

Traditional Uses, Phytochemistry, and Antimicrobial Activities of *Eugenia* Species – A Review

Authors

Angela Maria de Souza, Camila Freitas de Oliveira, Vinícius Bednarczuk de Oliveira, Fernando Cesar Martins Betim, Obdulio Gomes Miguel, Marilis Dallarmi Miguel

Affiliation

Postgraduate Program in Pharmaceutical Sciences, Federal University of Parana, Curitiba, Parana, Brazil

Key words

Eugenia species, Myrtaceae family, chemical composition, antimicrobial activity, toxicity

received April 16, 2018

revised June 26, 2018

accepted July 5, 2018

Bibliography

DOI <https://doi.org/10.1055/a-0656-7262>

Published online July 17, 2018 | *Planta Med* 2018; 84: 1232–1248 © Georg Thieme Verlag KG Stuttgart · New York | ISSN 0032-0943

Correspondence

Angela Maria de Souza
Postgraduate Program in Pharmaceutical Sciences, Department of Pharmacy, Federal University of Parana
Av. Prof. Lothário Meissner, 632, CEP 80210-170 Curitiba, Parana, Brazil
Phone: + 55 41 33 53 55 03, Fax: + 55 41 33 60 40 98
angelasouza68@hotmail.com

ABSTRACT

Antimicrobial resistance is a critical health problem, and pathogens responsible for common infections have developed resistance to antimicrobials, posing a threat to global health and placing a huge burden on health services. During the past two decades, the search for new bioactive agents in nature has become extremely important for promoting health and in the development of more efficient antimicrobials. The genus *Eugenia* is one of the largest in the Myrtaceae family, comprising approximately 1000 species from Mexico to Argentina, with a few species distributed in Australia and Africa. *Eugenia* species are used in folk medicine, with antidiabetic, antirheumatic, antipyretic, anti-inflammatory, antidiarrheal, antifungal, and antibacterial properties. This study systematically reviews the *Eugenia* species to compile the phytochemical composition and antimicrobial effects. In addition, we provide information regarding the traditional uses and cytotoxic activity of *Eugenia* species. We conducted a systematic literature search of specialized databases (Web of Science, Scielo, Lilacs, Pubmed, Science Direct, Scopus) and selected articles published between 1973 and 2015 using *Eugenia* and antimicrobial activity, *Eugenia* and toxicity, and *Eugenia* and chemical composition as key words. Ninety-three studies were included, and the phytochemical analyses from these studies show that *Eugenia* species are a rich source of flavonoids, tannins, triterpenes, and sesquiterpenes. Chemical constituents play an apparent role in the antimicrobial effects and reinforce the known antimicrobial potential of the *Eugenia* genus. It is worth mentioning that some *Eugenia* species cause significant cytotoxicity.

Introduction

The Myrtaceae family is a group of dicotyledonous plants comprising approximately 130 genera and 3800–5800 species of shrubs or trees. It has been found in all continents except Antarctica, with predominance in the tropical and subtropical regions of the world [1–3]. Approximately one-third of the species in this family belong to the genus *Eugenia*, with around 1000 species distributed from southern Mexico to northern Argentina. It is estimated that 350 species are native to Brazil, with a small number of species being found in Africa. The plants of this genus are perennial trees or shrubs with spherical and edible fruits [4, 5] that

have diverse pharmacological activities, including antidiabetic, antirheumatic, antidiarrheal, antipyretic, anti-inflammatory, antifungal, antibacterial, antioxidant, and cytotoxic properties. In addition, they have also been used to treat diseases of the stomach [6, 7].

Several known species from the *Eugenia* genus have been reported for their medicinal uses and chemical constituents, as well as antimicrobial and cytotoxic activities, including *Eugenia axillaris* (Sw.) Willd., *Eugenia beaurepaireana* (Kiaersk.) D. Legrand, *Eugenia brasiliensis* Lam., *Eugenia dysenterica* DC., *Eugenia punicifolia* (Kunth) DC., *Eugenia pyriformis* Cambess., *Eugenia rigida* DC., *Eugenia sulcata* Spring ex Mart, *Eugenia umbelliflora* O. Berg, and *Euge-*

► **Table 1** Data on the traditional use of *Eugenia* species in the studies selected through this systematic review.

Species	Extracts and/or part of the plant	Traditional uses	References
<i>E. axillaris</i> (SW.) Willd.	Decoction of the leafy branch tips	Aphrodisiac, antidiarrheic, and for bathing women after childbirth	[17, 18]
<i>E. beaurepaireana</i> (Kiaersk.) D.Legrand	No date	Anti-inflammatory, antidiarrheic, diuretic, antirheumatic, anti-febrile, antidiabetic, and antirheumatism	[7]
<i>E. brasiliensis</i> Lam.	Leaves, fruits, and bark infusions	Stomach diseases, antirheumatic, anti-inflammatory, antidiarrheic, and diuretic	[4, 7, 19]
<i>E. dysenterica</i> DC.	Leaves	Anti-inflammatory, antimicrobial, antihypertensive, antidiarrheic, purgative	[7, 8, 16, 18]
<i>E. punicifolia</i> (Kunth) DC.	No date	Hypoglycemic activity	[8]
<i>E. pyriformis</i> Cambess.	Leaves	Treatment for gout	[20]
<i>E. rigida</i> DC.	No date	Leukemia	[5]
<i>E. sulcata</i> Spring ex Mart	No date	Fever treatment and antidiarrheic	[21]
<i>E. umbelliflora</i> O.Berg	Aerial parts	Infections, inflammation, and diabetes	[22]
<i>E. uniflora</i> L.	Leaf and fruit infusions, hydro-alcoholic leaves extract	Exciting, febrifuges, antidysenteric, antidiarrheic, antihypertensive, antirheumatic, anti-inflammatory, hyperlipidemia, hypotriglyceridemic, hypoglycemic, bronchitis, coughs, fevers, anxiety, diuretic, stomach diseases, digestive disorders, verminosis, gout, vaso-relaxant, antioxidant, and with antimicrobial property	[7, 8, 11, 14–16, 23–31]

nia uniflora L., among others. Thus, the aim of the present study was to develop a systematic review to analyze whether plants in the *Eugenia* genus have antimicrobial and cytotoxic properties *in vitro*, as well as the chemical composition of the various species. This review demonstrates the importance of the *Eugenia* genus in providing secondary metabolites of pharmacological interest and establishes that further research of many species would be beneficial.

Search Strategy

This systematic review was carried out using bibliographic research in 2016, and includes articles published from 1973 to 2015. We used specialized databases (Web of Science, Scielo, Lilacs, Pubmed, Science Direct, Scopus, and an article selected from Google Scholar) and included *Eugenia* and antimicrobial activity, *Eugenia* and toxicity, and *Eugenia* and chemical composition as key words for the literature searches. The articles included in this manuscript were original articles. Further, articles containing isolated compounds identified via spectroscopic techniques and articles reporting antimicrobial and cytotoxic activity were included. Species of the genus *Eugenia* were selected according to the classification of *Kew Royal Botanic Garden* and *The Plant List*, excluding species not belonging to the genus. Duplicate items or items that were not within the review area of interest were excluded. The three major compounds identified in the species studied were selected for the chemical composition of the essential oil. The Endnote program was used to store the selected articles. Initially, two researchers selected articles by titles, and article abstracts were evaluated. Finally, the complete articles were read in whole, and references that met the inclusion criteria were included in the review. Disagreements were resolved

through consensus among researchers, and in the case of nonagreement, a third reviewer was consulted.

Initially, 1057 articles were selected. We excluded 227 duplicate articles, 53 of which were excluded with the help of an Endnote tool and 174 of which were manually excluded. Of the original 1057 articles, 673 did not fit the inclusion criteria and were excluded after reading the titles and abstracts, while 64 were excluded after reading the complete article. As such, this review includes 93 articles that reported the isolation of phytoconstituents, as well as the antimicrobial and cytotoxic properties of species from the genus *Eugenia*.

The *Eugenia* Genus

The *Eugenia* genus is considered the fourth most important genus of the family Myrtaceae for the production of essential oils after the *Eucalyptus*, *Melaleuca*, and *Psidium* genera. Essential oils from *Eugenia* species comprise approximately 300 compounds that have been previously identified, with cyclic sesquiterpenes predominating and monoterpenes found in smaller quantities. A few species produce aliphatic and aromatic compounds. These various types of terpenoid compounds are used in the pharmaceutical, cosmetic, and agrochemical industries [6, 8]. In addition to essential oils, flavonoids, triterpenoids, and tannins have also been identified in *Eugenia* species. Among the flavonoids, there is a predominance of polyhydroxy flavanols, and most of the isolated pentacyclic triterpenes have a lupan or oleanane skeleton [4].

The most studied *Eugenia* species are *E. uniflora* L. and *E. brasiliensis* Lam., which produce exotic fruits such as “pitanga” (*E. uniflora* L.) [9] and “grumixama” or “Brazilian cherry” (*E. brasiliensis* Lam.) [10]. These fruits are consumed fresh or in the form of juices and jellies and have high nutritional value, as well as being rich

► **Table 2** Chemical composition of essential oils from *Eugenia* species in the studies selected through this systematic review.

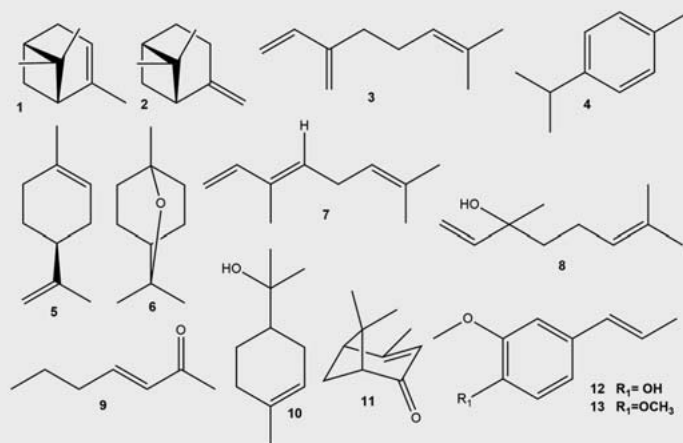
No	Species	Part of plant	Major components	References
1	<i>E. arenosa</i> Mattos	Leaves	Farnesyl acetate (70.4%) 59 , Aromadrendene (11.7%) 20 , Globulol (7.1%) 42	[31]
2	<i>E. argentea</i> Bedd.	Leaves	β -Caryophyllene (18.0%) 17 , δ -Cadinene (7.8%) 32 , Germacrene D (7.1%) 24	[15]
3	<i>E. austini-smithii</i> Standl.	Leaves	Trans-2-hexenal (33.6%) 9 , α -Terpineol (7.8%) 10 , Germacrene D (7.1%) 24	[32]
4	<i>E. axillaris</i> (SW.) Willd.	Leaves	Guaiol (35.4%) 44 , α -Pinene (15.5%) 1 , Germacrene D (12.1%) 24	[17, 33]
5	<i>E. bacopari</i> D.Legrand	Leaves	δ -Cadinene (15.8%) 32 , Aromadrendene (12.2%) 20 , Viridiflorene (7.9%) 27	[34]
6	<i>E. beaurepaireana</i> (Kiaersk.) D.Legrand	Leaves	Bicyclogermacrene (14.3%) 29 , Germacrene D (8.6%) 24 , β -Caryophyllene (8.0%) 17	[35, 36]
7	<i>E. biflora</i> (L.) DC.	Leaves	β -Pinene (27.85%) 2 , α -Pinene (27.34%) 1 , β -Caryophyllene (15.36%) 17	[37]
8	<i>E. brasiliensis</i> Lam.	Leaves	Cubenol (33.1%) 52 , Trans- α -Bergamotene (19.0%) 18 , Spathulenol (18.17%) 40	[10, 19]
9	<i>E. burkartiana</i> (D.Legrand) D.Legrand	Leaves	Bicyclogermacrene (14.2%) 29 , Germacrene D (8.8%) 24 , β -Caryophyllene (7.8%) 17	[34]
10	<i>E. calycina</i> Cambess.	Leaves	Bicyclogermacrene (19.3%) (29), Spathulenol (21.36%) 40 , β -Caryophyllene (8.57%) 17	[7]
11	<i>E. candolleana</i> DC.	Leaves	δ -Elemene (13.87%) 14 , Muurola-4,10(14)-dien-1 β -ol (8.68%) 49 , 1-Epi-cubenol (7.59%) 48	[38]
12	<i>E. cartagensis</i> O.Berg.	Leaves	Trans-2-hexenal (31.2%) 9 (E) β -Ocimene (16.2%) 7 , Germacrene D (12.3%) 24	[39]
13	<i>E. catharinensis</i> D.Legrand	Leaves	Ethyl palmitate (10.5%) 63 , Trans- α -Bergamotene (6.5%) 18 , α -Humulene (5.9%) 22	[34]
14	<i>E. chlorophylla</i> O.Berg.	Stem	Caryophyllene oxide (17.2%) 41 , Globulol (16.5%) 42 , t-Muurolol (16.8%) 51	[40]
		Leaves	Globulol (22.5%) 42 , α -Cadinol (9.4%) 35 , 1,10-di-epi-Cubenol (9.8%) 46	
		Flowers	β -Caryophyllene (12.8%) 17 , α -Cadinol (10.1%) 35 , Caryophyllene oxide (8.9%) 41	
15	<i>E. copacabanensis</i> Kiaersk.	Leaves	β -Pinene (50.4%) 2 , α -Pinene (20.2%) 1 , 1,10-di-epi-Cubenol (14.24%) 46	[8, 38]
16	<i>E. cuprea</i> (O.Berg) Nied.	Leaves	Spathulenol (12.1%) 40 , β -Caryophyllene (9.2%) 17 , Caryophyllene oxide (8.7%) 41	[31]
17	<i>E. dimorpha</i> O.Berg.	Leaves	α -Pinene (22.4%) 1 , α -Humulene (12.9%) 22 , 1,8-Cineole (9.9%) 6	[34]
18	<i>E. dysenterica</i> DC.	Leaves	γ -Cadinene (27.0%) 31 , β -Caryophyllene (14.8%) 17 , δ -Cadinene (13.0%) 32	[41]
19	<i>E. flavescens</i> DC.	Leaves	α -Curcumene (14.95%) 23 , α -Selinene (11.72%) 28 , δ -Cadinene (5.71%) 32	[37]
20	<i>E. foetida</i> Pers.	Leaves	Caryophyllene oxide (14.8%) 41 , Caryophyllene alcohol (9.1%) 39 , α -Cadinol (6.0%) 35	[42]
21	<i>E. haberi</i> Barrie	Leaves	α -Pinene (29.0%) 1 , α -Terpineol (19.4%) 10 , trans-2-Hexenal (11.2%) 9	[32]
22	<i>E. hiemalis</i> Cambess.	Leaves	Bicyclogermacrene (37.7%) 29 , β -Caryophyllene (7.4%) 17 , Germacrene D (7.0%) 24	[43]
23	<i>E. involucreta</i> DC.	Leaves	β -Caryophyllene (10.1%) 17 , Spathulenol (7.8%) 40 , β -Bisabolene (7.2%) 30	[44]
24	<i>E. joensonii</i> Kausel	Leaves	5-epi-Paradisilol (8.4%) 45 , δ -Selinene (7.9%) 26 , β -Selinene (7.2%) 25	[34]
25	<i>E. klappenbachiana</i> Mattos & D.Legrand	Leaves	Globulol (8.7%) 42 , Viridiflorene (6.9%) 27 , Spathulenol (5.9%) 40	[45]
26	<i>E. langsdorffii</i> O.Berg	Leaves	Epi-Longipinanol (13.6%) 37 , γ -Eudesmol (12.3%) 58 , Limonene (11.8%) 5	[46]
		Fruits	10-epi-Eudesmol (35.7%) 47 , 1,10-di-epi-Cubenol (15.6%) 46 , Caryophyllene oxide (7.5%) 41	
27	<i>E. melanadenia</i> Krub & Urb.	Leaves	1,8-Cineole (45.3%) 6 , α -Terpineol (10.6%) 10 , p-Cymene (8.2%) 4	[47]
28	<i>E. monteverdensis</i> Barrie	Leaves	α -Pinene (92.0%) 1 , Linalool (30.4%) 8 , trans-2-Hexenal (22.5%) 9	[32, 48]
		Fruits	α -Pinene (55.1%) 1 , Linalool (22.7%) 8 , Limonene (7.7%) 5	
29	<i>E. moraviana</i> O.Berg.	Leaves	β -Caryophyllene (14.5%) 17 , β -Elemene (11.8%) 16 , α -Copaene (7.9%) 15	[45]
30	<i>E. multicostata</i> D.Legrand	Leaves	α -Pinene (16.1%) 1 , Spathulenol (10.7%) 40 , Globulol (8.7%) 42	[31]
31	<i>E. neonitida</i> Sobral	Leaves	Bicyclogermacrene (24.3%) 29 , Germacrene D (18.7%) 24 , β -Caryophyllene (12.5%) 17	[49]
32	<i>E. octopleura</i> Krug & Urb.	Leaves	α -Pinene (43.0%) 1 , Limonene (23.6%) 5 , (E)- β -Ocimene (5.1%) 7	[50]
33	<i>E. patrisii</i> Vahl	Leaves	β -Bisabolene (16.52%) 30 , (E)-Muurola-3,5-diene (13.28%) 21 , β -Caryophyllene (11.07%) 17	[37]
34	<i>E. piauihiensis</i> O.Berg	Leaves	γ -Elemene (17.48%) 19 , β -Caryophyllene (16.46%) 17 , Bicyclogermacrene (8.11%) 29	[51]
35	<i>E. pitanga</i> (O.Berg) Nied.	Leaves	Germacrene D (29.3%) 24 , Bicyclogermacrene (22.4%) 29 , (E)- β -Ocimene (10.5%) 7	[31]
36	<i>E. platysema</i> O.Berg	Leaves	β -Selinene (17.9%) 25 , Aromadrene (12.6%) 20 , 7-epi- α -Selinene (10.4%) 33	[52]
37	<i>E. pluriflora</i> DC.	Leaves	(E)-nerolidol (24.6%) 36 , α -Pinene (24.0%) 1 , 1,8-Cineole (12.7%) 6	[52]
38	<i>E. protenta</i> McVaugh	Leaves	Selin-11-en-4 α -ol (18.3%) 54 , β -Elemene (16.9%) 16 , Germacrene D (15.6%) 24	[53]

continued

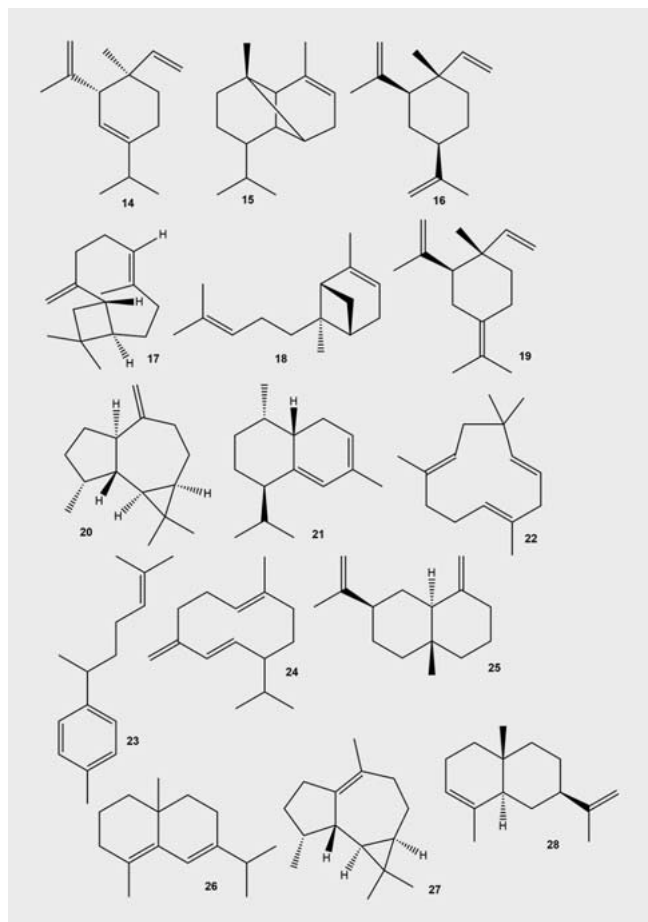
► **Table 2** Continued

N _o	Species	Part of plant	Major components	References
39	<i>E. puniceifolia</i> (Kunth) DC.	Leaves	Linalool (61.2%) 8 , β -Caryophyllene (22.7%) 17 , α -Cadinol (10.6%) 35	[54, 55]
40	<i>E. pyriformis</i> Cambess.	Leaves	β -Pinene (25.7%) 2 , Limonene (22.0%) 5 , 1,8-Cineole (14.7%) 6	[56]
41	<i>E. ramboi</i> D.Legrand	Leaves	β -Elemene (10.6%) 16 , Bicyclogermacrene (9.7%) 29 , β -Caryophyllene (8.2%) 17	[52]
42	<i>E. repanda</i> O.Berg	Leaves	β -Caryophyllene (16.3%) 17 , α -Humulene (10.2%) 22 , Bicyclogermacrene (9.4%) 29	[45]
43	<i>E. rhombea</i> (O.Berg) Krug & Urb.	Leaves	Cubenol (12.6%) 52 , α -Cadinol (12.5%) 35 , α -Pinene (12.1%) 1	[57]
44	<i>E. riedeliana</i> O.Berg	Leaves	Valerianol (28.1%) 53 , 10-epi-Eudesmol (12.6%) 47 , β -Caryophyllene (10.9%) 17	[58]
45	<i>E. rocana</i> Britton & P.Wilson	Leaves	Caryophyllene oxide (57.7%) 41 , 14-hydroxy-9-epi- β -Caryophyllene (10.3%) 55 , Verbenone (10.2%) 11	[59]
46	<i>Eugenia</i> sp.	Leaves	β -Caryophyllene (49.0%) 17 , 1,8-Cineole (26.0%) 6 , Zingiberene (24.7%) 34	[10, 32]
47	<i>E. speciosa</i> Cambess.	Leaves	α -Pinene (47.3%) 1 , Limonene (23.0%) 5 , Bicyclogermacrene (11.1%) 29	[31]
48	<i>E. stigmatica</i> DC.	Leaves	Physeteric acid (90.5%) 62 , δ -Tetradecalactone (2.2%) 60 , γ -Tetradecalactone (1.3%) 61	[43]
49	<i>E. stitipata</i> McVaught	Leaves	Germacrene D (38.3%) 24 , β -Caryophyllene (22.7%) 17 , Caryophyllene oxide (15.4%) 41	[60, 61]
50	<i>E. sulcata</i> Spring ex Mart	Leaves	α -Pinene (34.2%) 1 , β -Caryophyllene (24.6%) 17 , 1,8-Cineole (19.0%) 6	[21, 31, 55]
51	<i>E. supraaxilaris</i> Spreng.	Leaves	Limonene (21.8%) 5 , β -Pinene (17.4%) 2 , α -Humulene (8.7%) 22	[1]
		Fruits	Eugenol (35.5%) 12 , <i>Methyl</i> eugenol (32.8%) 13 , Myrcene (12.8%) 3	
52	<i>E. umbelliflora</i> O.Berg	Leaves	α -Pinene (24.7%) 1 , Viridiflorol (17.7%) 43 , β -Pinene (13.2%) 2	[52, 62]
53	<i>E. uniflora</i> L.	Leaves	Curzerene (47.3%) 38 , Selina1,3,7(11) trien-8-one (43%) 50 , Selina-1,3,7(11)-trien-8-one epoxide (29.0%) 57	[13, 63]
		Fruits	Selina1,3,7(11) trien-8-one (48.2%) 50 , Curzerene (42.6%) 38 , Germacrone (17.3%) 56	[27, 64]
54	<i>E. uruguayensis</i> Cambess.	Leaves	α -Pinene (23.5%) 1 , β -Pinene (11.8%) 2 , β -Caryophyllene (9.5%) 17	[52]
55	<i>E. xiririicana</i> Mattos	Leaves	Spathulenol (15.4%) 40 , β -Pinene (14.1%) 2 , Globulol (8.6%) 42	[31]
56	<i>E. zuchowskiae</i> Barrie	Leaves	α -Pinene (28.3%) 1 , β -Caryophyllene (13.2%) 17 , α -Humulene (13.1%) 22	[18, 32]

Arabic numeral in bold corresponds to the chemical structures shown in ► **Figs. 1–6**



► **Fig. 1** Chemical structures of monoterpenes α -pinene (**1**), β -pinene (**2**), myrcene (**3**), cymene (**4**), limonene (**5**), 1,8-cineole (**6**), (*E*)- β -ocimene (**7**), linalool (**8**), trans-2-hexenal (**9**), α -terpineol (**10**), verbenone (**11**), eugenol (**12**), and *Methyl* eugenol (**13**) isolated from *Eugenia* species.



► **Fig. 2** Structures of sesquiterpene hydrocarbons δ -elemene (14), α -copaene (15), β -elemene (16), β -caryophyllene (17), trans- α -bergamotene (18), γ -elemene (19), aromandrene (20), (E)-muuro-la-3,5-diene (21), α -humulene (22), α -curcumene (23), germacrene d (24), β -selinene (25), δ -selinene (26), viridiflorene (27), and α -selinene (28) isolated from *Eugenia* species.

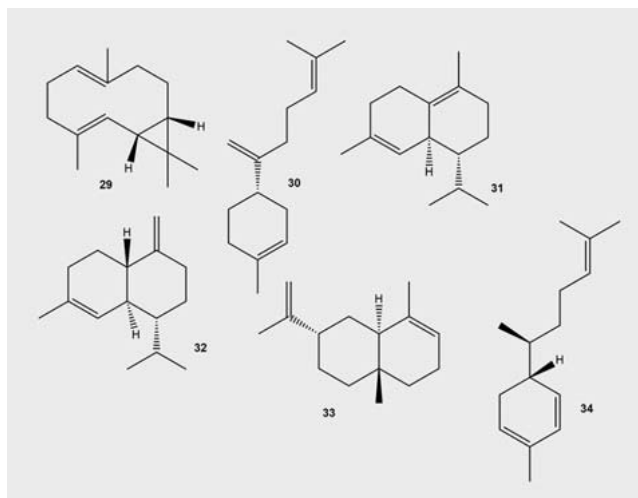
in calcium, phosphorous, provitamin A, vitamin C, carotenoids, and phenolic compounds (anthocyanins) [11]. In addition, these compounds have therapeutic properties that are widely used in folk medicine, such as diuretic, antirheumatic, antipyretic, anti-diarrheal, and antidiabetic properties [12, 13]. The essential oils are used in the Brazilian cosmetic industry, attributable to their astringent properties and pleasant smell [14].

Traditional uses

In traditional medicine, most of the plants of the genus *Eugenia* have been used to treat a wide variety of ailments such as infectious diseases, intestinal infections, and gastrointestinal disorders, as well as in the treatment of wounds or as repellents or insecticides against domestic and agricultural pests [15, 16]. The traditional uses of *Eugenia* species are described in ► **Table 1**.

Phytochemical constituents of *Eugenia* genus

An investigation of the chemical constituents of *Eugenia* species resulted in the isolation and identification of sesquiterpenes,



► **Fig. 3** Structures of sesquiterpene hydrocarbons bicyclogermacrene (29), β -bisabolene (30), γ -cadinene (31), β -cadinene (32), 7-epi- α -selinene (33), and zingiberene (34) isolated from *Eugenia* species.

monoterpenes, aliphatic compounds, triterpenes, flavonoids, tannins, and cyanidins.

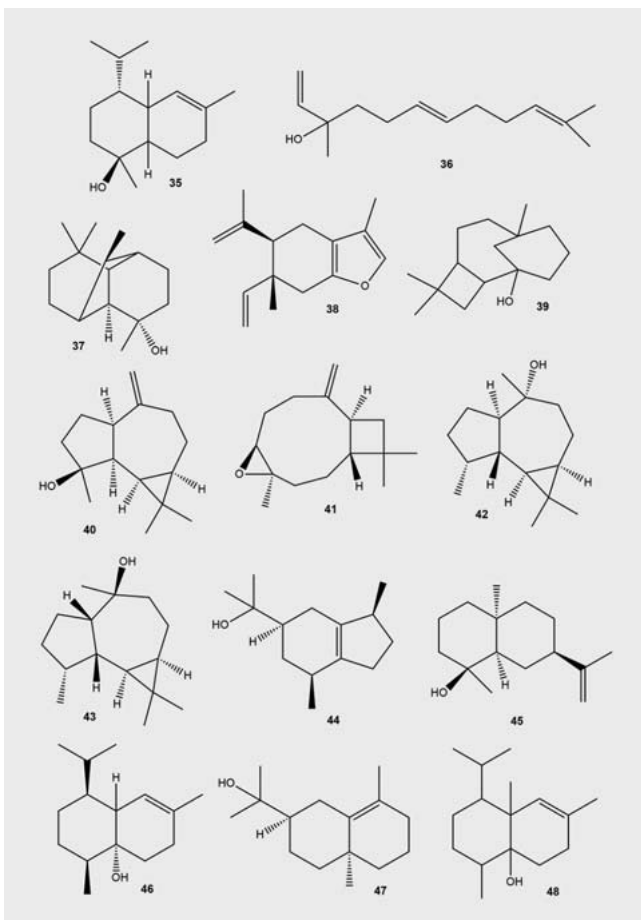
Essential oils

To obtain the essential oils, fresh samples of *Eugenia* species are collected and then identified, and an exsiccated sample is deposited in an herbarium. Most reports focus on the composition of essential oils from the plant leaves, however, in some studies, the stem, fruit, and flowers were analyzed. The most commonly used extraction processes were hydrodistillation and supercritical fluid extraction. The compounds were characterized using mass spectrometry, retention indexes, and retention times. We compared the results of each study to the current literature and spectra from databases.

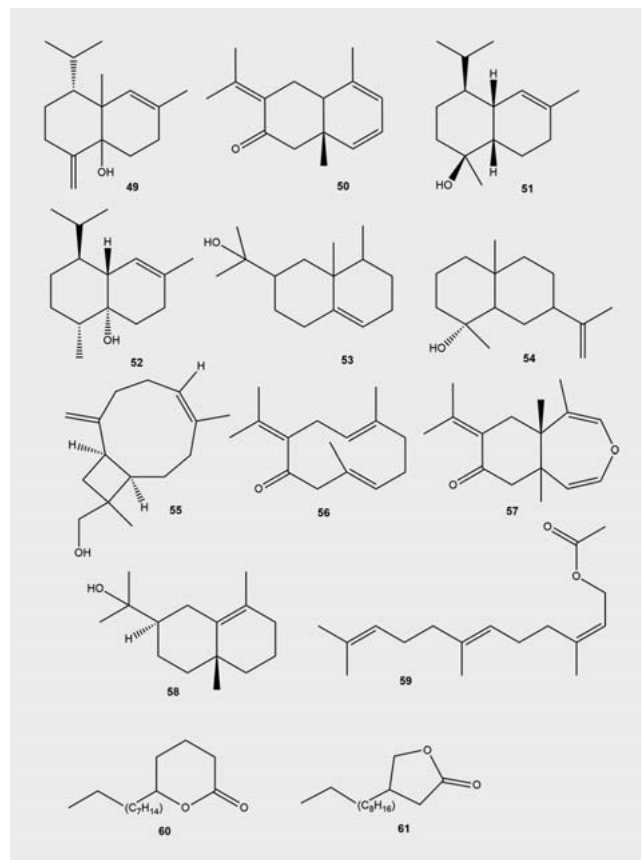
The essential oils from 56 species of *Eugenia* were analyzed, and approximately 500 compounds were identified. Sesquiterpenes (hydrocarbons and oxygen derivatives) were found and classified as the main class of volatile constituents, together with monoterpenes in smaller amounts. Some species produce small amounts of aromatic and aliphatic compounds, with concentrations below 1%. However, 90.0% of the compounds identified in *Eugenia stigmatisata* DC. were aliphatic compounds. Further, the aliphatic compounds from *Eugenia burkatiana* D.Legrand (7.9%), *Eugenia catharinensis* D.Legrand (10.5%), and *Eugenia joenonii* Kausel (14.6%) differed from the other species analyzed. The amount of each component is given as a percentage of the total oil and, in general, 80–90% of the oil was identified. The essential oils from *Eugenia* species are characterized by chemical diversity (► **Table 2**), and their molecules are shown in ► **Figs. 1–6**.

Triterpenes

The reported triterpenes were isolated from the stem and leaves of five species of *Eugenia* and are described in ► **Table 3**, and their structures are shown in ► **Fig. 7**. The triterpenic acids present in



► **Fig. 4** Structures of oxygenated sesquiterpene α -cadinol (35), (E)-nerolidol (36), epi-longipinanol (37), Curzerene (38), Caryophyllene alcohol (39), Spathulenol (40), Caryophyllene oxide (41), Globulol (42), Viridiflorol (43), Guaiol (44), 5-epi-paradisilol (45), 1,10-di-epi-cubenol (46), 10-epi-Eudesmol (47), and 1-epi-cubenol (48) isolated from *Eugenia* species.

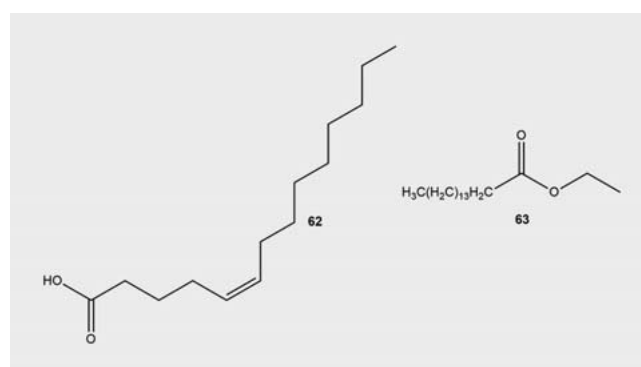


► **Fig. 5** Structures of oxygenated sesquiterpene muurola-4,10(14)-dien-1 β -ol (49), selina-1,3,7(11) trien-8-one (50), t-muurolol (51), cubenol (52), valerianol (53), selin-11-en-4 α -ol (54), 14-hydroxy-9-epi- β -caryophyllene (55), germacrone (56), selina-1,3,7(11)-trien-8-one epoxide (57), γ -eudesmol (58), farnesyl acetate (59), tetradecalactone (60), and γ -tetradecalactone (61) isolated from *Eugenia* species.

many botanical families have also been isolated from species in the *Eugenia* genus, including betulinic acid, which has several biological properties, including cytotoxic and anticancer potential [65]. Other compounds, such as α , β -amirins, have been identified in *Eugenia* species. The structural characteristics of the compounds were determined via ^1H and ^{13}C nuclear magnetic resonance spectroscopy and are compared to experimental data described in the literature.

Polyphenols and cyanidins

Several species of *Eugenia* are used in traditional medicine as antibacterial and anti-inflammatory agents, attributable to high concentrations of polyphenolic compounds, hydrolysable tannins, and flavonoids. Natural phytoalexins (also called stilbenes) having several important biological activities, including anticancer properties, were isolated from *E. rigida*. The first stilbene reactant isolated from the genus *Eugenia* was (Z)-3,4,3',5'-tetramethoxystilbene [5]. Further, euglobals were found in *E. umbelliflora*. Euglobals are substances that occur exclusively in the *Eucalyptus* genus



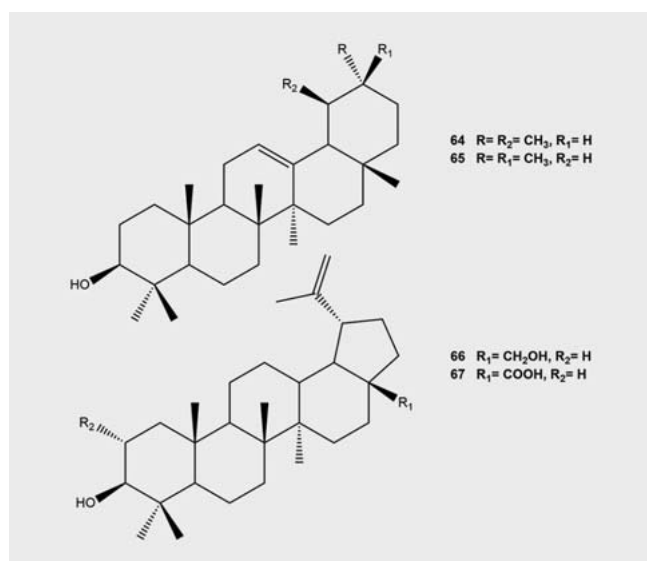
► **Fig. 6** Structures of aliphatic compounds physeteric acid (62) and ethyl palmitate (63) isolated from *Eugenia* species.

of the family Myrtaceae and have known biological activities, including chemoprotective, antileishmanial, and antimalarial properties [67]. These compounds are described in ► **Table 3**, and their chemical structures are shown in ► **Figs. 8–10**.

► **Table 3** Isolated compounds from *Eugenia* species in the studies selected through this systematic review.

Species	Part of plant	Components	References
<i>E. beaurepaireana</i> (Kiaersk.) D.Legrand	Leaves	α -Amirin 64 β -Amirin 65	[36]
<i>E. brasiliensis</i> Lam.	Leaves	α -Amirin 64 β -Amirin 65 Betulin or 3 β ,28-dihydroxy-lup-20(29)-ene 66 Quercetin or 3,5,7,3',4'-Pentahydroxyflavone 70 Catechin or (+)-(2R,3S)-5,7,3',4'-Tetrahydroxyflavan-3-ol 68 Gallocatechin or (+)-(2R,3S)-5,7,3',4',5'-Pentahydroxyflavan-3-ol 69	[4]
<i>E. dysenterica</i> DC.	Leaves	Procyanidin-B1 71 Catechin 68 Dimeric procyanidin gallate 72	[66]
<i>E. florida</i> DC.	Leaves	Betulinic acid 64	[65]
<i>E. rigida</i> DC.	Leaves	(Z)-3,4,3',5'-Tetramethoxystilbene 73 (E)-3,4,3',5'-Tetramethoxystilbene 74 (Z)-3,5,4'-Trimethoxystilbene 75 (E)-3,5,4'-Trimethoxystilbene 76	[5]
<i>E. umbelliflora</i> O.Berg.	Leaves	Taxaferol Mixture of α - and β -Amirin 64 and 65 Mixture of Betulin and Betulinic acid 66 and 67 Betulinic acid 67	[22]
	Fruits	Trimethoxy ellagic acid 77 Eugenial A similar to Euglobal A 78 Eugenial B similar to Euglobal B 79 Delphinidin 3-O- β -glucopyranoside 80 Cyanidin 3-O- β -glucopyranoside 81 Petunidin 3-glucoside 82 Pelargonidin 3-glucoside 83 Peonidin 3-glucoside 84 Malvidin 3-glucoside 85	[22, 67, 68]

Arabic numeral in bold corresponds to the chemical structures shown in ► **Figs. 7–10**



► **Fig. 7** Structures of triterpenes isolates α -amirin (**64**), β -amirin (**65**), betulin (**66**), and betulinic acid (**67**) isolated from *Eugenia* species.

Biological activities

Antimicrobial activity

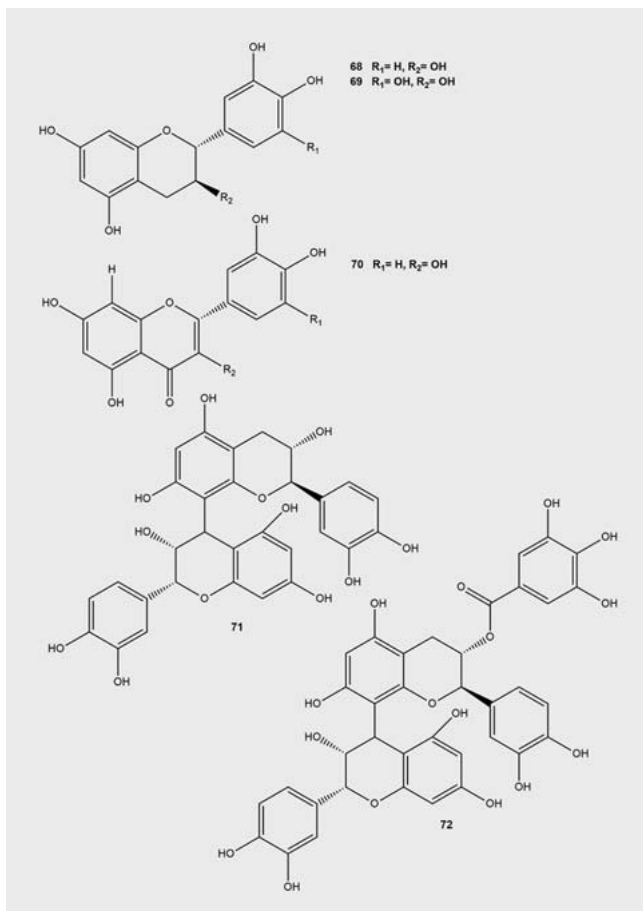
Some *Eugenia* species were investigated for their antibacterial and antifungal activities. Studies of the antimicrobial activity of *Eugenia* species are reported in ► **Table 4**.

Preparations of essential oils, leaf extracts, stems, and seeds of *Eugenia* species have been widely researched for their activities against gram-positive and gram-negative bacteria, as well as some species of yeast-like fungi, and compared to the activity of standard drugs. There are few studies on the antimicrobial activity of the isolated compounds.

Different antimicrobial activity assays with different antibiotic and antifungal controls were used, including agar diffusion, disc diffusion, bioautography, macrodilution, and microdilution.

Eugenia species were tested against ATCC and clinical isolates of gram-positive and gram-negative bacteria, as well as yeast-like fungi.

When the results were analyzed, the minimum inhibitory concentration (MIC) values were classified as having good inhibitory potential (less than 100 $\mu\text{g/mL}$), moderate inhibitory potential (between 100 and 500 $\mu\text{g/mL}$), weak inhibitory potential (between 500 and 1000 $\mu\text{g/mL}$), or the absence of inhibitory potential (above 1000 $\mu\text{g/mL}$) [20].



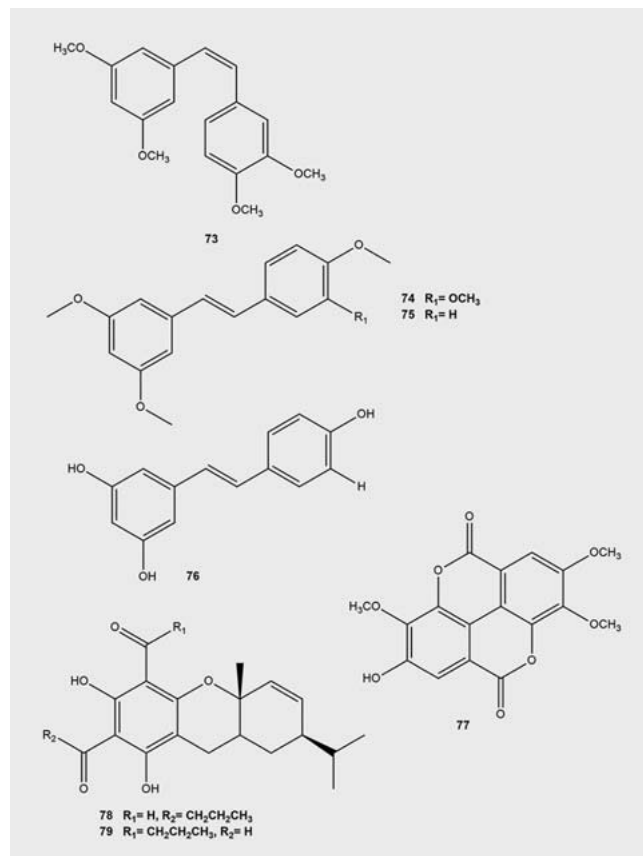
► **Fig. 8** Structures of polyphenolic compounds isolates catechin (68), gallocatechin (69), quercetin (70), procyanidin-B1 (71), and dimeric procyanidin gallate (72) isolated from *Eugenia* species.

According to this established profile, the *Eugenia calycina*, *E. pyriformis*, *E. umbelliflora*, *E. uniflora*, and *Eugenia uruguayensis* species demonstrated good inhibitory potential against gram-positive and gram-negative bacteria, as well as yeast-like fungi. Samples of ethanolic, methanolic, and ketonic extracts and essential oil evaluated against strains of several microorganisms showed MIC values ranging from 7 to 100 µg/mL. The antimicrobial activity observed has been attributed to the presence of different bioactive compounds that have an impact on the growth and metabolism of microorganisms. Medicinal plants are known to produce antimicrobial substances belonging to many chemical classes, such as alkaloids, lignins, phenolic compounds, and terpenoids [20].

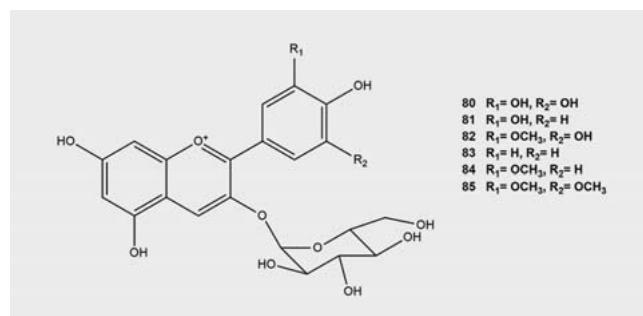
Moderate antimicrobial potential was observed against strains of gram-positive and gram-negative bacteria, as well as yeast-like fungi, with MIC values ranging from 156.2 to 500 µg/mL in several *Eugenia* species.

Antimicrobial activity in the presence of standard antibiotics

The compounds present in plants are capable of retarding or inhibiting the growth of bacteria, yeasts, and yeast-like fungi when used alone. However, there is also the possibility of using them in combination with conventional antimicrobials to improve their



► **Fig. 9** Structures of polyphenolic compounds isolates (Z)-3,4,3',5'-tetramethoxystilbene (73), (E)-3,4,3',5'-tetramethoxystilbene (74), (Z)-3,5,4'-trimethoxystilbene (75), (E)-3,5,4'-trimethoxystilbene (76), trimethoxy ellagic acid (77), eugenial A (78), and eugenial B (79) isolated from *Eugenia* species.



► **Fig. 10** Structures of cyanidins isolates delphinidin 3-O-β-glucopyranoside (80), cyanidin 3-O-β-glucopyranoside (81), petunidin 3-glucoside (82), pelargonidin 3-glucoside (83), peonidin 3-glucoside (84), and malvidin 3-glucoside (85) isolated from *Eugenia* species.

effectiveness [20]. The MIC of an *E. uniflora* ethanolic extract was reduced in the presence of the antibiotics amikacin, gentamicin, kanamycin, neomycin, and tobramycin at concentrations of 16 and 32 µg/mL when tested against clinical isolates of *Staphylococcus aureus*, demonstrating a synergistic effect [23]. However, the same samples evaluated against clinical isolates of *Escherichia coli*

► **Table 4** Antimicrobial activity of *Eugenia* species selected through this systematic review.

<i>Eugenia</i> species	Extraction/isolation procedure	Antimicrobial activity assay/control	Microorganisms and results	References
<i>E. axillaris</i> (Sw.) Willd.	Essential oil of leaves/hydrodistillation	Microdilution method/gentamicin sulfate and amphotericin B	<i>Bacillus cereus</i> ATCC 14579 = 625 µg/mL <i>Staphylococcus aureus</i> ATCC 29213 = 625 µg/mL <i>Pseudomonas aeruginosa</i> ATCC 27853 = 625 µg/mL <i>Escherichia coli</i> ATCC 25922 = 625 µg/mL <i>Candida albicans</i> ATCC 10231 = 625 µg/mL <i>Aspergillus niger</i> ATCC 16401 = 625 µg/mL	[17]
<i>E. bacopari</i> D. Legrand	Essential oil of leaves/hydrodistillation	Agar diffusion method/no date	<i>Staphylococcus aureus</i> ATCC 6538 p = 7–11 mm	[69]
<i>E. beaure-paireana</i> (Kiaersk.) D. Legrand	Essential oil of leaves/hydrodistillation	Microdilution method/gentamicin	<i>Staphylococcus aureus</i> ATCC 25923 = 1110 µg/mL <i>Escherichia coli</i> ATCC 25922 = 556.6 µg/mL <i>Pseudomonas aeruginosa</i> ATCC 27853 = 278.3 µg/mL	[62]
<i>E. brasiliensis</i> Lam.	Essential oil of leaves/hydrodistillation	Microdilution method/no date	<i>Staphylococcus saprophyticus</i> = 500–1000 µg/mL <i>Staphylococcus aureus</i> = 1000 µg/mL <i>Escherichia coli</i> = 1000 µg/mL <i>Pseudomonas aeruginosa</i> = 500–1000 µg/mL	[19]
	Essential oil of leaves/hydrodistillation	Microdilution method/gentamicin	<i>Staphylococcus aureus</i> ATCC 25923 = 156.2 µg/mL <i>Escherichia coli</i> ATCC 25922 = 624.9 µg/mL <i>Pseudomonas aeruginosa</i> ATCC 27853 = 624.9 µg/mL	[62]
	ethanol extract/maceration Fractions: hexane, dichloromethane, and ethyl acetate	Microdilution method/gentamicin	<i>Staphylococcus aureus</i> ATCC 25923 = 1560–6250 µg/mL <i>Escherichia coli</i> ATCC 25922 = 390–6250 µg/mL <i>Pseudomonas aeruginosa</i> ATCC 27853 = 780–6250 µg/mL	[4]
<i>E. calycina</i> Cambess.	Ethanol extract of bark and leaves/maceration Fractions were prepared from the ethanolic extracts (hexane, dichloromethane, and ethyl-acetate)	Microdilution method/vancomycin, gentamicin, and itraconazole	<i>Bacillus cereus</i> ATCC 14579 = 250–2000 µg/mL <i>Bacillus subtilis</i> ATCC 6633 = 1000–2000 µg/mL <i>Micrococcus roseus</i> ATCC 1740 = 1000–2000 µg/mL <i>Micrococcus luteus</i> ATCC 9341 = 1000–2000 µg/mL <i>Staphylococcus epidermidis</i> ATCC 12229 = 1000–2000 µg/mL <i>Staphylococcus aureus</i> ATCC 6538 = 500–2000 µg/mL <i>Staphylococcus aureus</i> ATCC 25923 = 1000–2000 µg/mL <i>Enterobacter aerogenes</i> ATCC 13048 = 1000–2000 µg/mL <i>Escherichia coli</i> ATCC 11229 = 1000–2000 µg/mL <i>Pseudomonas aeruginosa</i> ATCC 9027 = 2000 µg/mL <i>Pseudomonas aeruginosa</i> (clinical isolate) = 2000 µg/mL <i>Salmonella</i> spp. ATCC 19430 = 1000–2000 µg/mL <i>Serratia marcescens</i> ATCC 14756 = 1000–2000 µg/mL <i>Candida parapsilosis</i> ATCC 22019 = 250–2000 µg/mL <i>Enterobacter cloacae</i> (clinical isolate) = 1000–2000 µg/mL <i>Candida parapsilosis</i> (clinical isolate) = 250–2000 µg/mL <i>Candida albicans</i> (clinical isolate) = 500–2000 µg/mL <i>Cryptococcus</i> sp. D (clinical isolate) = 15.62–2000 µg/mL <i>Cryptococcus gatti</i> (clinical isolate) = 31.2–2000 µg/mL <i>Cryptococcus neoformans</i> (clinical isolate) = 31.2–2000 µg/mL	[6]
<i>E. chlorophylla</i> O.Berg	Essential oil of leaves, steam, and flowers/hydrodistillation	Microdilution method/bacitracina and ketoconazole	<i>Streptococcus mutans</i> ATCC 15175 = 50–500 µg/mL <i>Streptococcus sobrinus</i> (clinical isolate) = 50–500 µg/mL <i>Staphylococcus aureus</i> ATCC 6538 = 500 µg/mL <i>Kocuria ryzophila</i> ATCC 9341 = 100–500 µg/mL <i>Staphylococcus aureus</i> ATCC 6538 = 500 µg/mL <i>Candida albicans</i> ATCC 1023 = 500 µg/mL	[40]
<i>E. dysenterica</i> DC.	Essential oil of leaves/hydrodistillation	Microdilution method/fluconazole, amphotericin B and itraconazole	<i>Cryptococcus neoformans</i> = < 250 µg/mL <i>Cryptococcus gatii</i> (clinical isolate) = < 250 µg/mL	[70]
<i>E. mansoni</i> O.Berg	Ethanol, aceton, and chloroform extract of leaves/maceration	Agar diffusion method Microdilution method/nystatin and gentamicin	<i>Pseudomonas aeruginosa</i> ATCC 27853 = resistant <i>Staphylococcus aureus</i> ATCC 6538 p = sensitive (+) <i>Listeria innocua</i> (clinical isolate) = sensitive (+) <i>Aspergillus niger</i> ATCC 2601 = sensitive (+) <i>Mycobacterium tuberculosis</i> H37Rv/ATCC 27294 = sensitive (+)/200 µg/mL	[71]

continued

► **Table 4** *Continued*

Eugenia species	Extraction/isolation procedure	Antimicrobial activity assay/control	Microrganisms and results	References
<i>E. montevedensis</i> Barrie	Essential oil of leaves/hydrodistillation	Microdilution method/gentamycin	<i>Bacillus cereus</i> ATCC 14579 = 1250 µg/mL <i>Staphylococcus aureus</i> ATCC 29213 = 1250 µg/mL <i>Escherichia coli</i> ATCC 25922 = 1250 µg/mL	[48]
<i>E. pyriformis</i> Cambess.	Ethanol extracts of leaves, flowers, roots, stems, and fruits/maceration	Microdilution method Agar diffusion method/ chlorhexidine and rifamycin	<i>Candida albicans</i> ATCC 10231 = 12.5–50 µg/mL <i>Saccharomyces cerevisiae</i> ATCC 2601 = 25–50 µg/mL <i>Bacillus subtilis</i> ATCC 6633 = 25–50 µg/mL <i>Bacillus cereus</i> ATCC 11778 = 12.5–50 µg/mL <i>Micrococcus luteus</i> ATCC 9341 = 25–50 µg/mL <i>Enterococcus faecalis</i> ATCC 51299 = 50 µg/mL <i>Staphylococcus aureus</i> ATCC 6538 = 12.5–25 µg/mL <i>Escherichia coli</i> ATCC 25922 = 12.5 µg/mL <i>Pseudomonas aeruginosa</i> ATCC 27853 = 50 µg/mL <i>Proteus mirabilis</i> ATCC 25922 = 50 µg/mL <i>Salmonella typhimurium</i> ATCC 14028 = 2–50 µg/mL <i>Enterobacter cloacae</i> (clinical isolate) = 12.5–50 µg/mL <i>Serratia marcescens</i> (clinical isolate) = 25–50 µg/mL	[30]
	Ethanol extract fractions: hexane, chloroform, and ethyl acetate, hydroalcoholic. Acetonic extract/Soxhlet	Microdilution method/ vancomycin and fluconazole	<i>Enterococcus faecalis</i> ATCC 29212 = 62.5–1000 µg/mL <i>Staphylococcus aureus</i> ATCC 25923 = 62.5–250 µg/mL <i>Escherichia coli</i> ATCC 25922 = 250–1000 µg/mL <i>Klebsiella pneumoniae</i> ATCC 700603 = 250–1000 µg/mL <i>Pseudomonas aeruginosa</i> ATCC 27853 = 250–1000 µg/mL <i>Candida albicans</i> ATCC 40175 = 7.81–62.5 µg/mL <i>Candida krusei</i> ATCC 40147 = 7.81–31.25 µg/mL <i>Candida parapsilosis</i> ATCC 40038 = 7.81–62.5 µg/mL	[20]
<i>E. pluriflora</i> DC.	Essential oil leaves of leaves/hydrodistillation	Agar diffusion method/ no date.	<i>Staphylococcus epidermidis</i> ATCC 12228 = 7–11 mm <i>Staphylococcus aureus</i> ATCC 6538 p = 7–11 mm <i>Candida albicans</i> ATCC 10231 = 7–11 mm <i>Micrococcus luteus</i> ATCC 9341 = 11–16 mm <i>Saccharomyces cerevisiae</i> ATCC 160 = 11–16 mm	[69]
<i>E. repanda</i> O.Berg	Ethanol extract/maceration	Agar diffusion method Microdilution method/ nystatin and gentamicin	<i>Pseudomonas aeruginosa</i> ATCC 27853 = resistant <i>Staphylococcus aureus</i> ATCC 6538p = resistant <i>Listeria innocua</i> (clinical isolate) = sensitive (+) <i>Aspergillus niger</i> ATCC 2601 = sensitive (+) <i>Mycobacterium tuberculosis</i> H37Rv ATCC 27294 = sensitive (+)/200 µg/mL	[71]
<i>E. stipitata</i> McVaugh	Essential oil of leaves/hydrodistillation	Agar diffusion method/ tetracycline	<i>Listeria monocytogenes</i> ATCC 7973 = 12 mm <i>Staphylococcus aureus</i> ATCC 25923 = 14 mm <i>Pseudomonas aeruginosa</i> ATCC 27853 = 11 mm	[60]
<i>E. umbelliflora</i> O.Berg	Essential oil of leaves/hydrodistillation	Microdilution method/ gentamycin	<i>Staphylococcus aureus</i> ATCC 25923 = 119.2 µg/mL <i>Escherichia coli</i> ATCC 25922 = 477 µg/mL <i>Pseudomonas aeruginosa</i> ATCC 27853 = 477 µg/mL	[62]
	Methanol extracts of leaves and fruits/maceration Fractions: dchloromethane and ethyl acetate	Microdilution method/ ketoconazole	<i>Aspergillus flavus</i> ATCC 9170 = > 1000 µg/mL <i>Aspergillus fumigatus</i> ATCC 26934 = > 1000 µg/mL <i>Aspergillus niger</i> ATCC 9092 = > 1000 µg/mL <i>Rhizopus sp</i> (clinical isolate) = > 1000 µg/mL <i>Microsporium canis</i> (clinical isolate) = 300 > 1000 µg/mL <i>Microsporium gypseum</i> (clinical isolate) = 300– > 1000 µg/mL <i>Trichophyton mentagrophytes</i> ATCC 9972 = 600– > 1000 µg/mL <i>Trichophyton rubrum</i> (clinical isolate) = 400– > 1000 µg/mL <i>Epidermophyton floccosum</i> (clinical isolate) = 300– > 1000 µg/mL <i>Cryptococcus neoformans</i> ATCC 32264 = > 1000 µg/mL <i>Candida albicans</i> ATCC 1023 = > 1000 µg/mL <i>Candida tropicalis</i> ATCC 7349 = > 1000 µg/mL	[72]
	Methanol extracts of leaves and fruits/maceration Fractions: dchloromethane and ethyl acetate	Microdilution method/ vancomycin	<i>Bacillus cereus</i> ATCC 14579 = 7–300 µg/mL <i>Enterobacter cloacae</i> ATCC 35030 = 900 µg/mL <i>Escherichia coli</i> ATCC 11775 = 900 µg/mL <i>Pseudomonas aeruginosa</i> ATCC 27853 = 900 µg/mL <i>Salmonella typhimurium</i> ATCC 14028 = 900 µg/mL <i>Staphylococcus aureus</i> ATCC 6538P = 6–100 µg/mL <i>Staphylococcus saprophyticus</i> ATCC 35552 = 10–200 µg/mL <i>Streptococcus agalactiae</i> ATCC 13813 = 2–400 µg/mL	[73]

continued

► Table 4 Continued

Eugenia species	Extraction/isolation procedure	Antimicrobial activity assay/control	Microrganisms and results	References
<i>E. uniflora</i> L.	<i>n</i> -Hexane fraction of leaves/maceration	Disc diffusion/trimethoprim, sulfamethoxazole, and para-chlorocresol	<i>Escherichia coli</i> = 5.000 µg/mL <i>Aspergillus flavus</i> = 5.000 µg/mL	[24]
	Essential oil leaves of leaves/hydrodistillation	Disc diffusion/ketoconazole	<i>Epidermophyton floccosum</i> = 12–18 mm <i>Trichophyton mentagrophytes</i> = 16–18 mm <i>Trichophyton rubrum</i> = 15–20 mm	[74]
	Essential oil of leaves/hydrodistillation	Agar diffusion method Microdilution method/ sulphadiazine and cephalothine	<i>Candida albicans</i> (clinical isolate) = 208.3 µg/mL <i>Candida parapsilosis</i> (clinical isolate) = 208.3 µg/mL <i>Candida guilhermondii</i> (clinical isolate) = 109.4 µg/mL <i>Candida globosa</i> (clinical isolate) = 187.5 µg/mL <i>Candida lipolytica</i> (clinical isolate) = 93.7 µg/mL <i>Candida laurentii</i> (clinical isolate) = 208.3 µg/mL <i>Trichosporon asahii</i> (clinical isolate) = 312.5 µg/mL	[75]
	Essential oil leaves/hydrodistillation	Disc diffusion Microdilution method/ fluconazole and chloramfenicol	<i>Candida dubliniensis</i> ATCC 7978 = 230 µg/mL <i>Candida tropicalis</i> ATCC 13803 = 900 µg/mL <i>Candida albicans</i> ATCC 18804 = 1.800 µg/mL <i>Candida glabrata</i> ATCC 90030 = 930 µg/mL <i>Candida parapsilosis</i> (clinical isolate) = 3.750 µg/mL <i>Candida grubii</i> KN99 (serotype A) = 450 µg/mL <i>Candida gattii</i> R265 (serotype B) = 220 µg/mL <i>Cryptococcus neoformans</i> JEC21 (serotype D) = 110 µg/mL <i>Saccharomyces cerevisiae</i> BY4742 = 220 µg/mL	[76]
	Ethanol extract/maceration	Microdilution method/ amphotericin B and itraconazole	<i>Candida krusei</i> = 250 µg/mL <i>Aspergillus fumigatus</i> = > 500 µg/mL	[77]
	Essential oil leaves/hydrodistillation	Microdilution method/ no date	MIC90 Clinical Isolates: <i>Staphylococcus aureus</i> methicillin-resistant (MRSA), <i>Staphylococcus aureus</i> methicillin-sensitive (MSSA), <i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i> , <i>Salmonella typhimurium</i> , <i>Salmonella enteritidis</i> = 50.800–92.400 µg/mL	[78]
	Essential oil leaves/hydrodistillation	Macrodilution method/ no date	<i>Paracoccidioides brasiliensis</i> = 62.5–250 µg/mL	[27]
	Ethanol extracts of leaves/maceration	Microdilution method/ pennicilin G and eritromicin	<i>Micrococcus roseus</i> ATCC 1740 = 2.187 µg/mL <i>Micrococcus luteus</i> ATCC 9341 = 273 µg/mL <i>Bacillus cereus</i> ATCC 14576 = 1.094 µg/mL <i>Bacillus stearothermophilus</i> ATCC 1262 = 2.187 µg/mL <i>Bacillus subtilis</i> ATCC 6633 = 2.187 µg/mL <i>Enterobacter aerogenes</i> ATCC 13048 = 17.500 µg/mL <i>Escherichia coli</i> ATCC 8739 = 17.500 µg/mL <i>Staphylococcus aureus</i> ATCC 6538 = 2.187 µg/mL <i>Staphylococcus aureus</i> ATCC 25923 = 2.187 µg/mL <i>Staphylococcus epidermidis</i> ATCC 12228 = 273 µg/mL <i>Pseudomonas aeruginosa</i> ATCC 27853 = 8.750 µg/mL <i>Serratia marcescens</i> ATCC 14756 = 35.000 µg/mL <i>Enterobacter cloacae</i> (clinical isolate) = 17.500 µg/mL <i>Candida albicans</i> (clinical isolate) = 547 µg/mL	[28]
	Ethanol extracts of leaves/maceration Fractions: hexane, chloroform, and ethyl acetate	Agar diffusion method Microdilution method/ no date	n = 80, <i>Pseudomonas aeruginosa</i> (clinical isolate) = 1.090–17.500 µg/mL	[79]
	Ethanol extracts of leaves/maceration	Agar diffusion method Microdilution method/ ceftriaxone	<i>Staphylococcus aureus</i> ATCC 25923 = 250 µg/mL <i>Staphylococcus epidermidis</i> ATCC 14990 = 52 µg/mL <i>Pseudomonas aeruginosa</i> ATCC 27853 = 14 mm <i>Escherichia coli</i> ATCC 14942 = 11 mm	[80]
	Ethanol extracts of leaves/maceration	Microdilution method/ amphotericin B, mebendazole, nystatin and metronidazole	<i>Candida albicans</i> = > 1.024 µg/mL <i>Candida krusei</i> = > 1.024 µg/mL <i>Candida tropicalis</i> = 1.024 µg/mL	[81]

continued

► **Table 4** Continued

<i>Eugenia</i> species	Extraction/isolation procedure	Antimicrobial activity assay/control	Microrganisms and results	References
	Methanolic extracts of leaves/maceration	Microdilution method/ no date	<i>Pseudomonas aeruginosa</i> = 10 µg/mL <i>Shigella sonnei</i> = 156 µg/mL <i>Bacillus cereus</i> = 39 µg/mL	[25]
	Methanolic extracts of leaves/maceration	Agar diffusion method/ chloramphenicol and nystatin	<i>Staphylococcus aureus</i> ATCC 6538P = sensitive (+) <i>Bacillus subtilis</i> ATCC 6633 = sensitive (+) <i>Micrococcus luteus</i> ATCC9341 = sensitive (+++) <i>Staphylococcus epidermidis</i> ATCC12228 = resistant <i>Escherichia coli</i> ATCC 25922 = resistant <i>Candida albicans</i> ATCC 10231 = resistant	[82]
	Hydroalcoholic extracts of leaves/maceration process with ethanol-water (90–10%)	Microdilution method Bioautography method/ tetracycline, vancomycin, penicillin and nistatin	<i>Escherichia coli</i> ATCC 25922 = 500 µg/mL <i>Pseudomonas aeruginosa</i> ATCC 15442 = > 1000 µg/mL <i>Bacillus subtilis</i> ATCC 6623 = > 1000 µg/mL <i>Staphylococcus aureus</i> ATCC 25923 = 250 µg/mL <i>Candida albicans</i> (clinical isolate) = > 1000 µg/mL <i>Candida krusei</i> (clinical isolate) = 31.2 µg/mL <i>Candida parapsilosis</i> (clinical isolate) = 125 µg/mL <i>Candida tropicalis</i> (clinical isolate) = 31.2 µg/mL	[83]
	Hydroalcoholic extracts/percolation	Microdilution method/ ampycilin and nistatyn	<i>Staphylococcus aureus</i> ATCC 6538 = 80 µg/mL <i>Salmonella choleraesuis</i> ATCC 10708 = 100 µg/mL <i>Pseudomonas aeruginosa</i> ATCC 15442 = 400 µg/mL <i>Candida albicans</i> ATCC 10231 = 500 µg/mL <i>Aspergillus niger</i> ATCC 16404 = 900 µg/mL	[29]
<i>E. uruguayensis</i> Cambess.	Extracts/maceration with EtOH/H ₂ O 70:30, acetone and CHCl ₃	Microdilution method/ no date	<i>Staphylococcus aureus</i> ATCC 6538 p MSSA = 31.3 µg/mL <i>Staphylococcus aureus</i> ATCC 700699 MRSA = 31.3 µg/mL <i>Staphylococcus aureus</i> ATCC 43300 MRSA = 31.3 µg/mL <i>Staphylococcus aureus</i> USA 100 MRSA = 31.3 µg/mL	[84]
	Essential oil of leaves/hydrodistillation	Agar diffusion method/ no date	<i>Staphylococcus epidermidis</i> ATCC 12228 = 11–16 mm <i>Escherichia coli</i> ATCC 25922 = 11–16 mm <i>Saccharomyces cerevisiae</i> ATCC 160 = 10–16 mm	[69]

at a concentration of 128 µg/mL showed no synergistic effects [85]. An ethanolic extract from *E. uniflora* leaves evaluated against *Candida tropicalis* (ATCC 13803) alone and in combination with the antifungal metronidazole reduced the MIC of metronidazole from 128 to 32 µg/mL, a fourfold reduction [81].

The checkerboard method was used to evaluate synergistic interactions between *E. pyriformis* and vancomycin or fluconazole. A combination of the hydroalcoholic fraction from the *E. pyriformis* leaves and vancomycin exhibited synergism against *Enterococcus faecalis*, with a fractionated inhibitory concentration index (FICI) of 0.37. FICI values are interpreted as synergistic (FICI < 0.5), additive (0.5 < FICI < 4), or antagonistic (FICI > 4) [20]. In addition, combinations of fluconazole with an *E. pyriformis* crude leaf extract and acetone extract showed activity against *Candida krusei* and *Candida parapsilosis*, with FICI values between 0.24 and 0.50. Further, a synergistic interaction was observed when an ethyl acetate fraction of *E. pyriformis* leaves was combined with vancomycin or fluconazole to treat *Candida albicans*, *C. krusei*, and *C. parapsilosis* resulted in FICI values between 0.24 and 0.37 [20].

Cytotoxicity

The cytotoxic activity of *Eugenia* species is reported in ► **Table 5**. In these studies, several extraction methods were used to obtain extracts, fractions, and essential oils from leaves, fruits, and seeds of some *Eugenia* species. Effective results against growth in differ-

ent tumor cell lineages and *Artemia salina* were observed. Specimens of *A. salina* Leach (brine shrimp), a marine microcrustacean, were used as target organisms to detect bioactive compounds in plant extracts, and toxicity tests against these animals have shown a good correlation with antitumor activity [86]. Medium lethal concentrations (LC₅₀) were used to estimate the toxicity of *A. salina*, providing a general toxicity analysis, and several studies correlated this method with antiviral, antiparasitic, and antitumor activity [87–89]. The essential oil of *Eugenia zuchowskiae* Barrie was cytotoxic, with 100% death when used to treat cell lines at 100 µg/mL [18]. *E. zuchowskiae* Barrie extracts comprise α -pinene, β -caryophyllene, and α -humulene compounds. α -Pinene has exhibited cytotoxic activity in Hep G2 human hepatocellular carcinoma cells, and α -humulene has been shown to be active in several tumor cell lines [90].

Conclusions, Discussion, and Future Perspectives

Species of *Eugenia* have been investigated in recent decades, revealing a great diversity in chemical composition. Hydrocarbons and oxygenated derivatives have been identified in the essential oils of *Eugenia* species, while in extracts of the aerial parts, the compounds triterpenes, flavonoids, tannins, and cyanidins have

▶ **Table 5** Cytotoxic activity of *Eugenia* species in the studies selected through this systematic review.

Species	Extraction	Cytotoxicity assays	Cell lines	Cytotoxic activity	Reference
<i>E. axillaris</i> (Sw.) Willd	Essential oils of leaves/hydrodistillation dichloromethane extraction	<i>In vitro</i> cytotoxicity assay MTS	PC-3 (human prostatic adenocarcinoma) MDA-MB-231 (human mammary adenocarcinoma) MCF7 (human mammary adenocarcinoma) Hs 578T (human ductal carcinoma) Hep G2 (human hepatocellular carcinoma)	PC-3 = 67.47% MDA-MB-231 = 42.66% MCF7 = 30.21% Hs 578 T = 95.79% Hep G2 = 92.21% Cytotoxicity expressed as percentage kill at 250 µg/mL for Hs 578T and Hep G2; and at 100 µg/mL for PC-3, MDA-MB-231 and MCF7	[17]
<i>E. calycina</i> Cambess.	Essential oils of leaves/hydrodistillation Fractions obtained of Dichloromethane: F1, F2, F3, and F4	<i>In vitro</i> cytotoxicity assay MTT cervical cancer cell lines	Cervical cancer cell lines (HeLa ECACC 93021013)	EO CC50 = 137.4 ± 9.6 µg/mL F1 CC50 = 120.0 ± 9.4 µg/mL F2 CC50 = 117.6 ± 9.6 µg/mL F3 CC50 = 151.1 ± 8.3 µg/mL F4 CC50 = 139.2 ± 5.1 µg/mL	[7]
<i>E. cartagensis</i> O.Berg	Essential oils of leaves/hydrodistillation	<i>In vitro</i> cytotoxicity assay MTT	Colorectal carcinoma cells (HCT-15 and SW 620) Malignant melanoma cells (MCF7, M-14 and SK-Mel-28) Malignant melanoma cells (Malme-3M and UACC-257) Mammary adenocarcinoma cells (MDA-MB-231) Mammary ductal carcinoma cells (MDA-MB-435) Ovarian adenocarcinoma cells (OVCAR-5 cells)	Cytotoxic against HCT-15 and SW 620 cells at a concentration of 100 µg/mL, with 100 and 84.1% cell death, respectively. These oils were less active against MCF7 (73.5%), M-14 (45.3%), and SK-Mel-28 (41.3%) cells and were inactive against MDA-MB-468 cells, Malme-3M and UACC-257 cells, MDA-MB-231 cells, MDA-MB-435 cells, and OVCAR-5 cells.	[39]
<i>E. dysenterica</i> DC.	Ethanol extract of leaves/maceration	<i>In vitro</i> cytotoxicity in <i>Rhesus neonato</i> monkey cells	<i>Rhesus neonato</i> monkey cells (MA-104)	Disruption of the cell layer observed at a concentration of 5000 µg/mL	[16]
<i>E. montevidensis</i> Barrie	Essential oils of leaves and fruits/hydrodistillation	<i>In vitro</i> cytotoxicity assay MTT	Human MDA-MB-231 breast adenocarcinoma cells Human Hs 578T breast ductal carcinoma cells	MDA-MB-231 or Hs 578 T human tumor cells (0% killing at 100 µg/mL)	[48]
<i>E. uniflora</i> L.	Ethanol extract of leaves/maceration	Brine shrimp lethality bioassay	<i>Artemia salina</i> Leach eggs varying concentrations 1 to 1000 µg/mL	LC ₅₀ values above 250 µg/mL, with a 95% confidence interval (194.2–433.7)	[88]
	Methanol extract of leaves/maceration	Brine shrimp lethality bioassay	<i>Artemia salina</i> Leach eggs varying concentrations 10 to 1000 µg/mL	LC ₅₀ values above 250 µg/mL	[25]
	Ethanol extract of leaves/maceration	<i>In vitro</i> cytotoxicity assay	J774 macrophages	8% cytotoxic activity in J774 macrophages at a concentration of 100 µg/mL	[91]
	Ethanol extract of fruits/maceration	MTT assay Tritiated thymidine incorporation assay GRX MitoTracker Green MitoTracker Flow cytometry assays Cell	HSC line was obtained from livers of C3H/HeN mice that were infected by transcutaneous penetration of cercariae from the <i>Schistosoma mansoni</i> BH strain (GRX)	Viability cell was significantly decreased on cells treated with 50 µg/mL of extract for 72 h and on cells treated with 100 µg/mL for 48 and 72 h. Proliferation cell: The reduction of cell proliferation was dose dependent at the cell counting assay and the cells treated with 100 µg/mL of extract usually, not increased in three days of treatment. Mitochondrial content was significantly reduced in GRX cells treated with 50 and 100 µg/mL of an extract at all times studied. The cells treated with 50 and 100 µg/mL of extract for 24 h showed a 13% increase in the number of GRX cells in the G0G1 phase and a reduction in the S phase. We did not observe an increase in apoptosis in cells treated for 24 and 48 h. However, the percentage of necrotic cells increased significantly in cells treated with 50 and 100 µg/mL for 48 h.	[26]

continued

▶ Table 5 Continued

Species	Extraction	Cytotoxicity assays	Cell lineages	Cytotoxic activity	Reference
	Methanolic extracts of leaves and seeds Fraction: ethyl acetate, <i>n</i> -butanol and aqueous fraction	<i>In vitro</i> cytotoxicity assay splenocytes from BALB/c mice	Splenocytes from BALB/c mice Each sample was evaluated in six concentrations (1, 5, 10, 25, 50, and 100 g/mL) in triplicate	Ethyl acetate fraction of leaves = 50 and 100 µg/mL Ethyl acetate fraction of seeds = 25, 50, and 100 µg/mL Butanol fraction of seeds = 100 µg/mL Control saponin	[92]
	Essential oils of leaves/hydrodistillation	<i>In vitro</i> cytotoxicity assay MTT	Vero cell line	IC ₅₀ = 117.4 ± 11.9 µg/mL	[77]
	Essential oils of leaves/hydrodistillation	<i>In vitro</i> cytotoxicity assays (3T3 cells) neutral red	Balb/c 3T3 fibroblast	IC ₅₀ = > 1 mg/mL (no potential cytotoxic at concentrations > 1 mg/mL)	[93]
<i>E. supraaxillaris</i> Spreng.	Essential oils of leaves and fruits/hydrodistillation	<i>In vitro</i> cytotoxicity assay tumor cell lines	Tumor cell lines (cervix, colon, larynx, liver, and breast)	Cervix IC ₅₀ = 0.62 µL leaves and 1.30 µL fruits Colon IC ₅₀ = 0.43 µL leaves and 0.43 µL fruits Larynx IC ₅₀ = 0.54 µL leaves and 0.87 µL fruits Liver IC ₅₀ = 0.40 µL leaves and 0.38 µL fruits Breast IC ₅₀ = 0.40 µL leaves and 1.40 µL fruits	[1]
<i>E. zuchowskiae</i> Barrie	Essential oils of leaves/hydrodistillation	<i>In vitro</i> cytotoxicity assay MTT	MCF-7, MDA-MB-468, and UACC-257 human tumor	MCF-7 = 100% kill MDA-MB-468 = 100% kill UACC-257 = 100% kill Expressed as % kill at 100 µg/mL concentration	[18]

been identified. In view of the chemical diversity described, *Eugenia* species are likely a promising source of bioactive compounds. Of the *Eugenia* species known, only 350 have been investigated for their chemical composition and biological activity, demonstrating a shortage of studies for this genus. *E. uniflora* was the most studied species, attributable to its popular use. It is important to consider that *Eugenia* species are used in folk medicine, and several therapeutic properties have been reported, including antibacterial and antifungal activity against various microorganisms. Several studies evaluating the antimicrobial activity of extracts and derivatives used in combination with commercial antimicrobials revealed synergistic effects against microorganisms, potentializing the efficacy of these agents. However, some studies evaluating the bioactivities did not present a positive control or use a comparator to infer value to the results obtained, such as MIC or IC₅₀ values. Finally, we observed that cytotoxicity studies performed with *Eugenia* species presented wide methodological variations, making it difficult to compare the observed biological effects.

Studies exploring the association between the various phytochemicals and their biological activities may lead to the discovery of new bioactive compounds with therapeutic potential in *Eugenia* species that are native to Brazilian flora. Natural sources should be further explored and may result in the discovery of chemically diverse and biologically active compounds, including promising drugs in the search for new antimicrobial agents. Detection of these agents is important, as the increase in pathogen resistance to commercially available antimicrobials is a global health problem. Thus, this review suggests that species in the *Eugenia* genus have promising biological activities, supporting the need for future research on the development of drugs from the extracts and chemical constituents.

Acknowledgements

The authors extend their appreciation to the PhD Program in Pharmaceutical Sciences of the Federal University of Parana, Brazil.

Conflict of Interest

The authors declare no conflict of interest.

References

- 1] Aboutabl EA, Meselhy KM, Elkhreisy EM, Nassar MI, Fawzi R. Composition and Bioactivity of Essential Oils from Leaves and Fruits of *Myrtus communis* and *Eugenia supraxillaris* (Myrtaceae) Grown in Egypt. *J Essent Oil Bear Plants* 2011; 14: 192–200
- 2] Gu JQ, Park EJ, Luyengi L, Hawthorne ME, Mehta RG, Farnsworth NR, Pezzuto JM, Kinghorn AD. Constituents of *Eugenia sandwicensis* with potential cancer chemopreventive activity. *Phytochemistry* 2001; 58: 121–127
- 3] Stefanello MÉ, Pascoal AC, Salvador MJ. Essential oils from neotropical Myrtaceae: Chemical diversity and biological properties. *Chem Biodivers* 2011; 8: 73–94
- 4] Magina MDA, Dalmarco EM, Dalmarco JB, Colla G, Pizzolatti MG, Brighente IMC. Bioactive triterpenes and phenolics of leaves of *Eugenia brasiliensis*. *Quim Nova* 2012; 35: 1184–1188
- 5] Zaki MA, Balachandran P, Khan S, Wang M, Mohammed R, Hetta MH, Pasco DS, Muhammad I. Cytotoxicity and modulation of cancer-related signaling by (Z)- and (E)-3,4,3',5'-tetramethoxystilbene isolated from *Eugenia rigida*. *J Nat Prod* 2013; 76: 679–684
- 6] Ferreira FPS, Morais SR, Bara MTF, Conceição EC, Paula JR, Carvalho TC, Vaz BG, Costa HB, Romão W, Rezende MH. *Eugenia calycina* Cambess extracts and their fractions: Their antimicrobial activity and the identification of major polar compounds using electrospray ionization FT-ICR mass spectrometry. *J Pharm Biomed Anal* 2014; 99: 89–96
- 7] Sousa RMF, de Morais SAL, Vieira RBK, Napolitano DR, Guzman VB, Moraes TS, Cunha LCS, Martins CHG, Chang R, de Aquino FJT, do Nascimento EA, Oliveira A. Chemical composition, cytotoxic, and antibacterial activity of the essential oil from *Eugenia calycina* Cambess. leaves against oral bacteria. *Ind Crops Prod* 2015; 65: 71–78
- 8] Arruda RCO, Victório CP. Leaf secretory structure and volatile compounds of *Eugenia copacabanensis* Kiaersk. (Myrtaceae). *J Essent Oil Res* 2011; 23: 1–6
- 9] Malaman FS, Moraes LAB, West C, Ferreira NJ, Oliveira AL. Supercritical fluid extracts from the Brazilian cherry (*Eugenia uniflora* L.): relationship between the extracted compounds and the characteristic flavour intensity of the fruit. *Food Chem* 2011; 124: 85–92
- 10] Lima NP, Cerqueira SHF, Fávoro OA, Romoff P, Lago JHG. Composition and chemical variation of the essential oil from leaves of *Eugenia brasiliensis* Lam. and *Eugenia* sp. (Myrtaceae). *J Essent Oil Res* 2008; 20: 223–225
- 11] e Santos DN, de Souza LL, Ferreira NJ, Oliveira AL. Study of supercritical extraction from Brazilian cherry seeds (*Eugenia uniflora* L.) with bioactive compounds. *Food Bioprod Process* 2015; 94: 365–374
- 12] Peixoto CA, Oliveira AL, Cabral FA. Composition of supercritical carbon dioxide extracts of Pitanga (*Eugenia uniflora* L.) leaves. *J Food Process Eng* 2010; 33: 848–860
- 13] Costa DP, Santos SC, Seraphin JC, Ferri PH. Seasonal variability of essential oils of *Eugenia uniflora* leaves. *J Braz Chem Soc* 2009; 20: 1287–1293
- 14] Amorim ACL, Lima CKF, Hovell AMC, Miranda ALP, Rezende CM. Antinociceptive and hypothermic evaluation of the leaf essential oil and isolated terpenoids from *Eugenia uniflora* L. (Brazilian Pitanga). *Phytomedicine* 2009; 16: 923–928
- 15] Raj G, George V, Sethuraman MG. Chemical analysis of essential oil from the leaves of *Eugenia argentea* Bedd. *J Essent Oil Res* 2011; 23: 55–57
- 16] Cecílio AB, de Faria DB, Oliveira Pde C, Caldas S, de Oliveira DA, Sobral ME, Duarte MG, Moreira CP, Silva CG, de Almeida VL. Screening of Brazilian medicinal plants for antiviral activity against rotavirus. *J Ethnopharmacol* 2012; 141: 975–981
- 17] Schmidt JM, Noletto JA, Vogler B, Setzer WN. Abaco bush medicine: Chemical composition of the essential oils of four aromatic medicinal plants from Abaco Island, Bahamas. *J Herbs Spices Med Plants* 2006; 12: 43–65
- 18] Cole RA, Bansal A, Moriarity DM, Haber WA, Setzer WN. Chemical composition and cytotoxic activity of the leaf essential oil of *Eugenia zuchowskiae* from Monteverde, Costa Rica. *J Nat Med* 2007; 61: 414–417
- 19] Siebert DA, Tenfen A, Yamanaka CN, de Cordova CMM, Scharf DR, Simionatto EL, Alberton MD. Evaluation of seasonal chemical composition, antibacterial, antioxidant and anticholinesterase activity of essential oil from *Eugenia brasiliensis* Lam. *Nat Prod Res* 2015; 29: 289–292
- 20] Souza AMS, Armstrong L, Merino FJZ, Cogo LL, Monteiro CLB, Duarte MC, Miguel OG, Miguel MD. *In vitro* effects of *Eugenia pyriformis* Cambess., Myrtaceae: Antimicrobial activity and synergistic interactions with Vancomycin and Fluconazole. *African J Pharm Pharmacol* 2014; 8: 862–867
- 21] Lima BG, Tietbohl LAC, Fernandes CP, Cruz RAS, da Botas GS, Santos MG, Silva-Filho MV, Rocha L. Chemical composition of essential oils and anticholinesterase activity of *Eugenia sulcata* Spring ex Mart. *Lat Am J Pharm* 2012; 31: 152–155
- 22] Meyre-Silva C, Petry CM, Berté TE, Becker RG, Zanatta F, Delle-Monache F, Cechinel-Filho V, Andrade SF. Phytochemical analyses and gastropro-

- tective effects of *Eugenia umbelliflora* (Myrtaceae) on experimental gastric ulcers. *Nat Prod Commun* 2009; 4: 911–916
- [23] Coutinho H, Costa J, Falcao-Silva V, Siqueira-Junior J, Lima E. Fruits to potentiate the antibiotic activity: the effect of *Eugenia uniflora* and *Eugenia jambolanum* L. against MRSA. *Acta Alimentaria* 2012; 41: 67–72
- [24] Adebajo AC, Oloske KJ, Aladesanmi AJ. Antimicrobial activity of the leaf extract of *Eugenia uniflora*. *Phyther Res* 1989; 3: 451–455
- [25] Bouzada MLM, Fabri RL, Nogueira M, Konno TUP, Duarte GG, Scio E. Antibacterial, cytotoxic and phytochemical screening of some traditional medicinal plants in Brazil. *Pharm Biol* 2009; 47: 44–52
- [26] Denardin CC, Parisi MM, Martins LAM, Terra SR, Borojevic R, Vizzotto M, Perry MLS, Emanuelli T, Guma FT. Antiproliferative and cytotoxic effects of purple pitanga (*Eugenia uniflora* L.) extract on activated hepatic stellate cells. *Cell Biochem Funct* 2014; 32: 16–23
- [27] Costa DP, Filho EGA, Silva LMA, Santos SC, Passos XS, Silva MRR, Seraphin JC, Ferri PH. Influence of fruit biotypes on the chemical composition and antifungal activity of the essential oils of *Eugenia uniflora* leaves. *J Braz Chem Soc* 2010; 21: 851–858
- [28] Fiúza TS, Saboia-Morais SMT, De Paula JR, Tresvenzol LMF, Pimenta FC. Evaluation of antimicrobial activity of the crude ethanol extract of *Eugenia uniflora* L. leaves. *J Basic Applied Pharm Sci* 2008; 29: 245–250
- [29] Auricchio MT, Bugno A, Barros SBM, Bacchi EM. Antimicrobial and antioxidant activities and toxicity of *Eugenia uniflora*. *Lat Am J Pharm* 2007; 26: 76–81
- [30] Chavasco JM, Prado e Felipe BH, Cerdeira CD, Leandro FD, Coelho LF, Silva JJ, Chavasco JK, Dias AL. Evaluation of antimicrobial and cytotoxic activities of plant extracts from southern Minas Gerais cerrado. *Rev Inst Med Trop Sao Paulo* 2014; 56: 13–20
- [31] Apel MA, Sobral M, Schapoval EES, Henriques AT, Menut C, Bessiere JM. Essential oils from *Eugenia* species – part VII: sections Phyllocalyx and Stenocalyx. *J Essent Oil Res* 2004; 16: 135–138
- [32] Cole RA, Haber WA, Setzer WN. Chemical composition of essential oils of seven species of *Eugenia* from Monteverde, Costa Rica. *Biochem Syst Ecol* 2007; 35: 877–886
- [33] Pino JA, Bello A, Urquiola A, Aguero J. Leaf oil of *Eugenia axillaris* (Sw.) Willd. from Cuba. *J Essent Oil Res* 2003; 15: 15–16
- [34] Apel MA, Limberger RP, Sobral M, Henriques AT, Ntalani H, Menut C, Bassiere JM. Chemical composition of the essential oils from Southern Brazilian *Eugenia* species part II. *J Essent Oil Res* 2002; 14: 163–166
- [35] Apel MA, Sobral M, Schapoval EES, Henriques AT, Menut C, Bessière J. Chemical composition of the essential oils of *Eugenia beaurepaireana* and *Eugenia pyriformis*: section Dichotomae. *J Essent Oil Res* 2011; 16: 191–192
- [36] Magina MDA, Pietrowski EF, Gomig F, Falkenberg DDB, Cabrini DA, Otuki MF, Pizzollati MG, Brighente IMC. Topical antiinflammatory activity and chemical composition of the epicuticular wax from the leaves of *Eugenia beaurepaireana* (Myrtaceae). *Braz J Pharm Sci* 2009; 45: 171–176
- [37] Pereira RA, Zoghbi MGB, do Bastos MN. Essential oils of twelve species of Myrtaceae growing wild in the sandbank of the Resex Maracana, State of Para, Brazil. *J Essent Oil Bear Plants* 2010; 13: 440–450
- [38] Nakamura MJ, Monteiro SS, Bizarri CHB, Siani AC, Ramos MFS. Essential oils of four Myrtaceae species from the Brazilian southeast. *Biochem Syst Ecol* 2010; 38: 1170–1175
- [39] Moriarity DM, Bansal A, Cole RA, Takaku S, Haber WA, Setzer WN. Selective cytotoxic activities of leaf essential oils from Monteverde, Costa Rica. *Nat Prod Commun* 2007; 2: 1263–1268
- [40] Stefanello MÉA, Cervi AC, Ito IY, Salvador MJ, Wisniewski A jr., Simionatto EL. Chemical composition and antimicrobial activity of essential oils of *Eugenia chlorophylla* (Myrtaceae). *J Essent Oil Res* 2008; 20: 75–78
- [41] Duarte AR, Naves RR, Santos SC, Seraphir JC, Ferri PH. Genetic and environmental influence on essential oil composition of *Eugenia dysenterica*. *J Braz Chem Soc* 2010; 21: 1459–1467
- [42] Pino JA, Marbot R, Payo A, Chao D, Herrera P. Aromatic plants from Western Cuba. V: composition of the leaf oils of *Baccharis halimifolia* L. and *Eugenia foetida* (Sw.) Willd. *J Essent Oil Res* 2006; 18: 266–268
- [43] Apel MA, Sobral M, Schapoval EES, Henriques AT, Menut C, Bessiere JM. Chemical composition of the essential oils of *Eugenia hyemalis* and *Eugenia stigmatosa*. Part VI: section Biflorae. *J Essent Oil Res* 2004; 16: 437–439
- [44] Raseira M, Marin R, Apel MA, Limberger RP, Raseira MCB. Volatile components and antioxidant activity from some Myrtaceous fruits cultivated in Southern Brazil. *Lat Am J Pharm* 2008; 27: 172–177
- [45] Apel MA, Sobral M, Henriques AT, Menut C, Bessiere JM. Chemical composition of the essential oils from southern Brazilian *Eugenia* species. Part IV: section Racemosae. *J Essent Oil Res* 2002; 14: 290–292
- [46] de Moraes MM, da Camara CAG, dos Santos ML, Fagg CW. Essential oil composition of *Eugenia langsdorffii* O. Berg.: relationships between some terpenoids and toxicity against *Tetranychus urticae*. *J Braz Chem Soc* 2012; 23: 1647–1656
- [47] Pino JA, Marbot R, Bello A, Urquiola A. Essential oil of *Eugenia melanadenia* Krug et urb. from Cuba. *J Essent Oil Res* 2003; 15: 256–258
- [48] Villanueva H, Haber WA, Setzer WN. Chemical compositions of the leaf and fruit essential oils of *Eugenia monteverdensis* from Monteverde, Costa Rica. *J Essent Oil Bear Plants* 2009; 12: 443–446
- [49] Defaveri ACA, Sato A, Borré LB, Aguiar DLM, San Gil RAS, Arruda RCO, Riehl CAS. *Eugenia neonitida* Sobral and *Eugenia rotundifolia* Casar. (Myrtaceae) essential oils: composition, seasonality influence, antioxidant activity and leaf histochemistry. *J Braz Chem Soc* 2011; 22: 1531–1538
- [50] Tenorio AIS, Vargas D, Espinosa A, Diaz A, Gupta MP. Chemical composition of leaf essential oils of *Calyptanthes microphylla* B. Holts & ML, *Myrcia aff fosteri* Croat and *Eugenia octopleura* Krug & Urb from Panama. *J Essent Oil Res* 2011; 23: 29–33
- [51] Dias CN, Alves LP, Rodrigues KA, Brito MCA, Rosa Cdos DS, do Amaral FM, Monteiro Odos DS, Andrade EH, Maia JG, Moraes DF. Chemical composition and larvicidal activity of essential oils extracted from Brazilian legal Amazon plants against *Aedes aegypti* L. (Diptera: Culicidae). *Evid Based Complement Alternat Med* 2015; 2015: 490765
- [52] Apel MA, Limberger RP, Sobral M, Henriques AT, Ntalani H, Vérin P, Menut C, Bessière JM. Chemical composition of the essential oils from Southern Brazilian *Eugenia* species. Part III. *J Essent Oil Res* 2002; 14: 259–262
- [53] Zoghbi MGB, Guilhon GMSP, Sarges FN, Pereira RA, Oliveira J. Chemical variability of the volatiles from the leaves of *Eugenia protenta* McVaugh (Myrtaceae) growing wild in the North of Brazil. *Biochem Syst Ecol* 2011; 39: 660–665
- [54] Oliveira RN, Dias IJM, Camara CAG. Comparative study of the essential oil of *Eugenia puniceifolia* (HBK) DC. from different places of Pernambuco. *Braz J Pharmacogn* 2005; 15: 39–43
- [55] Ramos MFS, Monteiro SS, da Silva VP, Nakamura MJ, Siani AC. Essential oils from Myrtaceae species of the Brazilian Southeastern maritime forest (Restinga). *J Essent Oil Res* 2010; 22: 109–113
- [56] Stefanello MÉA, Wisniewski A, Simionatto EL, Cervi AC. Chemical composition and seasonal variation of essential oils of *Eugenia pyriformis* (Myrtaceae). *Lat Am J Pharm* 2009; 28: 449–453
- [57] Pino JA, Marbot R, Payo A, Chao D, Herrera P, Marti MP. Aromatic plants from western Cuba. I. Composition of leaf oil of *Gymnanthes lucida* Sw. and *Eugenia rhombea* (Berg) Krug et Urban. *J Essent Oil Res* 2005; 17: 278–280
- [58] Souza A, Cardoso-Lopes EM, da Silva MC, Cordeiro I, Young MCM, Sobral MEG, Moreno PRH. Chemical composition and acetylcholinesterase inhibitory activity of essential oils of *Myrcogenia myrcioides* (Cambess.) O. Berg and *Eugenia riedeliana* O. Berg, Myrtaceae. *Brazilian J Pharmacogn* 2010; 20: 175–179
- [59] Pino JA, Bello A, Urquiola A, Aguero J. Leaf oil of *Eugenia rocana* Britt. et Wils. from Cuba. *J Essent Oil Res* 2002; 14: 412–413

- [60] Medeiros JR, Medeiros N, Medeiros H, Davin LB, Lewis NG. Composition of the bioactive essential oils from the leaves of *Eugenia stipitata* McVaugh ssp Sororia from the Azores. *J Essent Oil Res* 2003; 15: 293–295
- [61] Franco MRB, Shibamoto T. Volatile composition of some Brazilian fruits: Umbu-caja (*Spondias citifera*), camu-camu (*Myrciaria dubia*), araca-boi (*Eugenia stipitata*), and cupuacu (*Theobroma grandiflorum*). *J Agric Food Chem* 2000; 48: 1263–1265
- [62] Magina MDA, Dalmarco EM, Wisniewski A, Simionatto EL, Dalmarco JB, Pizzolatti MG, Brighente IMC. Chemical composition and antibacterial activity of essential oils of *Eugenia* species. *J Nat Med* 2009; 63: 345–350
- [63] Rodrigues KA, Amorim LV, Oliveira JM, Dias CN, Moraes DF, Andrade EH, Maia JG, Carneiro SM, Carvalho FA. *Eugenia uniflora* L. essential oil as a potential anti-*Leishmania* agent: Effects on *Leishmania amazonensis* and possible mechanisms of action. *Evid Based Complement Alternat Med* 2013; 2013: 279726
- [64] Oliveira AL, Lopes RB, Cabral FA, Eberlin MN. Volatile compounds from pitanga fruit (*Eugenia uniflora* L.). *Food Chem* 2006; 99: 1–5
- [65] Faqueti LG, Petry CM, Meyre-Silva C, MacHado KE, Cruz AB, Garcia PA, Cechinel-Filho V, San Feliciano A, Monache FD. Euglobal-like compounds from the genus *Eugenia*. *Nat Prod Res* 2013; 27: 28–31
- [66] Prado LC, Silva DB, de Oliveira-Silva GL, Hiraki KR, Canabrava HA, Bispo-da-Silva LB. The gastroprotective effects of *Eugenia dysenterica* (Myrtaceae) leaf extract: the possible role of condensed tannins. *Biol Pharm Bull* 2014; 37: 722–730
- [67] Frighetto N, Welendorf RM, da Silva AMP, Nakamura MJ, Siani AC. Purification of betulinic acid from *Eugenia florida* (Myrtaceae) by high-speed counter-current chromatography. *Phytochem Anal* 2005; 16: 411–414
- [68] Kuskoski EM, Vega JM, Rios JJ, Fett R, Troncoso AM, Asuero AG. Characterization of anthocyanins from the fruits of Bagaçu (*Eugenia umbelliflora* Berg). *J Agric Food Chem* 2003; 51: 5450–5454
- [69] Limberger RP, Apel MA, Sobral M, Schapoval EES, Henriques AT. Volatile oil antimicrobial activity investigation from some Myrtaceae family species. *Braz J Pharm* 1998; 79: 49–52
- [70] Costa TR, Fernandes OFL, Santos SC, Oliveira CMA, Lio LM, Ferri PH, Paula JR, Ferreira HD, Sales BH, Silva M do R. Antifungal activity of volatile constituents of *Eugenia dysenterica* leaf oil. *J Ethnopharmacol* 2000; 72: 111–117
- [71] Bertucci A, Olivaro C, Da Silva PA, Ramos D, Cerdeiras MP, Vázquez A. Initial antimicrobial activity studies of plants of the riverside forests of the southern Uruguay River. *Braz J Pharmacogn* 2009; 19: 20–25
- [72] Machado KE, Cechinel Filho V, Cruz RCB, Meyre-Silva C, Cruz AB. Antifungal activity of *Eugenia umbelliflora* against dermatophytes. *Nat Prod Commun* 2009; 4: 1181–1184
- [73] Machado KE, Cechinel Filho V, Tessarolo ML, Mallmann R, Meyre-Silva C, Bella Cruz A. Potent antibacterial activity of *Eugenia umbelliflora*. *Pharm Biol* 2005; 43: 636–639
- [74] Lima EO, Gompertz OF, Giesbrecht AM, Paulo MQ. *In vitro* antifungal activity of essential oils obtained from officinal plants against dermatophytes. *Mycoses* 1993; 36: 333–336
- [75] Victoria FN, Lenardão EJ, Savegnago L, Perin G, Jacob RG, Alves D, da Silva WP, da Motta Ade S, Nascente Pda S. Essential oil of the leaves of *Eugenia uniflora* L.: antioxidant and antimicrobial properties. *Food Chem Toxicol* 2012; 50: 2668–2674
- [76] Lago JHG, Souza ED, Mariane B, Pascon R, Vallim MA, Martins RCC, Baroli AA, Carvalho BA, Soares MG, Dos Santos RT, Sartorelli P. Chemical and biological evaluation of essential oils from two species of Myrtaceae – *Eugenia uniflora* L. and *Plinia trunciflora* (O. Berg) Kausel. *Molecules* 2011; 16: 9827–9837
- [77] Correa-Royero J, Tangarife V, Durán C, Stashenko E, Mesa-Arango A. *In vitro* antifungal activity and cytotoxic effect of essential oils and extracts of medicinal and aromatic plants against *Candida krusei* and *Aspergillus fumigatus*. *Braz J Pharmacogn* 2010; 20: 734–741
- [78] Barbosa LN, Probst Ida S, Andrade BF, Alves FC, Albano M, da Cunha Mde L, Doyama JT, Rall VL, Fernandes Júnior A. *In vitro* antibacterial and chemical properties of essential oils including native plants from Brazil against pathogenic and resistant bacteria. *J Oleo Sci* 2015; 64: 289–298
- [79] Fiuzza TS, Sabóia-Morais SMT, Paula JR, Tresvenzol LMF, Carmo Filho JR, Pimenta FC. Antimicrobial activity of the crude ethanol extract and fractions from *Eugenia uniflora* leaves against *Pseudomonas aeruginosa*. *Lat Am J Pharm* 2009; 28: 892–898
- [80] Bernardo TH, Sales Santos Veríssimo RC, Alvino V, Silva Araujo MG, Evangelista Pires dos Santos RF, Maurício Viana MD, de Assis Bastos ML, Alexandre-Moreira MS, de Araújo-Júnior JX. Antimicrobial analysis of an antiseptic made from ethanol crude extracts of *P. granatum* and *E. uniflora* in Wistar Rats against *Staphylococcus aureus* and *Staphylococcus epidermidis*. *Sci World J* 2015; 2015: 751791
- [81] Santos KKA, Matias EFF, Tintino SR, Souza CES, Braga MF, Guedes GMM, Costa JGM, Menezes IRA, Coutinho HDM. Enhancement of the antifungal activity of antimicrobial drugs by *Eugenia uniflora* L. *J Med Food* 2013; 16: 669–671
- [82] De Souza GC, Haas APS, Von Poser GL, Schapoval EES, Elisabetsky E. Ethnopharmacological studies of antimicrobial remedies in the south of Brazil. *J Ethnopharmacol* 2004; 90: 135–143
- [83] Holecz FB, Pessini GL, Sanches NR, Cortez DAG, Nakamura CV, Filho BPD. Screening of some plants used in the Brazilian folk medicine for the treatment of infectious diseases. *Mem Inst Oswaldo Cruz* 2002; 97: 1027–1031
- [84] Barneche S, Cerdeiras MP, Lucarini R, Martins CHG, Olivaro C, Vazquez A. Anti-*Staphylococcus* activity of Uruguayan riverside forest plants. *Pharmacogn J* 2011; 3: 69–71
- [85] Coutinho HDM, Costa JGM, Falcão-Silva VS, Siqueira-Júnior JP, Lima EDO. Potentiation of antibiotic activity by *Eugenia uniflora* and *Eugenia jambolanum*. *J Med Food* 2010; 13: 1024–1026
- [86] McLaughlin JL, Rogers LL, Anderson JE. The use of biological assays to evaluate botanicals. *Drug Inf J* 1998; 32: 513–524
- [87] Meyer BN, Ferrigni NR, Putnam JE, Jacobsen LB, Nichols DE, McLaughlin JL. Brine shrimp: a convenient general bioassay for active plant constituents. *Planta Med* 1982; 45: 31–34
- [88] Siqueira JM, Ziminiani MG, Resende UM, Boaventura MAD. Activity-guided isolation of the constituents from bark of stem of *Duguetia glabruscula* – Annonaceae, using brine shrimp lethality test (BSL). *Quim Nova* 2001; 24: 185–187
- [89] Arcanjo D, Albuquerque A, Melo-Neto B, Santana L, Medeiros M, Citó A. Bioactivity evaluation against *Artemia salina* Leach of medicinal plants used in Brazilian Northeastern folk medicine. *Brazilian J Biol* 2012; 72: 505–509
- [90] Legaut J, Dahl W, Debiton E, Pichette A, Madelmont JC. Antitumor activity of balsam fir oil: production of reactive oxygen species induced by alpha-humulene as possible mechanism of action. *Plant Med* 2003; 69: 402–407
- [91] Santos KKA, Matias EFF, Tintino SR, Souza CES, Braga MFBM, Guedes GMM, Rolón M, Vega C, de Arias AR, Costa JGM, Menezes IRA, Coutinho HDM. Anti-*Trypanosoma cruzi* and cytotoxic activities of *Eugenia uniflora* L. *Exp Parasitol* 2012; 131: 130–132
- [92] Figueirôa Ede O, Nascimento da Silva LC, de Melo CM, Neves JK, da Silva NH, Pereira VR, Correia MT. Evaluation of antioxidant, immunomodulatory, and cytotoxic action of fractions from *Eugenia uniflora* L. and *Eugenia malaccensis* L.: correlation with polyphenol and flavanoid content. *Sci World J* 2013; 2013: 125027
- [93] Gallucci S, Neto AP, Porto C, Barbizan D, Costa I, Marques K, Benevides P, Figueiredo R. Essential oil of *Eugenia uniflora* L.: an industrial perfumery approach. *J Essent Oil Res* 2010; 22: 176–179