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REVIEW

Dragon's Blood: antioxidant properties for nutraceuticals and pharmaceuticals

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Abstract
Plants are the source of a large spectrum of phytochemicals, and the combined and concerted action of biologically active compounds lead to the potential beneficial properties of each plant matrix. A great attention is being addressed over the years toward herbs and medicinal plants. Dragon's Blood is a reddish resin oil extracted from *Croton lechleri* tree. It has been extensively used by indigenous cultures of the Amazon River since ancient times due to the beneficial nutraceutical and pharmaceutical properties. This perspective aims at providing a current framework on Dragon's Blood with focus on antioxidant properties for nutraceuticals and pharmaceuticals in a novelty integrated and multidisciplinary manner, highlighting the current knowledge, the main research lines, and emerging strategies. A literature quantitative research analysis approach was applied as starting point. The literature search was carried out by means of the Scopus database; 365 documents have been retrieved in the year range from 1854 to 2021, and a total of 269 terms were identified. Among the top-recurring keywords appear: unclassified drug, nonhuman, plant extract/s, Dragon's Blood, dracaena, Dragon Blood, chemistry, human, animal/s, plant resin. Source, chemical composition, potential nutraceutical, and therapeutical applications of Dragon's Blood are discussed here. The anti-inflammatory, wound healing, antidiarrheals, anticancer, antirheumatic, antiseptic, and antioxidant activities identified in the Dragon's Blood extracts can open novel perspectives for its use in food and pharmaceutical industries. While different bioactive compounds have already been identified in Dragon's Blood extract, only a few studies can be found in literature.

Keywords Medicinal plants · Natural products · Dragon's Blood · *Croton lechleri* · Antioxidant · Antibacterial · Antiviral · Anti-inflammatory

1 Introduction

Plants are the source of a large spectrum of phytochemicals, and the combined and concerted action of biologically active compounds lead to the potential beneficial properties of each plant matrix (Santini and Novellino 2017; Durazzo et al. 2018, 2020). A great attention is being addressed along the years toward the traditional medicine (Fitzgerald et al. 2020; Yeung et al. 2020) by exploiting the features, properties, and applications of herbs and medicinal plants (Naz et al. 2015; Begum et al. 2020; Durazzo et al. 2021a, b; Sharifi-Rad et al. 2021, Durazzo et al. 2022], taking into account biodiversity and sustainability (Guarino and Pignatti 2010; Pignatti and Cipriani 2010; Pignatti 2013; Attorre et al. 2018; Durazzo and Lucarini 2021; Chung et al. 2021).

In this context, Dragon's Blood tree (*Croton lechleri*) is particularly interesting for its beneficial properties associated since centuries to the red exudate produced, which is popularly known as grade blood or blood of water (Guerra et al. 2022). This species belongs to the *Euphorbiaceae* family and is found in the Amazon region in Brazil. It usually has a length of 5–6 m but can reach up to 20 m. What differentiates it from other trees is that a reddish sap is exuded when its bark is cut. Such sap is called blood of the dragon and is vastly used since centuries as a popular holistic medicine (Sun et al. 2019; Salazar-Gomez et al. 2022).

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This perspective aims at providing a current framework on Dragon's Blood with focus on antioxidant properties for nutraceuticals and pharmaceuticals in a novelty integrated and multidisciplinary manner, highlighting the current knowledge, the main research lines, and emerging strategies.

A literature quantitative research analysis approach was applied as starting point, to give a current snapshot of the current trend raised in the international research context by this topic. A search throughout the Scopus online database has been carried out by means of the string TITLE-ABS-KEY ("dragon's blood*"), and the "full records and cited references" were exported and processed using the VOSviewer software (version 1.6.16, 2020; www.vosviewer.com, accessed on 8 December 2021) (Waltman et al. 2010).

The search returned 365 publications covering the time range from 1854 to 2021, and a total of 269 terms were identified and visualized as a term map in Fig. 1. Figure 1 allows for the identification of the main terms correlated to Dragon's Blood, and also identifies the main existing research lines focused on this topic. It is interesting to observe that among the top-recurring keywords, appear: unclassified drug, nonhuman, plant extract/s, dragon's blood, dracaena, dragon blood, chemistry, human, animal/s, plant resin.

The most recent review is focused on the advanced research progress on anti-tumor effect of Chinese Dragon's Blood (Tian et al. 2021), whereas the most cited review is published by Gupta et al. in the *Journal of Ethnopharmacology* and it is addressed on botany, chemistry, and therapeutic uses of Dragon's Blood (Gupta et al. 2008) and in 2017, Bayerl published an interesting "Editorial" document on Dragon's Blood (Bayerl 2017).

The main subject areas explored are as follows: *Pharmacology, Toxicology and Pharmaceutics*, *Biochemistry, Genetics and Molecular Biology*, *Chemistry*, *Medicine*, *Agricultural and Biological Sciences*, *Environmental Science*, and others.

In the context of the environmental impact and sustainability perspective, it is worth mentioning the works on

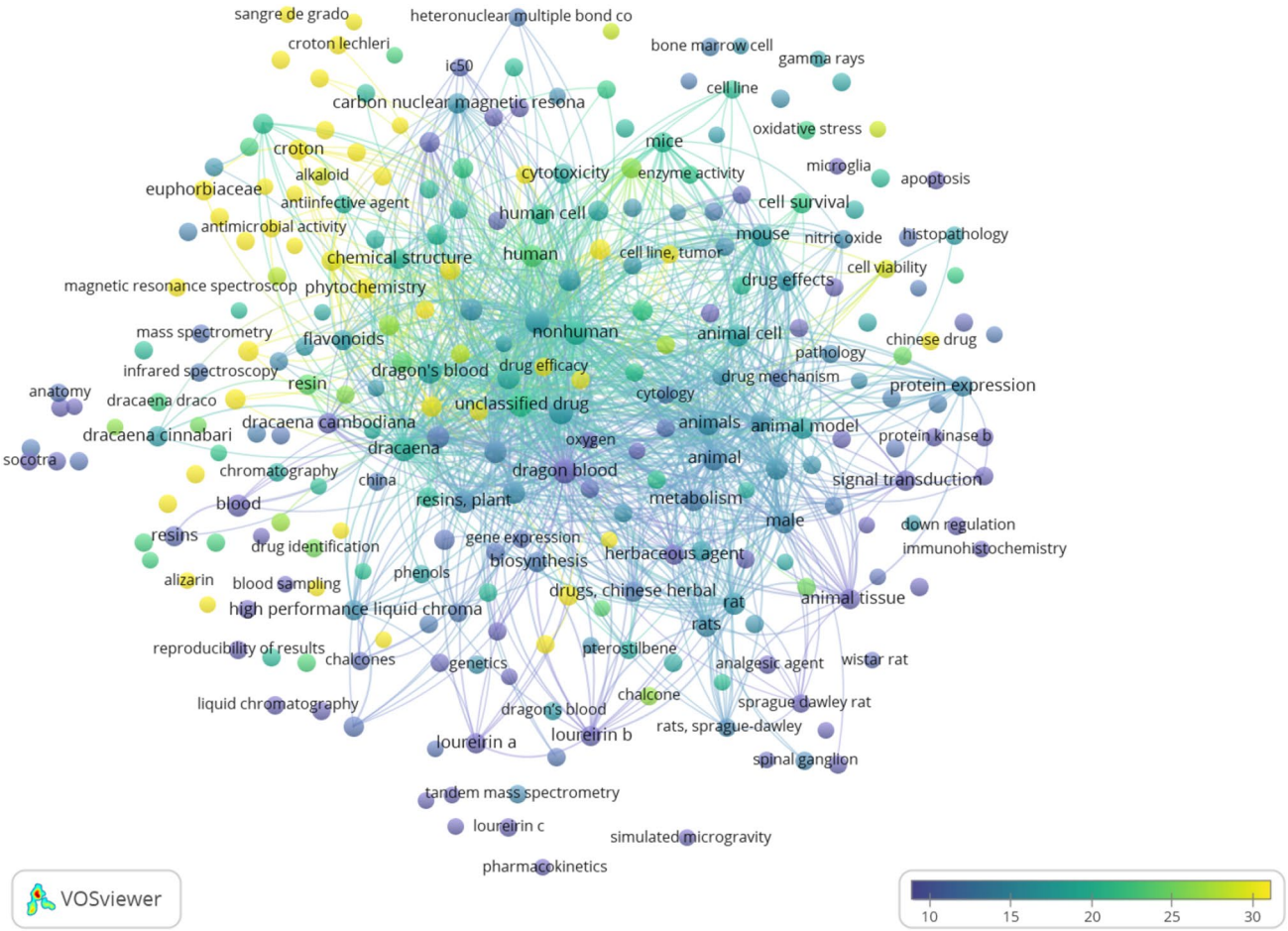

Fig. 1 Term map for the Dragon's Blood research. Bubble size represents the number of publications. Bubble color represents the citations per publication (CPP). Two bubbles are closer to each other if the terms co-appeared more frequently (bibliometric data were extracted from the Scopus online database and elaborated by the VOSviewer software)

sustainable land use management needed to conserve the Dragon's Blood tree of Socotra Island representing a vulnerable endemic umbrella species (Maděra et al. 2019); the socio economic roles of Dragon's Blood in participative rehabilitation of degraded forest and land (Letari et al. 2019); the Dragon's Blood secretion and its ecological significance (Jura-Morawiec et al. 2016, 2022).

Dragon's Blood can be used in the treatment of gastric diseases and infections, and it is also capable of healing wounds. Native people use the sap of the plant on burns and wounds to stop bleeding, speed up healing, and protect from infections (Jiang et al. 2017; Sun et al. 2019).

Dragon's Blood is one of the strongest healing agents known, it dries quickly when applied, and forms a second skin that promotes collagen formation and fibroblasts chemotaxis (Namjoyan et al. 2015). *Croton lechleri* ethanolic extract also exhibited antibacterial activity against superinfected skin ulcers in Colombian hospitalized patients (Corrales-Ramirez et al. 2013), and it had a highly significant bacterial inhibition when compared with the standard treatment in the clinic.

Different bioactive compounds were reported from Dragon's Blood resin (Jaronski et al. 2017). It is an astringent latex with cellulose and Dragon's Blood resin as active ingredients. It is composed of alcohol esters resinous, tannins (dimethylcedrusine, etc.), polyphenols (gallic acid, etc.), alkaloids (Namjoyan et al. 2015), proanthocyanidins, steroids (sitosterols, catechins), saponins, and lignans (Fan et al. 2014; Luo et al. 2015). Among the identified compounds, there are some that are linked directly with the properties of the Dragon's Blood. According to the literature, the alkaloid taspine proved to be the main active compound responsible for wound healing. It is associated with the formation of collagen, promoting healing by migrating fibroblasts to the injury site on the skin (Vaisberg et al. 1989; Namjoyna et al. 2015; Canedo-Téxon et al. 2019). Besides taspine, flavonoid compounds with antioxidant properties act as reducing agents, eliminating free radicals, since they donate hydrogen to free radicals. Flavans, flavanones, polymeric flavonoids, chromogen ketones, and flavanols can also be acknowledged, since they are secondary plant metabolites involved in the defense against ultraviolet radiation or aggression by pathogens, contributing to plant pigmentations and antioxidant. Additionally, these compounds also demonstrated benefits in the prevention of various diseases associated with oxidative stress, such as cancer, cardiovascular, and neurodegenerative diseases (Escobar et al. 2018). About proanthocyanidins, Rossi et al. (2011) showed that it is responsible for 90% of the dry weight of Dragon's Blood, characterized by its antioxidant and antibacterial properties. Regarding compounds in lower concentration, the lignan 3´,4-*O*-dimethylcedrusin is highlighted due to its participation in wound healing and there are korbein-A and korbein-B (De Martino et al. 2008). The main chemical compounds of Dragon's Blood are listed in Table 1.

2 Extraction and properties

Trees known as "dragon" or "dragon's blood" have shared healing properties, although they belong to distinct botanical families. *Croton lechleri (Euphorbiaceous)* is found in Peru, Ecuador, Colombia, and northern Brazil (Rossi et al. 2011). Also, *Croton urucurana* are usually sighted in the southeast, mid-west, and southern regions of Brazil, as well as in Argentina and Uruguay. Both species are relatives and their respective sap has a similar pharmacological activity. In the state of Minas Gerais (Brazil), Dragon's Blood is often called "water bleeds", as it grows near rivers and ponds (Martins et al. 2016). A large volume of latex was extracted indiscriminately in Colombia, Ecuador, and Peru, with the falling of the trees (Aguirre et al. 2001). As an example, in 1998, 50.607 L of *Croton lechleri* latex were exported mainly to Europe, United States, and Japan (Galy et al. 2000). Currently, the latex collection for commercial purposes occurs on a smaller scale that supplies regional communities. The Dragon's Blood latex extraction is similar to seringals, by cutting the trunk at breast height in a V-shape, then a reddish-colored sap exudes. Also, indigenous-influenced extraction is highlighted, where the incisions are made in tree trunks and the drops of latex are collected. This process begins when the tree aged 6–7 years or when its DAP (diameter to breast height) reaches approximately 25–27 cm. An incision is made at 1.30 m of the soil and the recommended extraction is at morning during the full moon for 5–9 h. This method produces regularly an average of 2.0–3.5 L of latex (Aguirre et al. 2001; Osakada 2009). Latex conservation can be done by adding sugarcane liquor to prevent the product from crystallizing. The final product should be packed in an airtight container and stored in refrigerated places. This latex has from 3 to 6 months of storage life (Vásquez and Bach 2015). Dragon's Blood has interesting properties for medicinal applications (Sun 2019). It can treat scarring by stimulating skin rejuvenation, which explains its antioxidant property. Other characteristics of Dragon's Blood are its antibacterial, antiviral, and anti-inflammatory activity, and can be exploited for several medicinal uses (Fig. 2).

2.1 Wound healing

The Dragon's Blood healing properties are associated to the two most active components present in the sap, taspine and dimethylcedrusin. Both are efficient in healing, but also in the treatment of gastric and duodenal ulcers (Sun et al. 2019). A process of taspine isolation and its use in

Table 1 Main chemical compounds of Dragon's Blood

Groups	Compounds	
Alkaloids	Taspine, pyridine, aportineindole, quinoline, tropanes, anthraquinones, unsaturated fatty acids, anthraquinones and triterpenes	
Phenolic compounds	Gallic acid, coumaric p-acid, sirinic acid, ferulic acid, vanillic acid, salicylic acid and others with less concentrations	
Polyphenol compounds	Stylbens, flavonoids, dihydroflavonoids, catechins, sirinic acid, and proanthocyanidins	
	Flavonoids	7,4'-Dihydroxyflavone, 7,4'-dihydroxy-dihydroflavone, 4'-methoxy-3′7-dihydroxyflavone, 4',7-dihydroxy-flavan, 7-hydroxy-4'-methoxyflavane, 4',7-dihydroxy-3'-methoxyflavan, 2'-methoxyisocotrin-5'-ol, socotrin-4'-ol, and cochinchinenin C
	Chalcones	4,4'-Trihydroxychalcone, 2'-methoxy-4,4'-dihydroxychalcone, 2'-methoxysocotrin-5'-ol and 2-methoxy-4,4'-dihydroxychalcone
	Dihydro-chalcones	Loureirin A, loureirin B, loureirin C, loureirinD,2,4,4'-trihydroxydihydrochalcone, cochinchinenin A, 4,4'-dihydroxy,4-hydroxy-2-methoxydihydrochalcone, 2,6-methoxydihydrochalcon, 4'-dihydroxy-4,6-dimethoxy-dihydrochalcone
	Flavanols	Catechin and epicatechin, gallocatechin, epigallocatechin
Tannins	Hydrolyzed	This compound has a central polyol group (mostly β-d-glucose, and also quinic acid, other phenols, and glycosides); and hydroxyls esterified by gallic acid (phenolic part)
	Condensed	The condensed one have a "polymeric" structure of flavan-3-ol, such as catechin, or flavan-3,4-diol, of leucocyanidin
Quinones	p-Benzoquinone and anthraquinone	

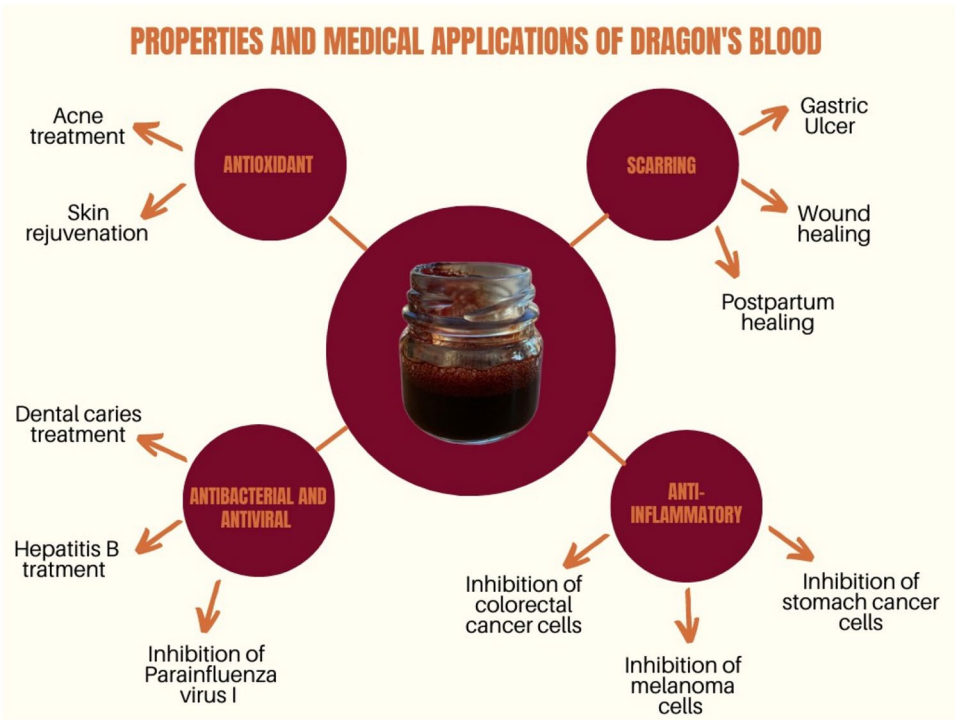

Fig. 2 Medicinal applications of Dragon's Blood

wound healing, acting on various mechanisms that lead to skin regeneration, in varicose ulcers and bedsores has been described (Vaisberg et al. 1989; Namjoyan et al. 2016; Guerra et al. 2022). Dragon's Blood polyphenols and proanthocyanidins are potent antioxidants that could act against free radicals that cause skin aging (Escobar et al. 2018). In cosmetics, these compounds increase the collagen synthesis reducing the wrinkles formation and promote skin rejuvenation, and also protect the skin against UV rays. It is very effective in the treatment of acne and can be combined with the essential oil of Cypress (*Cupressus Sempervirens*) or Pitanga (*Eugenia Uniflora*). Polyphenols also play an important role in healing and eliminating free radicals, mainly proanthocyanidins, which stimulate wound contraction and healing. In this way, the gel produced from the latex of *Croton lechleri* called also "Sangre de Drago", has a therapeutic effect (Namjoyan et al. 2015; Apaza Ticona 2021). A summary of the healing properties is shown in Fig. 3.

2.2 Antiviral and antibacterial activities

The latex of *Croton lechleri* Dragon's Blood plant has antibacterial and antiviral properties through its secondary metabolites belonging to phenol, terpenoids, alkaloids, leptins, polypeptides (Gupta and Gupta 2011; Bayerl 2017) groups, among others. The pure extract of the plant *Croton lechleri Mull Arg.* has secondary metabolites with antibacterial and antiviral properties as displayed in Fig. 4, including 2,4,6-trimethoxyphenol, 1,3,5-trimethoxybenzene, korberin A and B, crolechinic acid, proanthocyanidins, catechins, epicatechins, gallocatechins, galloepicatechins, flavonols phenol, terpenoids, alkaloids, leptins and polypeptides (Gupta and Gupta 2011; Lopes at al. 2013; Bayerl 2017) groups. Experiments have shown that sap inhibits the action of various types of viruses, such as herpes simplex, hepatitis virus (Olson 2015), influenza and parainfluenza (due to the influenza virus), cytomegalovirus, and respiratory syncytial viruses (Vilchez and Braulio 2018). The Shaman Pharmaceuticals Company developed a drug, named Virend®, containing antiviral compounds extracted and isolated from the Dragon's Blood bark and resin for the treatment of herpes. They also developed an oral drug called Provir® for the treatment of respiratory viral infections (King and Tempesta 1994; Snell 2001). *Croton lechleri* has a large community of endophytic fungi with great antibacterial potential against bacteria pathogenic to humans, especially against Gram-positive bacteria (Ferreira et al. 2021; Sebastiao 2018). It showed antibacterial effect on *Staphylococcus aureus* ATCC 43300 in concentrations above 77%. The antimicrobial activity of Dragon's Blood resin obtained from *Dracaena cinnabari* Balf f. dichloromethane extract was attributed to the high concentration of phenolics, flavonoids, and flavonols, being proposed as a natural food preservative (Gupta and Gupta 2011).

2.3 Anti-inflammatory activity

The intragastric administration of Dragon's Blood in carrageenan-inflamed or sciatic nerve-injured rats demonstrated its potent anti-inflammatory and analgesic effects by inhibiting hyperalgesia and paw edema, and by reducing the expression of cyclooxygenase-2 protein or preprotachykinin-A mRNA (Li et al. 2012) blocks the activation of nerve fibers that release pain signals to the brain, and functions as an

Fig. 3 Healing properties of Dragon's Blood

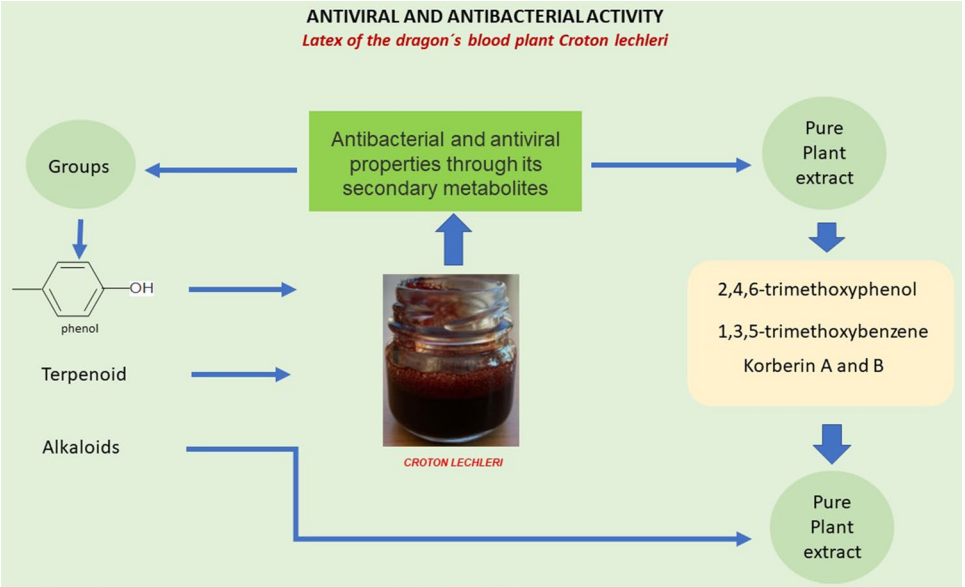

Fig. 4 Antiviral and antibacterial activity of Dragon's Blood blocks

antalgic. The analgesic effect of topical administration of Dragon's Blood, which was reported to last up to 6 h, has been exploited in gels containing 1–3% of resin in the treatment of relief of rheumatism arthritis and arthrosis, as well as against pain caused by herpes zoster, inflammation of the trigeminal nerve, bursitis, twists, and fibromyalgia (Pieters et al 1993). Resin can be formulated in creams or gels (in percentages of 3–5% of the total) with anti-inflammatory essential oils (e.g., copaiba, oregano, ginger, or wintergreen) that are also analgesics and can potentiate the bioactivities of Dragons' Blood. Immunomodulatory activity of this resin has also been demonstrated by affecting the activated T cells. In low doses, it is a phagocytosis inhibitor, and in higher doses has antioxidant and an activating effect of phagocytosis. It shows the ability to inhibit the proliferation of leukemic cells and cytostatic activity against KB and V-79 tumors. In veterinary, Dragon's Blood is also very efficient, treating skin infections, warts, wounds, abscesses, and otitis (Dietrich 2018).

2.4 Antioxidant and anticancer activities

Antioxidants are substances that block the harmful effect of free radicals. Natural antioxidants are phenolic compounds that are formed by benzene groups and hydroxyl substituents, which have oxy-reducing properties and the ability to stabilize intermediate compounds (Sandoval et al. 2006). The evaluation of combined and concerted action of bioactive compounds gives the measurement of antioxidant properties and indicator of health status (Durazzo 2017; Santini and Cicero 2020). The Dragon's Blood is an exceptionally high and stable antioxidant (Escobar et al. 2018; Pona et al. 2019). The antioxidant capacity of Dragon's Blood in the gastric mucosa has been studied in experimental animals. It was concluded that the bioactive extract presented a positive effect through the gastric route, confirmed by the lower lipid peroxidation. It has also been reported that 75% ethanol extract from Chinese Dragon's Blood suppressed cell growth and promoted apoptosis in human hepatoma HepG2 and SK-HEP-1 cells (Chen et al. 2020). Using RNA interference, the authors demonstrated the anti-hepatoma activity of the ethanolic extract partially through downregulation of Smad3, one of major members in TGF-β/Smad signaling pathway.

3 Current applications

The most relevant applications of Dragon's Blood are listed in Table 2. The development of formulations for the topical administration of Dragon's Blood using biopolymers is seldom reported in the literature. The production of a dressing containing silk fibroin and an aqueous solution with polyethylene oxide (PEO) of 1000 [KDa] at 3% (w/v) Dragon's Blood at 2% (v/v) has been described (Melo et al. 2018). The sample is characterized by continuous fibers with the presence of porous granules, which is one of the main requirements of dressings to accelerate cell migration. Also, tissue healing and antibacterial activity of chitosan and polyvinyl alcohol were tested with the addition of hydroalcoholic solution of *Croton lechleri* formulated in chitosan and polyvinyl alcohol semi-solid for tissue healing, and tested its antimicrobial activity against *S.* aureus, resulting a minimal inhibitory concentration of 0.025 g/10 mL (León and Santiago 2007). Chitosan and pullulan have been proposed to be used as local delivery systems for active ingredients from plant extracts for the treatment against periodontal

Table 2 Examples of current applications of Dragon's Blood

Applications	Results
Healing	Curative effect of the cream made with *Croton lechleri* Müll atomized latex extract (1.5%)
	The administration of Dragon's Blood increased the rate of wound repair in mice by 31%
	It was observed a significant improvement of wound healing from the third day. And on day 14, 95.73% were treated therapeutically and 78.10% with placebo
	At days 5 and 7, 80% of those who received phytotherapic treatment with Dragon's Blood improved the healing in postpartum cases
	Dragon's Blood was highly effective in the healing process: 92.5% of the cases had abundant tissue granulation and in 100% of cases avoided infection, inflammation, and dehiscence
Ulcer	The administration of Dragon's Blood to gastric mucous induced a higher cytoprotection, in consequence reduced the lipoperoxidation and helped in gastric ulcer treatment
	In diabetic patients, the ulcer area decreased substantially. One patient, for example, in the first week had an ulcer with an area of 237.50 cm^2 and in the twelfth week, it decreased to 174.80 cm^2
Diarrhea	The flow of sodium and water was reduced, which decreased the frequency and consistency of diarrhea. SP-303, a proanthocyanidin oligomer isolated from Dragon's Blood latex plant, was able to shorten the duration of the diarrhea by 21%
Dermatology	At concentrations of 125, 250, 500, and 1000 µg/mL, inhibitions on the collagen enzyme were observed at 5.67%, 17.33%, 33.41%, and 59.52% respectively, helping the skin rejuvenation
	The effectiveness of the Dragon's Blood-based gel and cream for the treatment of polymorphic acne of grade I and II was determined by the reduction of acne lesions on the skin of 100% of treated patients
	The hydration values, thickness of the dermis and elasticity increased in all groups after 6 weeks of application of the cream containing 3% of Dragon's Blood extract, thus, being efficiently useful in preventing or improving skin changes associated with stretch mark
Traumatic tympanic membrane	The healing rate and the average cure time of the treated group were better than the control group, so it can be concluded that Dragon's Blood powder can improve the cure rate and shorten the treatment time of the traumatic tympanic membrane
	In cases of cervicitis, after 5 days of Dragon's Blood application, 10% of the women did not show any improvements, 45% were cured and the other 45% presented great improvement of the infection
Gynecology	After 7 days applying Dragon's Blood moisturizer, the effect on *Candida albicans* was similar to Clotrimizol effect, implying that Dragon's Blood is efficient against candidiasis
Odontology	It shows that 97% of the patients in which *Croton lechleri* was applied had rapid healing. It was possible to demonstrate the benefits of Dragon's Blood after simple extraction of teeth, where healing has been achieved quickly
	The activity of *Croton lechleri* latex at concentrations of 75 and 100% showed antibacterial activity, and are acceptable to be considered as an accessible, natural, and low-cost inhibitory agent for prevention methods in dental caries
	The Dragon's Blood application resulted in a fast analgesic/anti-inflammatory effect, and the removal of tooth decay, disappearance of edema, bleeding and gingival redness was observed. It preserved the membrane of all cells functional functions, and viability of periodontal ligament cells
Cancer	Concentrations of 0.3 and 3.0 µg/µL of Dragon's Blood showed 100% action against the breast cancer cell line
	It was observed that 50% of the colorectal cancer cells were inhibited 24 h after the Dragon's Blood application in a concentration below 50 µg/µL
	An inhibition of 50% of melanoma cells was achieved by Dragon's Blood application in a period of 24 h in concentration below 5 µg/µL
	Maximum inhibition of stomach cancer cells was reached at concentrations > 200 µg/mL of Dragon's Blood after 18 h of the application
Virus	The inhibition desired for Parainfluenza I virus was reached at a concentration of 3.0 µg/mL of Dragon's Blood
	For herpes type I, 35.6 µg/mL of Dragon's Blood inhibited the activity of the virus, while for herpes type II, 20.5 µg/mL was necessary
	RSV (Respiratory Syncytial virus) had its activity inhibited with a concentration of 6.0 µg/mL of Dragon's Blood
	The desired inhibition was achieved with a concentration of 50 µg/mL of Dragon's Blood for the type B of hepatitis

pathogen microorganisms (Rodriguez-Garcia et al. 2010). Thickness of chitosan films was on average of 0.03 mm and for pullulan of 0.07 mm. Five plant extracts were tested, and among them was *Croton lechleri*. The results revealed that both biopolymers with added plant extracts have antibacterial activity and can be used as bio-adhesive film against periodontopathogens tested.

The stability of Dragon's Blood sap was studied considering several storage conditions, under different environments of temperature and relative humidity (Escobar et al. 2018). In addition, an accelerated aging treatment was performed,

subjecting the lyophilized Dragon's Blood sap to irradiation with UV light, and the effect of these stress conditions on its antioxidant activity was also evaluated. The results demonstrated that the concentration of the sap constituent's changes at different storage conditions. For example, the storage conditions were studied in a range of temperature from 4 to 21 ºC, and different conditions of relative humidity (0, 23, 44, and 56%). The presence of moisture was evaluated with respect to the Dragon's Blood degradation. Regarding the temperature, no significant effect was detected in the range studied (4 ºC and 21 ºC at a 0% relative humidity). However, applying UV light irradiation, a reduction of 20% of the sap concentration was observed. The antioxidant activity remained stable under the studied storage conditions (under different temperature and relative humidity) (Escobar et al. 2018). The high stability observed for Dragon's Blood sap can confer interesting characteristics in various industrial products, such as food, pharmaceuticals, nutraceuticals or cosmetics, paints or paper products, being possibly used as an antioxidant or as an ingredient.

Ingestion of crude extracts or tea formulations of *Croton lechleri* may cause mild nausea, bitter taste or diarrhea (Pona et al. 2019). The use of Dragon's Blood as a healing agent in concentrations of 0.1% and concentrations of 0.001% caused negative effects on the reproductive tract of Wistar Rats, since it caused a decrease in the values of membrane integrity, acrosome, and cell viability of sperm (Schmuch et al. 2013). To test and evaluate the potential toxic, cytotoxic, and mutagenic/genotoxic of *Croton lechleri*, a test with *Allium cepa* was performed by diluting 0.5, 1.0, 2.0, and 2.5 mL of the extract in 250 mL of water, using root growth, mitotic index, and the presence of micronuclei as parameters. It was observed that all the concentrations used of *Croton lechleri* inhibited the root growth of the roots of *Allium cepa*, evidencing its toxic potential. There was also a decrease in the mitotic index, mainly at the concentration of 2.5 mL, indicating cytotoxicity. In addition to cytotoxicity, the mutagenic potential was observed through the high micronucleus index, showing that the "dragon's sap" should be used with caution (De Almeida et al. 2019). In another study, to analyze long-term Dragon's Blood toxicity, rabbits were administered Guangxi Dragon's Blood at rates of 3.0 and 1.5 g/kg body weight, once a day for 90 days. It has been observed that the Dragon's Blood did not cause changes in the animal's pathological state, and had no significant effect on blood erythrocytes and leukocytes number, alanine aminotransferase, urea nitrogen, or weight. There was no functional damage to the liver or kidney. In the pathological examination under optical microscope, except for some expansion of the tiny blood vessel between myocardial cells, there was no damage to the liver, lungs, kidney, intestine or the adrenal glands, thus indicating that the use of Dragon's Blood did not show toxic reactions (Fan et al. 2014).

Application of nanotechnologies to plants' extracts of nutraceutical interest (Daliu et al. 2019; Zielińska et al. 2019; Souto et al. 2020a; Durazzo et al. 2021a, b) represents a key issue, such as the preparation, characterization, and dissolution characteristics of Dragon's Blood extract nanosuspensions (Wang et al. 2019); the silver nanoparticle's synthesis by Dragon's Blood resin ethanol extract and antiradiation activity (Wang et al. 2019); the assessment of bioreducing and stabilizing potential of Dragon's Blood resin extract in synthesis of silver containing nanoparticles (Hasan et al. 2015); surface-enhanced Raman scattering study of organic pigments using silver and gold nanoparticles prepared by pulsed laser ablation (Hasan et al. 2013; Fazio et al. 2013). Safety aspects and procedures should be taken into proper account in view of an optimal use of these techniques aimed to improve perspective applications of this important vegetal matrix (Zielińska et al. 2020; Souto et al. 2020b).

4 Conclusion

The latex of *Croton lechleri* or Dragon's Blood, which is known to be used in the Amazonic region, has potential application in medicine in the treatment of many diseases. The resin offers huge potential, and studies are needed to improve the extraction, to purify the compounds isolated from Dragon's Blood, and assess completely quality and control aspects. Also, the correct administration of *Croton lechleri* to ensure proper, safe, and responsible uses and applications should be investigated.

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Data availability Not applicable.

Declarations

Conflict of interest The authors declare no conflict of interest.

Institutional review board Not applicable.

Informed consent Not applicable.

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