in vivo* in Nile tilapia (*Oreochromis niloticus*). The oleoresin exhibited marked bactericidal activity under laboratory conditions, while fish receiving higher doses of this raw material in their diet demonstrated better immune response parameters and a lower degree of tissue damage following bacterial infection.

Despite numerous *in vitro* studies confirming the antibacterial activity of copaiba oleoresin against oral bacteria, pathogens responsible for periodontal disease, and multidrug-resistant strains (Tab. 2), there is still a lack of a sufficient number of randomized clinical trials evaluating the efficacy of these properties in humans. The strongest clinical evidence is currently provided by a randomized controlled trial conducted by Cardinelli et al. [19], in which a hydrogel

containing *Copaifera multijuga* oleoresin significantly accelerated healing of traumatic skin wounds. Although the study did not directly assess microbiological parameters, the results are consistent with previous reports indicating the anti-inflammatory and antimicrobial properties of copaiba oleoresin.

Additional clinical evidence was provided by a randomized controlled trial evaluating a dental varnish containing copaiba oil used in children. The preparation was applied to the tooth surface, and the incidence of dental caries was subsequently assessed based on clinical evaluation. The copaiba oil varnish showed promising protective effects against dental caries, suggesting its potential to control oral biofilm and prevent periodontal disease [23].

Analgesic and wound-healing effects

The analgesic properties of copaiba oleoresin are primarily attributed to BCP, which often accounts for 30-60% of its volatile fraction [3]. β-Caryophyllene is a selective agonist of the cannabinoid receptor type 2 (CB2), and activation of this receptor leads to the inhibition of the release of pro-inflammatory mediators and a reduction in the sensitization of nociceptors. Unlike cannabinoid receptor type 1 (CB1) agonists, β-caryophyllene does not produce psychoactive effects. Furthermore, diterpenes in copaiba oleoresin, such as copalic acid and kaureneic acid, may indirectly alleviate pain by reducing inflammation, a key mechanism underlying chronic pain development [35].

Experimental studies consistently confirm the analgesic effects of copaiba oleoresin, especially following its topical application to damaged skin [5, 15, 18, 24]. In a model of UVB-induced skin burns, a cream containing 3% copaiba oleoresin significantly reduced both sensitivity to mechanical and thermal stimuli [27]. These results indicate an analgesic (antinociceptive) effect associated with the inhibition of pain signal transmission in the nervous system.

In addition to its analgesic properties, a growing body of research indicates that copaiba oleoresin promotes wound healing. In a study published in 2024, conducted using a mouse model of acute allergic airway inflammation, it was shown that copaiba oleoresin significantly reduced the severity of the inflammatory response and promoted re-epithelialization by reducing elastic fiber fragmentation and increasing collagen deposition [25]. These results suggest that copaiba oleoresin supports tissue regeneration, although the strength of this effect may depend on the route of administration and

Tab. 2. Antimicrobial activity of copaiba oleoresin (*Copaifera* spp.). A review of *in vitro* studies and experimental data. **Source:** [3, 12, 20, 24-26].

Microorganism	Clinical significance	Method of confirming activity	Observed effect
Staphylococcus aureus	Skin and wound infections, atopic dermatitis	MIC, MBC, agar diffusion	Inhibition of the growth of Gram-positive *Staphylococcus epidermidis*
Staphylococcus epidermidis	Skin biofilm, infections of implants	MIC, growth tests	Bacteriostatic activity
Cutibacterium acnes (formerly *Propionibacterium acnes)*	Acne vulgaris	*In vitro* studies, dermatological formulations	Inhibition of bacterial growth associated with acne
Streptococcus mutans	Dental caries	MIC, biofilm tests	Inhibition of biofilm formation
Enterococcus faecalis	Endodontic infections	*In vitro* microbiological tests	Reduction of bacterial growth
Porphyromonas gingivalis	Periodontitis	Periodontal studies	Antibacterial and anti-inflammatory effects
Aggregatibacter Actinomyces comitans	Periodontal diseases	MIC, bacterial cultures	Inhibition of proliferation
Escherichia coli	Infections of the and urinary tract	MIC, MBC	Moderate susceptibility, usually lower than Gram-positive bacteria
Pseudomonas aeruginosa	Wound and burn infections	MIC, agar diffusion	Weaker activity than against Gram-positive bacteria
Klebsiella pneumoniae	Hospital-acquired infections	Growth tests	Partial susceptibility
Candida albicans	Candidiasis of the skin and mucous membranes	MIC, fungal cultures	Antifungal activity
Candida tropicalis	Opportunistic infections	MIC	Growth inhibition
Candida glabrata	Infections in with impaired immunity	MIC	Moderate antifungal activity

MIC (minimum inhibitory concentration) – the minimum concentration required to inhibit microbial growth; MBC (minimum bactericidal concentration) – the minimum concentration required to kill microorganisms.

the type of injury. Taken together, the available data indicate that copaiba oleoresin may simultaneously relieve pain and accelerate tissue repair, particularly in the context of inflammation and injuries to the skin and mucous membranes [5, 15, 18, 24].

Clinical evidence supporting the analgesic effects of copaiba oleoresin in humans remains limited. Studies published since 2021 have primarily focused on wound healing and modulation of the inflammatory response, while pain assessment has typically been a secondary endpoint. Nevertheless, numerous preclinical studies indicate that copaiba oleoresin has significant analgesic potential that may be clinically relevant [25].

USE OF COPAIBA

Use in cosmetology

The available scientific evidence on the use of copaiba oleoresin in cosmetology remains limited. As an active ingredient, it is most commonly used in functional formulations designed for the care of irritated, problematic, and inflamed skin. Copaiba oleoresin is primarily found in creams and serums for acne-prone skin, spot treatments for specific dermatological issues, including those affecting the oral cavity, and dermocosmetics. It is also used in regenerative formulations and in skincare products applied after sun exposure, where it acts as a soothing agent and helps restore the skin's barrier. Due to its anti-inflammatory properties and potential analgesic effects, copaiba oleoresin is also used in massage oils, lotions, and topical preparations to relieve musculoskeletal discomfort. Less commonly, it is used in hair and scalp care products to reduce irritation and alleviate inflammatory changes on the scalp [7, 25].

Copaiba oleoresin is suggested as a potential adjunct in the treatment of acne vulgaris [28]. However, current clinical evidence supporting its efficacy in treating this condition remains limited. One RCT demonstrated that a gel containing copaiba oleoresin exhibited significant clinical efficacy in the treatment of acne lesions [29]. Although earlier studies have also shown beneficial effects of preparations derived from *Copaifera* species, current randomised clinical trials remain lacking, making this an important research gap.

Scar formation is a natural stage of the skin healing process; however, disruptions in this process can lead to pathological scars. One clinical study evaluated the efficacy of a silicone gel enriched with copaiba oleoresin in preventing scar formation and improving scar appearance. The use of the tested formulation significantly improved the color, contour, elasticity, texture, and overall appearance of scars, and reduced their visibility, as assessed clinically and photographically using the Manchester Scar Scale (MSS). The preparation containing copaiba oleoresin was well tolerated, caused no significant adverse effects, and achieved a high level of patient satisfaction. These results suggest that copaiba oleoresin may be a promising ingredient to support the prevention and treatment of pathological scars. However, larger clinical trials are needed to confirm its efficacy and determine the role of this raw material in routine dermatological and cosmetological practice [24].

The anti-inflammatory properties of copaiba oleoresin are primarily attributed to β-caryophyllene, while the diterpenes may also support tissue repair and exhibit protective effects. For this reason, copaiba oleoresin appears to be a promising ingredient in formulations designed for the care of irritated, damaged, and oxidatively stressed skin. Its multifaceted biological activity makes it particularly attractive in dermocosmetics for skin with impaired epidermal barrier function, inflammation, and a need for intensive regeneration.

It should be emphasized, however, that most of the available scientific evidence comes from *in vitro* studies and animal models, while the number of clinical trials evaluating the efficacy of cosmetics containing copaiba oleoresin remains limited. Therefore, further well-designed clinical trials are necessary to determine the optimal concentrations of this ingredient, assess the safety of its long-term use, and verify the actual efficacy of cosmetic formulations containing copaiba oleoresin in clinical and cosmetological practice [12, 27].

Use in aromatherapy

Copaiba essential oil, which is the volatile fraction of copaiba oleoresin derived through distillation, is usually used in aromatherapy instead of raw copaiba oleoresin. Traditionally, this oil has been used to promote relaxation, reduce stress, improve sleep quality, support the treatment of respiratory tract infections, and alleviate pain. Despite its centuries-long history in traditional medicine, few clinical studies have evaluated its efficacy.

Clinical evidence was provided by a randomized controlled trial, which demonstrated that inhalation of copaiba essential oil in individuals performing a task that induced cognitive stress led to a significant reduction in anxiety levels, as assessed both by the participants' subjective reports and by objective physiological parameters. In individuals exposed to the essential oil, heart rate and salivary cortisol levels decreased, indicating an attenuation of the hypothalamic-pituitary-adrenal (HPA) axis stress response. Furthermore, electroencephalographic (EEG) analysis revealed reduced beta-wave activity in the frontal cortex, commonly interpreted as an indicator of reduced psychological tension and cortical arousal. Taken together, these results confirm the potential usefulness of copaiba essential oil in aromatherapy as a method to help reduce anxiety and psychological stress [30].

SAFETY AND TOXICOLOGICAL ASPECTS

The growing interest in copaiba oleoresin as an ingredient in therapeutic and cosmetic formulations underscores the need for a comprehensive assessment of its safety profile. Despite its natural origin, copaiba oleoresin may exhibit toxic effects depending on dose, exposure duration, and variations in its chemical composition.

Although copaiba oleoresin has been used in traditional medicine for centuries, toxicological safety data remain limited. To address this gap, Silva et al. conducted studies in rodents to evaluate the acute and subacute oral toxicity of a commercially available *Copaifera* spp. oleoresin. The study followed the Organisation for Economic Cooperation and Development (OECD) guidelines for toxicological studies and included both a single high-dose administration and a 28-day repeated-dose protocol. In the acute toxicity study, animals were administered a single oral dose of 2,000 mg/kg body weight. During the subsequent 14-day observation period, no deaths or severe signs of toxicity were observed. This allowed the test material to be classified as Category 5 according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS), indicating a low risk of acute toxicity. In the subacute study, female rats were administered oral doses of 25, 50, or 100 mg/kg body weight per day for 28 days. No adverse effects were observed on body weight gain, food and water intake, organ weights, or the results of hematological, biochemical, and histopathological tests. An interesting observation was a decrease in alkaline phosphatase activity in all groups receiving oleoresin, which, according to the authors, may indicate a potential hepatoprotective effect of the tested material [31].

Furthermore, available toxicological data indicate that copaiba oleoresin does not exhibit significant genotoxic or toxic effects on reproductive function at doses comparable to those used therapeutically. Almeida et al. found no genotoxic effects of copaiba oil or selected fractions in a mouse model, suggesting that these preparations do not cause detectable damage to genetic material [32]. Similarly, Cardinelli et al., in a comprehensive review of toxicological data on various species of the genus *Copaifera*, concluded that both copaiba oleoresins and the terpenes isolated from them exhibit a favorable safety profile [33]. Furthermore, Gonçalves et al. evaluated the effects of chronic oral administration of *C. multijuga* essential oil on reproductive function in male rats and found no significant impairment of reproductive capacity, semen quality, or fertility [34].

However, some safety concerns have arisen regarding pregnancy. In studies on pregnant rats, high doses of systemically administered *Copaifera reticulata* oleoresin were associated with adverse effects on fetal development, suggesting the possibility of embryotoxic effects at significant exposure levels [33]. Although these effects were observed at doses significantly higher than those used in therapeutic or cosmetic practice, these findings warrant a cautious approach to using copaiba-containing preparations in pregnant women until additional clinical data confirm their safety.

FUTURE PROSPECTS

Despite the growing number of preclinical studies, knowledge regarding the safety of copaiba oleoresin use in humans remains limited. Experimental studies suggest that certain components of the oleoresin may exhibit cytotoxic or genotoxic properties following metabolic activation, while selected sesquiterpenes have shown potential mutagenic properties in in silico predictive models. However, animal studies to date have not confirmed significant genotoxic effects at therapeutically relevant doses.

Furthermore, available absorption, distribution, metabolism, excretion, and toxicity (ADMET) models suggest that certain terpenes in copaiba oleoresin may cross the blood-brain barrier. It should be emphasized, however, that predictions based on computer models require confirmation in appropriately designed experimental and clinical studies [33].

Given the growing interest in copaiba oleoresin in dermatology, cosmetology, and regenerative medicine, high-quality clinical studies are needed to evaluate its pharmacokinetic profile, the safety of long-term use, potential drug interactions, and effects on markers of oxidative stress and inflammation in humans [35]. Another important area of research is evaluating the safety and efficacy of modern drug delivery systems, such as nanocarriers and controlled-release formulations, that aim to enhance the therapeutic efficacy of biologically active compounds derived from copaiba oleoresin [36].

Among the best-documented biological properties of copaiba oleoresin are its anti-inflammatory, antioxidant, antimicrobial, and tissue-regenerating effects [33]. These mechanisms are particularly important for maintaining skin homeostasis, as chronic inflammation and oxidative stress are among the main factors leading to tissue damage and accelerated skin aging [37]. For this reason, copaiba oleoresin is a promising, multifunctional ingredient for future dermatological and cosmetic formulations.

Studies on its pharmaceutical formulations also confirm the therapeutic potential of copaiba oleoresin. An example is the drug delivery system developed by Campanholi et al., which utilizes oleoresin from *Copaifera reticulata* in the treatment of skin wounds. The developed formulation exhibited satisfactory physicochemical stability while maintaining the biological activity necessary to support tissue regeneration [38]. In turn, Gushiken et al. [35] demonstrated that a nanostructured lipid emulsion containing *Copaifera langsdorffii* oleoresin

significantly accelerated wound healing by reducing inflammation and stimulating re-epithelialization, without causing local adverse effects. Thus, appropriately designed delivery systems for active ingredients can increase the bioavailability and therapeutic efficacy of copaiba oleoresin while simultaneously maintaining a favorable safety profile, which represents a promising direction for the further development of pharmaceutical and cosmetic formulations.

SUMMARY

The genus *Copaifera* is attracting increasing interest in pharmacology, aromatherapy, cosmetology, and medicine, particularly in complementary medicine, primarily because of its broad spectrum of biological activity. This review has demonstrated that copaiba oleoresin has well-documented anti-inflammatory, antimicrobial, and antioxidant properties.

Current data also indicate that copaiba oleoresin exhibits low acute and short-term toxicity. Available experimental studies have not shown a significant risk of genotoxic effects. However, it should be emphasized that some components of the oleoresin have shown potential mutagenic properties in *in silico* models or following metabolic activation. It remains unclear whether these observations have clinical significance, which represents one of the major gaps in the current state of knowledge.

Available scientific evidence supports the therapeutic and cosmetic potential of copaiba oleoresin. However, further well-designed clinical trials are necessary to determine the safety of its long-term use, optimal dosing, and efficacy in humans. Standardizing the composition of the oleoresin and further developing modern formulations will also be of great importance. This will enable the promising preclinical results to translate into reliable clinical and cosmetic applications.

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