Phytotechnological and Pharmaceutical Potential of *Eugenia* Genus

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Abstract *Eugenia* is the largest Neotropical genus belonging to the Myrtaceae family, comprising more than 1000 species spread across the Antilles, Southeast Asia, Pacific Islands, Argentina, southern Mexico, Cuba, Uruguay, Africa, and Brazil. *Eugenia* genus comprises species employed in folk medicine due to their antioxidant compounds, such as polyphenols, tannins, and flavonoids. Traditionally, plants are widely used to treat inflammatory diseases and metabolic disorders. Various species from this genus possess technological potential as well. The biological properties associated with the phytochemistry profile raise a significant number of potential intermediate and final products. Thus, we approach the technological products obtained from species of the *Eugenia* genus, their biological potential and the main techniques employed in the future development of products with commercial value.

Keywords Myrtaceae · Medicinal plants · Cerrado · Intermediate products

1 Introduction

Historical records from traditional Chinese, Ayurvedic and Amerindian medicine show that the widespread use of plants for medicinal and nutritional purposes comes from the beginning of humanity [1]. Thus, over the years, the use of natural products has become an alternative practice in conventional medicine around the world; the World Health Organization and government agencies have highlighted the need for

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studies that establish criteria for safety, efficacy, and quality, valuing the use of medicinal plants in the therapeutic scope [2, 3].

In this context, scientific research aims to prove its use in folk medicine, based on empirical knowledge, classifying and identifying its biochemical composition, and establishing its real benefits of use and better pharmacological properties [1]. Furthermore, the structural diversity of special metabolites present in plants represents a prosperous source of bioactive compounds [3]. Thus, the search for these substances becomes essential due to the ability to treat different pathophysiological conditions and contribute to the conservation and recognition of the biodiversity of Biomes and promoting the sustainability and development of natural resources.

Eugenia is the largest Neotropical genus belonging to the Myrtaceae family, comprising more than 1000 species spread across the Antilles, Southeast Asia, Pacific Islands, Argentina, Southern Mexico, Cuba, Uruguay, Africa, and Brazil [4, 5]. In Brazil, the genus has a wide geographic distribution, mainly in the Amazon, Atlantic Forest, and Cerrado [6, 7]. According to the current molecular classification, *Eugenia* belongs to the subtribe Eugeniinae of the tribe Myrteae, subfamily Myrtoideae [8–10].

The species' way of life consists of fruit trees, shrubs, or sub-shrubs, occupying the position of the second most diverse tree genus in species on the planet [9, 11, 12]. The flowers are axillary, branched, tiny, and fragrant with white or possibly pink petals [12]. The fruits are small, less than 10 cm in diameter, globose, pulpy, consisting of few seeds, usually 1–2 [9, 12], and consumed *in natura*; they are rich in minerals, vitamins, and phenolic compounds. Due to their characteristics, many plants are used in landscaping, domestic planting, reforestation, and urban afforestation. Other species, such as *Eugenia dysenterica* (Mart.) DC, are still used in folk medicine as laxatives, anti-inflammatory, and anti-rheumatic agents [13–16].

In addition, the species are rich in essential oils, extracts are also made from them (ethanolic, hydroalcoholic, acetone), and chemical compounds are isolated [17, 18], several nutrients and bioactive substances have been described supporting popular uses [13, 14]. Thus, *Eugenia* genus has aroused much commercial interest due to its edible fruits, ornamental characteristics, essential oils, and therapeutic potential.

2 The Pharmaceutical Potential of the *Eugenia* Genus

Species of the *Eugenia* genus have several biological properties, such as gastroprotective [19], antidiabetic [20], antioxidant [21], anticancer [22], anti-inflammatory [23], antimicrobial [17], antipyretic [24], among others [13]. These activities are related to the presence of special metabolites, such as phenolic compounds, mainly flavonoids (myricitrin, quercetin), terpenoids (monoterpenes, triterpenes, sesquiterpenes), and tannins [13, 15]. Traditionally, plants are widely used to treat inflammatory diseases and metabolic disorders [17].

The pharmaceutical potential has been described in several plants, including fruits, seeds, and leaves [13]. For example, extracts from *Eugenia selloi* (O.

Berg) B.D. Jacks.(fruit), *Eugenia kleinii* D. Legrand.(seeds), and *Eugenia brasiliensis* Lam.(pulp) showed anti-inflammatory and antioxidant activity due to the ability to modulate neutrophil migration. Two similar compounds across species that may enhance the observed potential were ellagic acid and quercetin [25–27]. Likewise, the presence of ellagic acid and other α- and β-amyrin pentacyclic triterpenoid constituents in *Eugenia umbeliflora* O. Berg leaves was reported, showing important anti-inflammatory effects on the extract the behavior of neutrophils and on the decrease of IL-β levels [28].

Antiparasitic activities have also been reported; studies with essential oil from the leaves of *Eugenia uniflora L.* and hydroalcoholic extract of *Eugenia pruniformis* Cambess, showed anti-leishmania (*Leishmania amazonesis*) potential against promastigote and amastigote forms using in vivo and in vitro experiments. Biological activity is probably associated with sesquiterpenes and terpenoid fractions [29, 30]. These results are promising and may help in the future in the treatment of leishmaniasis—an infectious, neglected tropical disease of great epidemiological importance [31].

Extracts from the leaves of *Eugenia punicifolia* (Kunth) DC. ("cerejeira do cerrado"), *E. dysenterica*, *E. umbeliflora,* and the fruit of *Eugenia mattosii* D. Legrand ("cerejeira anã") showed gastroprotective and antinociceptive effects in vivo, such as increased production of gastric mucus, blockage of production of hydrochloric acid, reduction of more than 60% of ulcerated areas, similar to that compared with cimetidine and omeprazole (medicines used in the treatment of gastritis). These studies indicated the presence of condensed tannins and proanthocyanidins as responsible for the observed biological effects [19, 32–34].

Despite antimicrobial properties, crude extracts from seeds (*E. Kleinii*, *E. brasiliensis*) and leaves (*E. brasiliensis*), obtained greater antifungal potential in *Candida albicans* biofilm than with nystatin (standard) in the phytochemistry of the extract. The majority presence of gallic acid and epicatechin was observed [14]. Likewise, antibiofilm activity was observed in *Lactobacillus acidophilus* from the extract of *E. brasiliensis* (pulp), in addition to catechin, flavonols, anthocyanins, and ellagitannins were found [27]. Essential oils of *E. umbeliflora*, *E. brasiliensis,* and *Eugenia beaurepairiana* (Kiaersk) D. Legrand("ingábaú") showed antibacterial properties against *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*, and extract/fractions of *E. mattosii* still show antimycoplasmic activity (*Mycoplasma pneumoniae* and *Mycoplasma genitalium*) [35, 36]. Furthermore, the essential oil of *Eugenia calycina* Cambess ("pitanga vermelha do cerrado") and its fractions showed selective activity against oral gram-negative bacteria (*Porphyromonas gingivalis*, *Prevotella nigrescens*, among others). These biological properties have been associated with the presence of oxygenated and non-oxygenated sesquiterpenes, thus making it a good measure in treating oral bacterial infections [37].

Ethanol extract from fruits and seeds of *Eugenia involucrata DC.* showed an antitumor effect on PANC-1 (pancreatic adenocarcinoma) cells, involving complex mechanistic pathways, such as oxidative stress and cell proliferation. The primary responsibility for the biological activity of the extract was epicatechin, catechin, and ellagic acid alone or in combination with other chemical constituents present

[22]. On the other hand, the study by Vitek et al. 2016, with an isolated compound (quercetin-3-O-(6″-O-galloil)-β-d-glucopyranoside) from the extract of *E. dysenterica* leaves, alone was shown to induce cytotoxicity in cells of the CCRF-CEM lineage (Lymphoblastic Leukemia of T cells) and antiproliferative and cell differentiation effects in a Kasumi-1 lineage (acute myeloid leukemia) [38].

Other reported activities of *Eugenia* spp. consists of antidepressant activity influenced by substances such as α-amyrin and β-amyrin, betulin, 29-hydroxy-oleanolic acid, and flavonoids [39], potential to inhibit acetylcholinesterase (AChE) activity, correlated with known compounds such as quercetin, catechin, epicatechin, procatechuic acid, and myricthrin [40]. Ability to interact with nicotinic cholinergic receptors [41], and finally, the species show low or no toxicity using in vivo and in vitro studies [25, 27, 42, 43]. Therefore, the phytochemical characteristics of the genus are a promising source in the discovery of bioactive compounds and the development of drugs, proving the great pharmaceutical potential of the species.

3 Phytotechnological Potential of the *Eugenia* Genus

Due to the growing recognition of the nutritional and therapeutic benefits of species of the *Eugenia* genus, many of the fruits are being consumed in an industrial version of ice cream/popsicles, juices, jams, sweets, and jellies, such as the "pitanga" of the *E. uniflora* species, the "cereja do rio grande" from *E. involucrata* and the "cagaita" belonging to *E. dysenterica* [44, 45].

In this context, residues from *Eugenia* spp. has been well investigated; Silva et al. [46], observed that the by-product of pitanga fruits (*E. uniflora*) had higher polyphenol content (total anthocyanins, yellow flavonoids, β-carotene, lycopene, resveratrol and coumarins) than their respective pulp, demonstrating that after processing the residues have prospects of use, such as nutraceutical supplements and food inputs [46]. The extract of *E. uniflora* leaves is a healthy alternative for replacing synthetic antioxidants, such as butylated hydroxytoluene (BHT), in goat and pork hamburgers [47, 48]. Due to its antioxidant potential, preserving the quality of the meat without adverse effects on its physical–chemical and sensory properties, and increasing the shelf life to storage time.

Bioactive peptides derived from plants have attracted significant interest from researchers and the pharmaceutical industry. They are chains of amino acids joined by covalent bonds with different biological functions [49]. For example, Lima et al. 2010, showed that a peptide isolated from the fruit of *E. dysenterica* promoted a laxative effect in rats due to the increase in intestinal peristalsis without causing diarrhea and toxic effects. The peptide was identified using modern and practical analysis methods such as high-performance liquid chromatography (HPLC). The molecular mass and degree of purity were determined using Tris/Tricine polyacrylamide gel electrophoresis matrix-assisted laser desorption/ionization-time of flight

mass spectrometry (MALDI-ToF) [50]. Thus promoting perspectives in the technological development of natural pharmaceutical peptides in treating irritable bowel syndrome and chronic constipation.

One application of renewable characteristics that has been studied is the use of the extract of the leaves of *E. dysenterica* as an additive in biofuel. Rial et al. [51], demonstrated the ability of the crude extract to reduce the oxidation of soy biodiesel after 120 days of storage much more effectively than quercetin (standard). This result was associated with flavonoids, tannins, steroids, and triterpenoids, promoting stability and better quality of biodiesel [51].

The spray drying technique also proves to be a promising strategy in developing bioactive intermediate products from *Eugenia* spp. [52]. The study by Iturri et al. [53], was shown to be a good technique in the preservation of phenolic compounds and in obtaining microparticles from the pulp extract of *Eugenia stipitata* McVaugh. In addition, innovatively, Differential Scanning Calorimetry (DSC) was used with the spray dryer to define the drying temperatures and the proportion of the wall material. Therefore, the microparticles with the best conservation of polyphenols and the best antioxidant potential were with maltodextrin (1:9) at 100 ºC. Hence, the association between these two techniques results in a quality product, with high concentrations of compounds being economically viable in industrial production [53].

Nanoemulsions have alternative products in the application. Nanoemulsions from the essential oil of *Eugenia brejoensis* Mazine leaves potential antibacterial foods. against *Pseudomonas fluorescens* bacteria found in food. No essential oil compounds were identified as sesquiterpenic hydrocarbons, β-(E)-Caryophyllene, δ-cadinene, and bicyclogermacrene [54]. From the extracts, emulsions are also made, as the catechin-rich *E. dysenterica* extract has shown in in vitro experiments, antimicrobial properties against *S. aureus* strains, and angiogenic activity [43]. Demonstrating the possibility of developing dermatological treatment from plant products, with a perspective on the cosmetics industry.

Other technological potentials of species of the *Eugenia* genus include serving as an additive in producing films (food and degradable biofilms) of active nanocomposites and in the coating of minimally processed foods due to antioxidant and antimicrobial activity [55, 56]. Furthermore, protect different organisms (*E. coli*, seeds, and *Drosophila melanogaster*) against toxicity caused by mercuric chloride residues through antioxidant mechanisms or chelation [57], promoting interesting perspectives in environmental conservation. Also, *Eugenia* spp. has shown good yield and extraction results by the supercritical fluid technique, indicating the use of green technologies as alternative and economic conditions in extractive processes [58–60].

Some species still show a predisposition in the development of quality insecticides, with low toxicity and sustainable footprint; an example is a study by Silva et al. [61], in which the essential oil of *E. calycina* showed larvicidal activity against *Aedes aegypti* mosquito, due to the synergistic effect of oxygenated sesquiterpene compounds (spathulenol, aromadendrane-4β,10α-diol and 1β-11-dihydroxy-5-eudesmene), with low toxicity in HeLa (human epithelial cell) and Vero (African monkey renal cell) cell lines [61]. Therefore, in addition to the biological properties

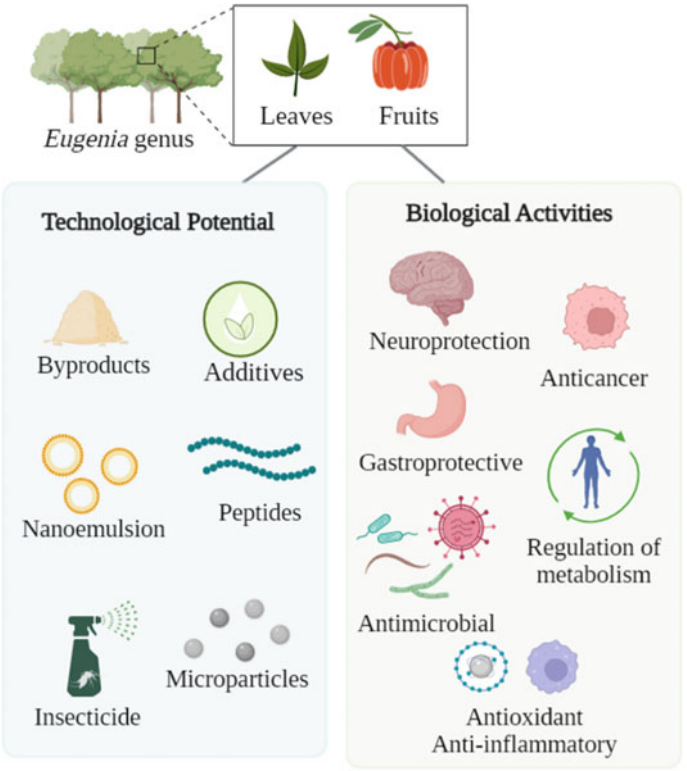

Fig. 1 Illustration of the biological and technological potential of the *Eugenia* genus

Eugenia spp. also demonstrates great technological potential in the development of products with commercial value (Fig. 1).

4 Food Application of *Eugenia* spp.

In recent decades, the food industry and the consumer market have been increasingly interested in phenolic-rich edible fruits as they slow down the rancidity process, improve the quality and the nutritional value of foods, and promote well-being and health [62]. *Eugenia* spp. is an innovation hotspot for food purposes, because of the presence of (i) favorable sensory characteristics and (ii) bioactive phytochemicals with biological activity stronger than that observed in fruits traditionally consumed by the urban population, so being considered superfruits, which encourages its use as nutraceuticals [13, 15, 63, 64]. Nutraceuticals are substances that, other than nutrition, are also used as medicine. A nutraceutical presents physiological benefits or protects chronic body processes, such as aging and chronic diseases. In other terms,

nutraceuticals may be used to improve health, increasing life expectancy [65]. Thus, *Eugenia* spp. has great economic potential since the regular intake of its superfruits should be beneficial for human health [13, 64].

Two *Eugenia* species stand out for food applications: *E. uniflora* and *E. dysenterica*. These species are traditionally consumed in Brazil in natura or prepare several culinary recipes, such as ice creams, jams, jellies, and beverages. Recently, *E. uniflora* was added to traditional kombucha, which contributed to diversifying and improving this beverage's chemical and bioactive characteristics, revealing a sweeter kombucha, with floral and fruity aromas and with a greater antioxidant activity [66]. Since the antioxidant compounds are highly unstable molecules, microencapsulation of *E. uniflora* juice by spray drying demonstrated to be a suitable alternative for the encapsulation and protection of antioxidants for the food industry [67].

E. uniflora extracts could also be used in the food industry as natural aroma enrichment of processed foods, in food packaging, or as food preservatives. The characteristic flavor of *E. uniflora* fruits is attributed to the presence of sesquiterpenes and ketones [68]. The flavor intensity of these fruits obtained by supercritical carbon dioxide extraction is correlated to the temperature increase (>50 °C) [69]. The antioxidant molecules in *E. uniflora* could be essential to protect *in natura* or processed food. Biopolymer films loaded with nanocellulose from soybean straw and activated with *E. uniflora* leaf extract displayed a greater resistance and stiffness, higher barrier properties to UV/Vis light, and higher antioxidant activity than those without the extract [55]. *E. uniflora* leaf extract was effective against color deterioration and lipid and protein oxidation, without impairing the sensorial characteristics, on lamb burgers with fat replacement by chia oil emulsion, representing a promising alternative to replace synthetic antioxidants by natural products in lamb burgers [47].

Although its laxative capacity [50], *E. dysenterica* can be used in the food industry [63]. Wines, juices, jellies, and raisins with high antioxidant properties and good consumer acceptance were elaborated using *E. dysenterica* pulp [70–73]. Moreover, *E. dysenterica* fruit extract has the potential to be used as an ingredient of diabetic and obese food formulations since it can inhibit α-amylase and α-glucosidase, key enzymes in carbohydrate metabolism, slowing postprandial hyperglycemia [74], and it presents functional properties to both prevent and treat obesity and associated diseases [75, 76]. Recently, *E. dysenterica* juice also demonstrated a postprandial glucose-lowering effect [77]. To prevent deterioration of the bioactive compounds in *E. dysenterica,* spray drying methodology was shown to be a suitable alternative during dehydration of the leaves and fruit [52, 78].

Other *Eugenia* species, considered unexplored Brazilian fruits, has the potential to be applied in the food industry. *E. calycina* presents three times more ellagic acid than blackberry and black raspberry, the main richest classical foods in ellagic acid [62]. Using a thermal ultrasound approach, phenolic compounds extraction from *E. calycina* was more efficient [79]. Fresh and spray dried *Eugenia jambolana* Lam ("jambolan") has already been used to prepare caprine frozen yogurt containing the probiotic strain *Bifidobacterium animalis* subsp. *lactis* BI-07. The preparation presented a good consumer acceptance and maintained high probiotic survival

rates along with 90-day frozen storage, proving to be a high-quality dairy product for the crescent, healthy-oriented market [80]. The stability of anthocyanins- and anthocyanidins-enriched extracts and formulations of fruit pulp of *E. jambolana* was investigated. The anthocyanins-enriched Sephadex extract presented good stability (36% content reduction) after 1 year at 5 °C [81].

Eugenia pyriformis Cambess ("uvaia") can be considered an energetic matrix containing fructose, sucrose, glucose, and maltotetraose. This fruit presents high levels of macronutrients (ash, lipids, proteins, fibers) and minerals. It contributes to the dietary reference intake regarding dietary fibers and micronutrients, such as Fe, Cu, K, Mg, and Mn. Moreover, *E. pyriformis* presented high levels of total flavonoids, phenolic compounds, and antioxidant activity, terpenes the majority (46.75%) of identified volatile compounds [82, 83]. The influence of in vitro gastrointestinal digestion on the bioaccessibility and bioactivity of phenolic compounds was investigated for *E. pyriformis* fruits. Flavonoids increased their relative intensity, while phenolic acids reduced their power, suggesting that such compounds are more susceptible to being degraded during the digestive process, presumably due to less chemical complexity than flavonoids, which were found mainly in glycosylated form [84].

E. stipitata ("arazá") is being considered a superfruit because of the high content of minerals such as K, Ca, and Mg, sucrose, fructose, maltotetraose, phenolic compounds, and flavonoids, with a good antioxidant capacity, revealing a relevant potential to be used as a functional food [64, 85]. Storage stability tests of freeze-dried *E. stipitata* powders revealed that shelf-lives, calculated considering 90% properties retention as the acceptability limit, were 34 and 50 days to an arazá/maltodextrin mixture and an arazá/Arabic-gum mixture, respectively [86]. Microparticles of maltodextrin and *E. stipitata* pulp (1:9, 100 °C) obtained by spray-drying guided by differential scanning calorimetry (DSC) had good bioactivity conservation after in vitro gastrointestinal digestion, conserving 61% of total polyphenols, and 101%, 85% and 31% of antioxidant capacity. These microparticles had a spherical morphology, presented good thermal stability, and can be stored at a temperature range from 20 to 40 °C without becoming sticky [53].

E. brasiliensis ("grumixama") is also considered a good source of bioactive compounds, such as anthocyanins, flavonols, and ellagitannins [87]. Human urine and plasma after ingestion of polyphenol-rich juice of purple *E. brasiliensis* revealed that a single dose of grumixama juice increased the plasma antioxidant capacity and 114 metabolites were assessed in urine, including 17 amino acids, 47 organic acids, and several other metabolites involved mainly with amino acid metabolism and mitochondrial metabolism [88]. Altogether, these data indicate that *Eugenia* spp. may serve as a raw material for the food industry.

5 Conclusion

Species of the *Eugenia* genus are a promising source of bioactive and biotechnological compounds. Essential oils and plant extracts contain special metabolites such

as flavonoids, terpenoids, and tannins, responsible for triggering various biological activities (regulation of metabolism, neuroprotection, gastroprotection, etc.), thus making it an alternative measure as a therapeutic complement and treatment of diseases. In addition, the species show perspective in the industry with the development of technological products playing the role of drugs, environmental remediators, food inputs, additives, insecticides, among others.

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