Therapeutic potential of extracts from Amazonian plants with antimicrobial activity

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The search for new treatment alternatives in medicine has encouraged the use of extracts obtained from therapeutic plants. The Amazon region presents a wide variety of plants used in the treatment and/or prevention of diseases, among which four species can be highlighted: Cipó-pucá (*Cissus sicyoides*), Cipó-d'alho (*Mansoa standleyi*), Murici (*Byrsonima crassifólia*) and Jambu (*Spilanthes acmella*). The therapeutic potentials of these plants are recognized for their antimicrobial action and their broad health benefits. All these benefits are attributed to compositions rich in phenolic, sulfur and nitrogen compounds, carotenoids, among other bioactive compounds. To obtain these extracts, it is necessary to use an extraction method that provides a non-toxic final product with a desirable and safe composition, such as extraction with supercritical fluid. Thus, the use of extracts of Amazonian plants obtained with supercritical CO_2 for the treatment and/or prevention of diseases is a good alternative for these natural bioactive compounds and free of toxic residues.

Keywords: Activity Antimicrobial; Supercritical fluid

1. Introduction

In recent years, the interest in bioactive compounds of natural origin has been increasing due to its effectiveness in the prevention and/or treatment of various diseases [1, 2]. These compounds naturally contained in plant raw materials are often used in the form of extracts in Brazil, specifically in the Amazon region. The plants and their extracts have ethno-pharmacological characteristic, due to their great biological potential, which led to their use in folk medicine [3, 4, 5].

The use of natural therapeutic products represents a good alternative in the substitution of synthetic medicines.

The effects associated with the extensive use of synthetic drugs can cause serious damage to several organs of the human body, since many of them present long-term contraindications, for instance, some drugs used in the treatment of chronic diseases such as diabetes and hypertension [6]. In addition, there are several diseases caused by bacteria, protozoa and fungi that present strains resistant to potent antibiotic and antifungal agents, imposing the need for the development of new drugs [7, 8]. Thus, in order to overcome this limitation of the use of synthetic drugs, researchers and pharmaceutical industries have shown a great interest in plants with medicinal potential that are safe and effective and that are recognized for their antimicrobial action and wide health benefits [9].

Among the Amazonian plants that have been used in folk medicine and that are object of scientific studies, the following species stand out: Cipó-pucá (*Cissus sicyoides*), Cipó-d'alho (*Mansoa standleyi*), Murici (*Byrsonima crassifolia*) and Jambu (*Spilanthes acmella*). These plants have been investigated and have shown positive results regarding their antimicrobial activity against pathogenic microorganisms such as bacteria, protozoa and fungi involved in the cause of various diseases [10, 11, 3, 12]. Furthermore, their potential antioxidants and their use in the treatment and/or prevention of diseases such inflammation, hyperlipidemia, diabetes, hypertension and increased immunity have also been proven [13, 14, 15, 16]. The therapeutic potential of these plants is attributed to compositions rich in phenolic, sulfur and nitrogen compounds, carotenoids, among other bioactive compounds [17, 18, 19, 20, 21, 22].

Obtaining plant extracts rich in bioactive compounds can be accomplished by various methods such as solvent extraction. However, there is a need to use products free of contamination by solvents, in order to ensure the application of the plant extracts in food products and medicines. A suitable and widespread technology for the extraction has been the method with supercritical fluid. Supercritical extraction using carbon dioxide (CO_2) as supercritical fluid has already been studied to obtain bioactive compounds from natural sources, without drawbacks such as the use of organic solvents that present toxicity and contaminate extracts [23, 24, 25]. The visible interest of the scientific community in this technology has been encouraged by the versatility of CO_2, whose properties can be adjusted to obtain extracts with desirable chemical composition and ensuring a safe separation process for both human health and the environment [26].

Thus, the use of extracts of Cipó-pucá, Cipó-d'alho, Murici and Jambu, obtained by extraction with supercritical CO_2, in the treatment and/or prevention of diseases, represents a great opportunity for the pharmaceutical companies to provide a quality, natural, of high content of bioactive compounds and free of toxic waste product.

2. Plant extracts in the treatment/prevention of diseases

The use of plant extracts by mankind to cure or relieve illnesses has been taking place for a long time, a fact that is striking in the evolution of Eastern and Western populations. The knowledge of primitive and indigenous peoples was of great importance in the discovery of drugs from natural products and/or precursors of simple organic synthesis to reach a drug [27], A good example is *curare*, an extract obtained from several plants by the natives, commonly used in arrows to paralyze animals during hunting and fishing, which later gave rise to a muscle relaxant used in certain surgical procedures, such as in the abdomen and removal of the tonsils [28]. Another important plant is poppy, a plant whose another important natural product is withdrawn, the opium, which has been known for centuries as a sedative and anesthetic, and its effect is attributed to morphine, currently given to patients with chronic pain [29, 27].

Salgueiro barks were also widely used for analgesic and antipyretic activities due to the presence of salicylates, especially salicin. This compound represented a watershed in the production of drugs from plant extracts and was later synthesized, giving rise to acetylsalicylic acid (AAS), a drug widely used for its analgesic, anti-inflammatory and antipyretic activities in the treatment of rheumatoid arthritis and inhibition of platelet aggregation [29, 27, 28].

The pharmaceutical industry keeps increasing its interest in plant extracts, because these are sources of new substances with great therapeutic potential for treatment and/or prevention of various diseases, such as Chagas disease (*Tripanossoma cruzi*), various types of leishmaniasis as human Leishmania (*Leishmania chagasi*) [30] and Amazonians Leishmania [31], besides helping to combat dengue and chikungunya fevers, due to the ovicidal and larvicidal effects of some plant extracts, which inhibit the proliferation of eggs and larvae of the *Aedes aegypti* [32].

Many extracts from several plant species showed antimicrobial activity *in vitro* against different pathogenic bacteria and fungi [33, 34, 35, 36, 37, 38, 39]. In addition, many extracts can be used for the treatment of breast, colon and stomach cancer, since they have antioxidant and cytotoxic against breast tumor cells, representing an indicator for testing in future studies. Thus they are candidates to be sources of natural antioxidant compounds, replacing synthetic ones, and then contributing to the prevention of possible diseases [37, 36, 40].

3. Cipó-pucá (*Cissus sicyoides*)

The genus *Cissus* belongs to the family Vitaceae, being represented by 48 endemic species, of which 42 are described in Brazil [41]. It is considered a plant of the neotropical region that includes part of Florida, Mexico, the islands of the Caribbean and South America and is usually found in the Amazon region. *Cissus sicyoides* L. is also known as Cipó-pucá, Cipó-puci, Vegetal Insulin, Anil-trepador and Bejuco-caro. It is a climbing plant that can reach up to 6 meters in length, has a fleshy articulated branch, leaves of oval shape with sharp apex, yellowish or reddish flowers and round fruits with a strong aroma, with color variations from violet to black [42, 43, 44, 45, 46]. The fruits are edible *in nature* and may have potential use as food coloring [47]. The leaves have been widely used in Brazilian popular medicine, since the presence of secondary metabolites proves the effectiveness of the plant against various diseases [46, 48].

The composition of the different parts of the plant is distinct. The bioactive compounds present in leaves and stem are represented by groups such as carotenes (α-carotene and β-carotene) [13], phenolic compounds such as flavonoids (kaempferol and quercetin) [49], resveratrol [50], tannins [45], coumarins and steroids [51]. It was also detected the presence of essential oils [45], which are natural products of plants of lipid nature and that presents a great variety of structures [52]. Essential oils consist mainly of terpene hydrocarbons, simple and terpene alcohols, aldehydes, ketones, phenols, esters, ethers, oxides, peroxides, furans, organic acids, lactones, coumarins and even sulfur compounds [53, 54]. In the fruit composition, anthocyanins were found [47], which are the main compounds responsible for the pharmacological activities of the plant [45, 49].

The aerial parts of the plant, leaf and stem, are traditionally the most used in the preparation of infusions or teas [48, 15, 55]. The therapeutic potentials of Cipó-pucá are traditionally used by folk medicine to treat rheumatism, epilepsy, stroke, abscesses, arthritis and type 2 diabetes mellitus, and treat respiratory diseases [14, 44, 15, 56, 57]. In addition, pharmacological effects were detected in the treatment and/or prevention of dysfunctions such as hypertension, vasoconstriction of arteries, veins and capillaries. It was also considered that the anti-inflammatory effect has a positive influence on the treatment of diseases such as cancer [58, 59, 60], besides presenting gastroprotective activity [61].

The ethno-pharmacological use reports that the Cipó-pucá extract has anti-inflammatory and antidiarrheal actions, due to the abundant presence of flavonoids in the extract, being the main responsible for the pharmacological effects of the plant, presenting an important role in oxidative stress, acting as antioxidants and free radical scavengers [59, 57]. Furthermore, flavonoids, resveratrol, tannins and coumarins are specifically responsible for the bacteriostatic action that stops the growth of certain bacteria, impairing their proliferation [17, 45]. There are other properties that are also attributed to Cipó-pucá such as anti-flu and anti-thermal [60], antioxidant, antibacterial and antifungal [15, 62].

According to García and collaborators [17], Cipó-pucá has antibacterial activity showing inhibitory capacity against bacteria that cause food poisoning, which causes acute effects in the gastrointestinal tract and in some cases, the severity can be such that patients come to death (*Bacillus cereus, Bacillus subtilis, Bacillus megaterium, Staphylococcus aureus, Escherichia coli* and *Salmonella typhimurium*) [63]. Multiresistant bacteria cause blood infections and are related to medical device implants (*Staphylococcus epidermidis*) [64]; those responsible for

generalized infections (*Serratia marcescens*) [65], those that cause infections of the urinary tract and of wounds, meningitis in neonates or infants and rheumatoid arthritis (*Proteus* vulgaris) [66, 67, 68] and those that cause arthritis in patients with HIV, Lupus, ocular and respiratory infections (*Moraxella lacunata*) [69]. Besides that, Silva and collaborators [70] demonstrated that the plant has antifungal activity, inhibiting the growth of fungi, responsible for skin and nail mycotic infections, allergic diseases such as asthma and rhinitis (*Cladosporium sphaerospermum*) [71, 72] and those causing lung diseases such as hemorrhagic pneumonia (*Cladosporium cladosporioides*) [73, 74].

4. Cipó-d'alho (*Mansoa standleyi*)

The genus *Mansoa* DC is a plant that belongs to the family Bignoniaceae, distributed especially in the neotropical region [75]. It is found in forests in Brazil, Argentina and Southeast Mexico, being Brazil the main center of diversity with a large occurrence in the Amazon. The genus *Mansoa* DC is composed of 11 species and *M. standleyi* is the species with the highest occurrence in the Northeast of the state of Pará [76, 77, 78, 18, 79]. The plant is a climbing shrub, which reaches up to 3 m in height, has opposite and composed leaves, which exhibit a bright olive-green color, has flowers of red-violet color, differing from other species only because it presents a fruit with capsular form with 9-10 cm long [79, 80]. *M. standleyi* is popularly known as Cipó-d'alho, which means garlic vine, because of its characteristic garlic smell and aroma (*Allium sativum*) that exhales after the smashing of plant. The species is used as an ornamental plant, because of its attractive flowers, and is also used as a condiment, and for medicinal purposes. Presents therapeutic potential, besides it attributes similar to those of garlic, such as aroma and taste, and volatile compounds present in the plant, which are mainly responsible for their biological properties [81, 18, 82, 21].

The main chemical constituents identified in the leaves of the Cipó-d'alho were sulfur compounds such as diallyl disulfide, dialyl trisulfide and diallyl tetrasulfide [83, 18, 20]. Also, the chemical analysis of the essential oil present in the leaves of the Cipó-d'alho led to the identification of triterpenoids, flavonoids, naphthoquinones and amino acids [84, 21]. Just like garlic, when the leaves or other organs are crushed, the alliin and alliinase are mixed, forming allicin, one of the compounds responsible for the characteristic odor of garlic [79, 80]. Allicin is a volatile and highly unstable compound, representing the most important and abundant bioactive compound (60-80%) in garlic, due to its high concentrations of functional activity [85, 22].

This plant has several uses in traditional medicine. Among them the most cited are for treatment of influenza, fever, pain, arthritis and rheumatism [86, 82, 79]. Its therapeutic effects are also highlighted in the reduction of the blood fat, in the prevention of thrombosis and allergies and in the treatment of fatigue and muscular pain [87]. Moreover, according to Santhosha and collaborators [88], Cipó-d'alho provides protection against the development of breast cancer, and this therapeutic effect is attributed to dialysate trisulfide. The sulfur compounds alone or in association are involved with their inhibitory potential of weeds, promoted by the plant essential oil [83]. It also presents antioxidant, antibacterial and antifungal activies, attributed to the presence of allyl sulfide and, mainly, allicin present in the essential oil, which is a potential antioxidant [89, 85, 22]. Furthermore, it has shown great potential inhibitory to growth of microorganisms, including bacteria, fungi and virus [90, 91]. Its antifungal action acts in inhibiting the growth of fungal spores. In a study by Santos and collaborators [12] on an evaluation of the antifungal potential of essential oil of Cipó-d'alho leaves, the oil was presented as an alternative for use in the control of candidiasis, an infection caused by fungi of the genus *Candida (Candida albicans)*, which affect the lips, mouth, oropharynx, vagina and the gastrointestinal tract [92].

It was also observed antibacterial activity of the extract of Cipó-d'alho on the bacteria responsible for alimentary infections like *Staphylococcus aureus, Salmonella* spp. and *Escherichia coli* [93], which are well known by the general public and present a range of symptoms, in which the most common include stomach pain, nausea, vomiting, diarrhea and sometimes fever. Depending on the etiologic agent involved, the clinical picture may be more severe and prolonged, presenting severe dehydration, bloody diarrhea, acute renal failure and respiratory failure [63].

5. Murici (*Byrsonima crassifolia*)

Muricizeiro (*Byrsonima crassifólia*), as it is popularly called, is a species belonging to the genus *Byrsonima*, from the family Malpighiaceae, originating in the North, Northeast and central region of Brazil. It is popularly called Murici, Murici-da-várzea, Murici-da-mata, Murici-amarelo, among other names. The Murici tree is three to five meters high, with twisted branches, single leaves, bunched flowers and rounded fruits of yellowish color of about 1 to 2 cm diameter [16, 94, 95]. Although the fruit is mainly consumed as juice, ice cream and liqueurs [96], it is also used in the treatment and/or prevention of various diseases, as well as the leaves, seeds and stem bark [97, 98, 8, 99].

Therapeutic studies on the plant have been performed for the treatment of diarrhea, dysentery, indigestion, skin infections, wound healing, diabetes, among other diseases [100, 101, 16]. In general, Murici tree can be considered a plant with great antioxidant potential and antifungal function, as these properties are found in all parts of the plant [3, 102, 103, 104]. Although that some species of genus *Byrsonima* have demonstrated the presence of antibacterial, antifungal, anti-protozoal and anti-inflammatory activities [105, 106, 96, 107, 108, 98].

The fruits are rich in phenolic compounds [109] such as flavonoids (catechins, epicatechin, quercetin, kaempferol [16], pyrocatechol and proanthocyanidins), glycolipids, terpenoids (triterpenes), gallic acid and derivatives such as pyrogallol [110], esters [111] and carotenoids (lutein) [112]. Some studies have shown that the fruit able to reduce the levels of glucose, triglycerides, LDL (low density lipoprotein) lipoproteins also called "bad cholesterol" and raise the level of the HDL (high Density lipoprotein) lipoprotein known as "good cholesterol," and antioxidant substances, in addition to stimulating insulin production, with terpenoids (sesquiterpene lactones) being the main responsible for this therapeutic effect [102, 97]. Besides that, Murici exhibits highly active antifungal activity by inhibiting fungi that cause skin infections such as mycoses and dermatophytoses (*Epidermophyton floccosum*, *Trichophyton rubrum*, *Microsporum canis*) [113], being attributed to triterpenes this inhibitory effect [114].

Leaves are sources of glycolipids [115] flavonoids such as myricetin, phenolic compounds such as gallic acid, catechins and epicatechins [116]. Leaf extracts have antidepressant effects, due to the presence of flavonoids such as rutin, quercetin and hesperidin [117]. Due to its antiprotozoal effect, leaf extracts can be used to treat diseases such as giardiasis (*Giardia lamblia*), an infection of the small intestine [118, 119], leishmaniasis (*Leishmania mexicana*), which causes skin lesions [120] and Chagas disease (*Trypanossoma cruzi*), characterized by causing fever of varying intensity, malaise, problems in the lymph nodes and enlargement of the liver and spleen [105, 121].

The seed contains linoleic, oleic, stearic and palmitic acids [96]. As in fruits, seeds also have antihyperglycemic and antihyperlipidemic effects [102], as well as being an anti-inflammatory potential in both acute and chronic inflammatory models due to the compound called birsonimadiol, which when administered orally represents a powerful therapeutic drug for the treatment of inflammation [98].

The stem bark is an excellent source of flavonoids such as catechins, epicatechins [122, 123] and quercetins, β-amirin, betulin, betulinic acid, oleanolic acid, gallic acid and phytosterol (β-sitosterol) [99]. Has activity against spasms [124]. It is antidepressant [125] and acts as an anti-inflammatory [126]. It is widely used as a home remedy for diarrhea, vaginal discharge, toothache, lung problems, wounds, ulcers and as febrifuge [127, 106], being this therapeutic effect attributed to its antimicrobial activities. Its antibacterial activity is able to inhibit several bacteria, including those responsible for pharyngitis, deep infection in muscles, skin and intestine, erysipelas and toxic shock syndrome (*Streptococcus pyogenes*) [128, 129, 130], urinary and hospital infections (*Pseudomonas aeruginosa*) [131], food poisoning and intestinal infections transmitted by the ingestion of contaminated food (*Staphylococcus aureus, Escherichia coli, Salmonella typhi* and *Shigella flexneri*) [132, 63], oropharynx (*Streptococcus pneumoniae*) [133], infections related to medical implants (*Staphylococcus epidermidis*) [134], abscesses, pneumonia, septic arthritis, meningitis, bacteremia and septic shock in immunosuppressed patients (*Micrococcusluteus*) [135], besides inhibiting bacteria associated with dental caries and oral diseases (*Streptococcus mutans* and *Porphyromonas gingivalis*) [106, 136, 99, 137, 113, 138]. It also shows antifungal activity against meningoencephalitis causing lung damage and secondary damage to skin, bones and kidneys (*Cryptococcus neoformans*) [139] and dermatophytosis causing mycosis (*Microsporum gypseum, Miscrosporum canis, Trichophyton mentagrophytes, Epidermophyton floccosum* and *Trichophyton rubrum*) [140, 94, 136, 137].

6. Jambu (*Spilanthes acmella*)

Spilanthes is a botanical genus of the family Compositae or Asteraceae, composed of approximately 60 species existing in regions of tropical climate like America, Africa and India. *Spilanthes acmella*, a species native to Brazil is popularly known as Jambu or Agrião-do-Pará. It is cultivated throughout the year and can reach between 50 and 60 centimeters in height [141, 142, 143, 144]. The species is used for many years as an ornamental, medicinal and food plant. In cuisine, it is used in the composition of salads, soups, appetizers and traditional dishes [145, 143, 146]. Its flowers and leaves have pungent taste, which cause a sensation of salivation, numbness and tingling [147, 148].

The mastication of the plant is made to relieve toothache and diseases of the gums and throat [148]. The extract obtained by decoction in water is used as laxative and diuretic [149, 150]. It is also used to treat other diseases such as rheumatism, fever, hemorrhoids, asthma and sore throat [149, 151, 152].

Several classes of bioactive compounds of Jambu have been identified, isolated and characterized. Among them, alkylamides, steroids, flavonoids and esters [153, 154, 155], can be highlighted. In addition, among the N-alkylamides, Spilanthol was found as the main lipid component [156]. Spilanthol is an amide also abundant in other species of the genus *Spilanthes*, which has anti-inflammatory and analgesic properties and antibacterial, antifungal, acaricidal, larvicidal and ovicidal activities [157, 158, 159, 10, 160, 11, 161, 162].

The antibacterial activity of Spilanthol present in extracts of Jambu acts in the inhibition of the bacteria responsible for pneumonia and urinary infection (*Klebsiella pneumoniae*) [163], pharyngitis, erysipelas and toxic shock syndrome (*Streptococcus pyogenes*), diphtheria (*Corynebacterium diphtheriae*) [164] and the cause of dental caries (*Streptococcus mutans*) [165], presenting greater activities than some commercial drugs.

The antifungal activity of this compound causes the inhibition of pathogenic fungi producing aflatoxins (*Aspergillus flavus, A. parasiticus* and *A. niger*) which, when ingested, cause chronic aflatoxicosis resulting in longer pathological conditions, including decreased immunity and cancers, or acute aflatoxicosis resulting in death [163, 166]. *Aspergillus flavus* also causes aspergillosis, a lung disease that ranges from local inflammation of the airways to severe and life-

threatening infections [167]. Other tests were performed on Jambu extracts and greater antifungal activity was observed in the fight against candidiasis than the standard commercial drug (fluconazole). Antifungal effects were also demonstrated in the microorganisms that cause cryptococcosis (*Cryptococcus neoformans*), a disease characterized by nodules or abscesses in the lungs, subcutaneous tissues and joints, and skin diseases such as chilblains (*Microsporum gypseum*) [168]. Besides Spilanthol, antifungal activities present in Jambu extracts are also related to the alkamides, saponins and sesquiterpenoids [169, 166, 154].

Other investigations with extracts of Jambu presented analgesic, anti-thermal and anti-inflammatory activities attributed to flavonoids and steroids such as β-sitosterol [170, 171, 172, 173, 160, 174, 150]. Besides these activities, Jambu also showed antioxidant, vasorelaxant [175] and neuroprotective effects, acting in the treatment and/or prevention of encephalic or medullary lesions caused by ischemia, stroke, seizures or trauma [176].

7. Obtention of plant extracts by supercritical CO_2

Extracts have been used as medicaments for a long time, due to the presence of bioactive compounds present in different parts of plants. To potentiate their therapeutic effects, these compounds must be identified and isolated by extraction methods. Studies have been carried out to compare different methods of extracting bioactive compounds with the objective of finding the best alternative for its application in therapeutic products [177]. There are several methods for extracting bioactive compounds in plants, among these, traditional extraction methods with organic solvents and supercritical extraction may be mentioned [178, 179].

Extraction with organic solvents (such as water, ethanol and methanol) is frequently used for the isolation of bioactive compounds [180, 181]. It is characterized as a separation method of easy execution, but it has some disadvantages such as the production of toxic waste, the degradation of bioactive compounds by the use of high temperatures and long extraction times, which represents an economic loss and an environmental problem [182, 183, 184].

Extraction with supercritical fluid is defined as a modern and efficient extraction method and has been recognized as a promising procedure, because it does not release toxic waste from solvents in the environment, allows the extraction of extracts with high purity, has the ability to separate the specific bioactive compounds through their selectivity, uses smaller extraction times and can be conducted at low temperatures, preserving the quality of the compounds, as well as being technically feasible for almost any vegetable [185, 186, 187, 188, 189].

This method uses different pressure and temperature values to transform gases into supercritical fluids. This change from gaseous state to supercritical state allows it to exhibit some properties of liquids and of gases, with penetration capacity being an intermediate characteristic between the two states. Therefore, the supercritical state of fluids can be defined as the state in which the liquid and gas are mixed together, forming a homogeneous fluid [188]. In this physical state, the fluid can penetrate more easily into solid plants, resulting in better yields in the extractions [190, 191].

Carbon dioxide (CO_2) is the most used supercritical fluid in this type of extraction because it has moderate critical temperature (31.3 ºC) and pressure (7.38 MPa), and is inexpensive, ecological, safe, non-toxic, non flammable and presents a high degree of purity and high penetration capacity [192, 193, 194]. It is more effective for the extraction of compounds with low polarity like essential oils, carotenoids and fatty acids, but can be used in the extraction of compounds of high polarity, like phenolic compounds, making use of modifiers, also known as co-solvents (such as water and ethanol) [190, 191], to improve the yield and the selectivity of extracts [186].

Several researches, to obtain vegetable extracts with supercritical CO_2 were developed with the purpose of optimizing the process and reducing costs. Among the extracts obtained with supercritical CO_2 that present high therapeutic potential, the Rosemary, Jambu, Fennel, Clove, Black Sesame, Copaiba, Jucá and Açaí can be highlighted.

The Rosemary leaf presented more satisfactory results of yield and antioxidant activity [195]; the extract of the Jambu flower, which presented high selectivity to obtain the spilantol [196]; the extract of the fennel seed, which constituted an excellent source of bioactive compounds, such as anethole and fenchone, as well as fatty acids [197]; the extract of Clove, which presented high content of eugenol, compound that has high antifungal activity [198, 199, 200]; the extracts of the Black Sesame seed, the leaf and the oleoresin of Copaiba, in which the anti-inflammatory and neuroprotective effects against strokes were verified against the sesquitherpenes, including β-caryophyllene, this therapeutic effect [201, 202, 203]; the extract of Jucá fruits, which presented anti-inflammatory capacity, being used in bioactive dressings for the healing of wounds [204]; and extract of Açaí fruits, which showed potential applications for nutraceutical purposes due to the high content of anthocyanins [205].

It is important to note that one of the main reasons that may hinder the more widespread use of plant extracts is that most of the studies reported so far in the literature generally employ unpurified extracts to conduct bioactivity studies in cells and animals [196]. For this reason, the extraction of plant bioactive compounds with supercritical CO_2 has aroused the interest of food, cosmetic and pharmaceutical industries as an alternative to replace the conventional extraction processes that are harmful to humans and to the environment.

8. Conclusions

Given that diseases and pain are the conditions that most limit productivity and decrease the quality of humans life, and that many drugs cause gastrointestinal damage, cardiovascular problems, intolerance, respiratory depression and physical and psychological dependence, extracts from Cipó-pucá, Cipó-d'alho, Murici and Jambu, obtained by extraction with supercritical CO_2, represent an important gain in human investments in health, food and cosmetic areas, due to their expressive therapeutic potentials. Moreover, it is a great opportunity for obtaining bioactive compounds of natural origin which can be used for the treatment and/or prevention against various diseases.

The chemical identification and estimation of the antimicrobial activity of these extracts have fundamental importance for their application by pharmaceutical companies and can be used to establish parameters in the development of products, assisting in their quality and, therefore, their safety and efficacy. Thus, these extracts can act as an optional form of therapy taking into account the additional benefits when compared to conventional medicines.

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