

Biology-Botany

Therapeutic applications of *Eugenia klotzschiana* O.Berg: A Systematic Bibliographic Review

Aplicações terapêuticas de *Eugenia klotzschiana* O. Berg:
Uma Revisão Bibliográfica Sistemática

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ABSTRACT

Eugenia klotzschiana O.Berg is an endemic plant from the Brazilian Cerrado biome with substantial chemical and genomic diversity. This systematic review aimed to identify the therapeutic applications of the plant in the SciELO, Bireme, LILACS, PubMed/Medline, Web of Science, Google Scholar, and Science Direct bibliographic databases, using the START Program for identifying and selecting studies. Forty-six articles were obtained, of which 42 were excluded and four were included in the review. The described therapeutic applications were the antioxidant, antimicrobial, antiparasitic, and cytotoxic activities of fruits, flowers, and leaves. The small number of published articles indicates the need for developing studies on the therapeutic potential of *Eugenia klotzschiana* O.Berg.

Keywords: Ethnobotany; Chemical composition; START; Phytotherapeutics

RESUMO

Eugenia klotzschiana O.Berg é uma planta endêmica do Cerrado que possui considerável diversidade química e genômica. Esta revisão sistemática objetivou identificar as aplicações terapêuticas da planta nas seguintes bases de dados bibliográficas: SciELO, Bireme, LILACS, PubMed/Medline, Web of Science, Google Acadêmico, Science Direct, com a utilização do Programa START para a identificação e seleção dos artigos. Um total de 46 artigos foram obtidos, dos quais 42 publicações foram excluídas e 4 foram incluídas no estudo. As aplicações terapêuticas descritas foram as atividades: antioxidante, antimicrobiana, antiparasitária e citotóxica dos frutos, flores e folhas. O pequeno número de trabalhos publicados indica a necessidade do desenvolvimento de estudos sobre as potencialidades terapêuticas da *Eugenia klotzschiana* O.Berg.

Palavras-chave: Etnobotânica; Composição química; START; Fitoterápicos

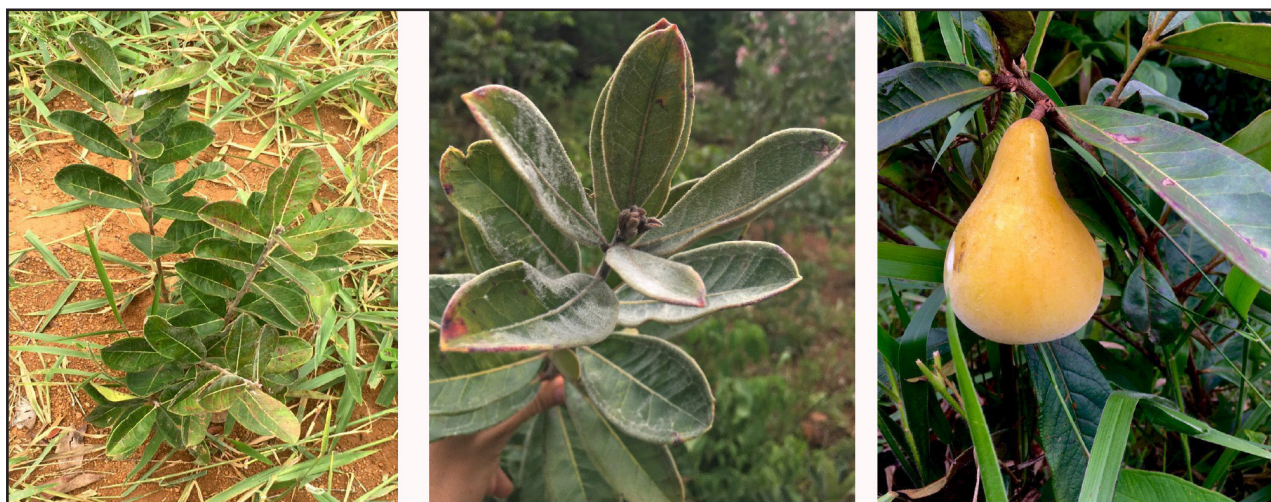
1 INTRODUCTION

The Myrtaceae family is extensively distributed in different Brazilian vegetation formations (Gressler, Pizo, & Morellato, 2006), representing an ancient lineage of the middle Cretaceous within the order Myrtales and an important floristic component in areas of the pan-tropical region with high biodiversity (Vasconcelos et al., 2017).

This botanical family has significant potential uses in both ethnomedicine and ethnopharmacology of traditional peoples. Its leaves and flowers have plenty of phenolic compounds used for distinct gastrointestinal disorders and as anti-inflammatories and antihypertensives (Lucena et al., 2014; Araújo et al., 2019).

The *Eugenia klotzschiana* O.Berg, popularly known as *perinha-do-cerrado* (Brazilian pear), is an endemic plant of the Cerrado biome (Brazilian savanna) (Siqueira, 2014) with a shrub size and clump formation habit. Interestingly, the specimens are independent superficially but interconnected subterraneously (Oliveira et al., 1999) (Figure 1).

Figure 1 - *Eugenia klotzschiana* O.Berg (1) - Shrub, (2) - Leaves, (3) - Fruit



Source: Ribeiro, C.L.

Eugenia klotzschiana O.Berg is a species popularly known as the Brazilian pear that belongs to the Myrtaceae family and is strictly distributed in the Cerrado biome area (Carneiro et al., 2017^a). This biome has high floristic biodiversity (Ferreira et al., 2017),

and the Myrtaceae family is among the most relevant in the neotropical ecosystems, mainly along the Atlantic Forest and Cerrado regions, representing around 10 to 15% of the diversity of these biomes (Costa, 2009).

In its natural habitat, the species may reach a primary development of approximately one meter in height and, under cultivation conditions, around 12 meters. Its flowers are typically white and fragrant, and the fruits are fleshy with yellow skin, white and soft pulp, acidic, and aromatic with about two to four seeds per fruit (Faria, Costa, & Junqueira, 2006).

This species grows in tropical climate regions and adapts to permeable and drained soils in the biome regions of *cerrado ralo*, *cerrado sensu stricto*, *campo limpo*, and *campo sujo* (Faria, Costa, & Junqueira, 2006). It is distributed among the Brazilian states of Goiás, Bahia, Mato Grosso do Sul, Minas Gerais, and São Paulo (Medeiros, 2011). However, there are also records of its presence in the Noel Kempff Mercado National Park, in Bolivia, growing in moist *campo sujo* vegetation between Serranía de Huanchaca and Campamento Huanchaca 2, at an altitude of 600-650 m. It is worth noting that reports of this species closest to Bolivia occurred in Camapuã, MS, Brazil (Villarroel & Proença, 2013).

Eugenia klotzschiana O.Berg presents a high chemical and genomic diversity, partially due to the ability to adapt to various biotic and abiotic conditions. Brazilian biomes show high habitat diversity due to environmental conditions, such as distinct climates, altitudes, and soil types that somewhat force plants to express unique adaptive factors (Basso et al., 2005).

Hence, complex chemical compounds and bioactive natural products are expressively diverse, making nature an extraordinary but little-known platform for models that can guide the production of cosmetics, medicines, food supplements, and other bioproducts (Valli & Bozani, 2019).

Only a few studies have been conducted on this species, highlighting the lack of phytochemical screenings of leaves, fruits, stems, and roots (Vicente, 2020). In this

context, the present study screened the therapeutic properties of *Eugenia klotzschiana* O.Berg and their correlation to phytochemical information in the specialized literature.

2 MATERIALS AND METHODS

A bibliographical survey was performed to answer the question: What are the described therapeutic applications for *Eugenia klotzschiana* O.Berg?

The inclusion criteria were full open-access articles published in national and international journals, in Portuguese, English, and/or Spanish, describing the medicinal use of *Eugenia klotzschiana* O.Berg. The exclusion criteria were scientific productions not published as full articles (theses, dissertations, and abstracts). After searching the databases, an exploratory reading was performed and the studies that did not meet the inclusion criteria were excluded.

The consulted bibliographic databases were SciELO (Scientific Electronic Library Online), Bireme, LILACS (Latin American and Caribbean Literature on Health Sciences), PubMed/Medline (Medical Literature Analysis and Retrieval System online), Web of Science, Google Scholar, and Science Direct. The initial descriptors were "*Eugenia klotzschiana*", "Biological Activities" and "Chemical Composition". However, only Google Scholar presented results. Hence, only the plant's name composed the search descriptor in the remaining databases. The bibliographical search was carried out in May 2023, and occurred without time restrictions.

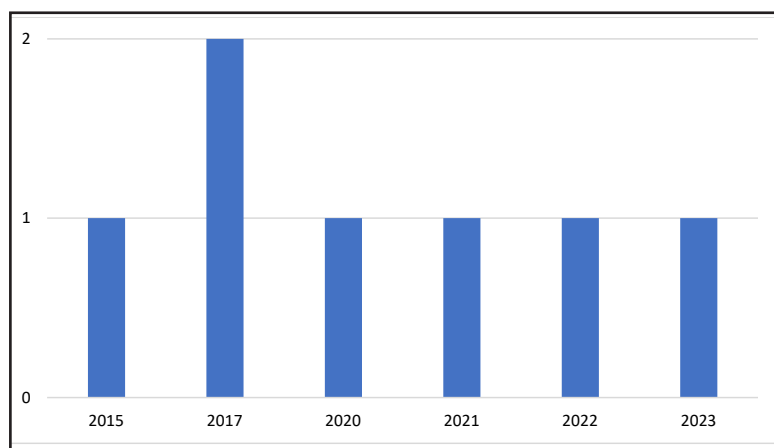
The articles were identified and selected with START software, version 3.3 beta 0.3, developed to perform systematic reviews in bibliographic databases (Hernandes et al., 2020). Then, the results were organized in a Prisma 2009 flowchart template (Moher et al., 2015). One reviewer extracted the data, and two others repeated the process later to verify consistency.

3 RESULTS AND DISCUSSION

The database searches with the keyword "*Eugenia klotzschiana*" resulted in 46 records, of which 42 (91.3%) were excluded because they neither addressed the plant's therapeutic potential nor fit the inclusion criteria. The other four (8.7%) articles were included.

The articles retrieved with the search term *Eugenia klotzschiana* O.Berg in the title and/or abstract were published between 2015 to 2023 (Figure 2).

Figure 2 – Number of articles published on *Eugenia klotzschiana* O.Berg until May 2023



Source: Authors

The compiled articles showed three studies on the plant, but without analyzing its therapeutic capacity. Sanches et al. (2021) investigated the characterization and storage of fruits, evaluating the chemical and physical changes in storage at room temperature. These authors concluded that fruits should be harvested ripe because they present better coloration, flavor, and dimensions than in other development stages and are less acidic. Mariano *et al.* (2022) evaluated and determined volatile organic oils from the fruits, identifying around 38 types with monoterpenes and sesquiterpenes. Corvalán et al. (2023) analyzed the nuclear genomics of *Eugenia klotzschiana* O.Berg.

The present review included the study by Takao et al. (2015), even though *Eugenia klotzschiana* O.Berg was not the main species. The authors screened distinct species from the Cerrado flora, with *Eugenia klotzschiana* O.Berg among them.

Studies on *Eugenia klotzschiana* O.Berg have increased over the last few years but are still scarce. However, only four of these were included in this study.

There are only a few studies demonstrating the potential of this species for evaluating the antioxidant capacity of *Eugenia klotzschiana* O.Berg and the expression of phenolic content (Takao, Imatomi, & Gualtieri, 2015). Moreover, the fruits of this species present carotenoids, flavonoids, phenolic compounds, and ascorbic acid, consequently showing antioxidant activity (Carneiro et al., 2019)(Table 1).

Table 1 – List of studies with therapeutic applications of *Eugenia klotzschiana* O.Berg

Described activity	Studied part of the plant	Article
Antioxidant	Fruits	Carneiro <i>et al.</i> , 2019
	Leaves	Takao <i>et al.</i> , 2015
	Leaves, Flowers	Carneiro <i>et al.</i> , 2017 ^a
Antimicrobial	Leaves, Flowers	Carneiro <i>et al.</i> , 2017 ^a
Antiparasitic	Flowers	Carneiro <i>et al.</i> , 2017 ^b
Cytotoxic	Flowers	Carneiro <i>et al.</i> , 2017 ^b

Source: Authors

This species is also included in the Brazilian List of Plants for the Future (Vieira, Camillo, & Coradin, 2018). The natural manifestation of *Eugenia klotzschiana* O.Berg is virtually disappearing due to agricultural practices in plant development regions, so it becomes a priority to cultivate and commercialize this species (Corvalán et al., 2017).

The studies included in the systematic review were published by Brazilian research groups from the following institutions: Department of Botany, Federal University of São Carlos (UFSCar), Federal Institute of Science and Technology of Goiás - Campus Rio Verde (GO), and Federal Institute of Education, Science, and Technology of Southern Minas Gerais - Campus Pouso Alegre (MG).

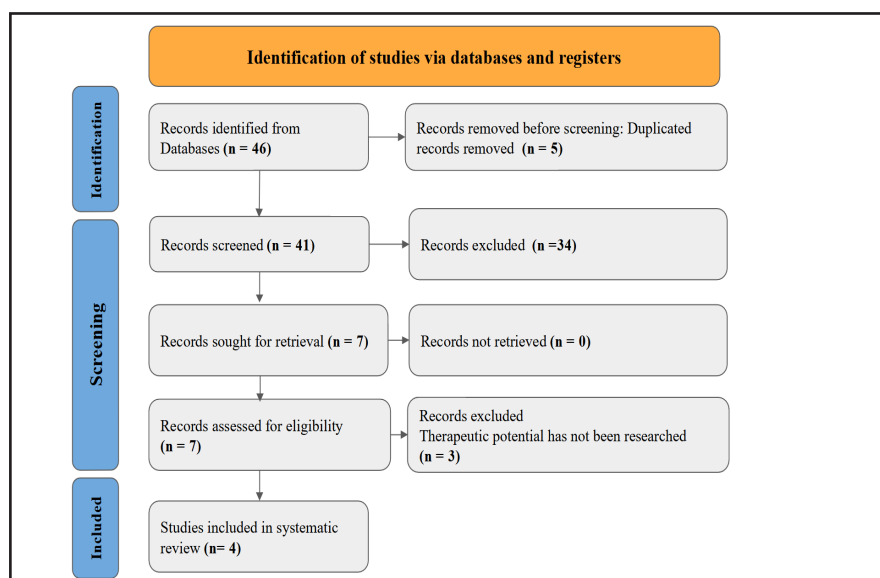
The articles were published in the following Brazilian scientific journals: Anais da Academia Brasileira de Ciências, Brazilian Archives of Biology and Technology, Revista Virtual de Química, and Brazilian Journal of Biology. The keywords used in these studies were free radical scavenging, *Eugenia klotzschiana*, Myrtaceae, essential

oil, flowers, *Trypanosoma cruzi*, cytotoxic analysis, cerrado pear, nutrients, flavonoids, antioxidant capacity, antioxidant activity, antibacterial activity, Brazilian pear, drying, *Eugenia klotzschiana*, and sesquiterpenes.

Investigations elucidating the therapeutic potentials highlighted the leaves, flowers, and roots, as observed in the present study. Among these organs, research has shown a higher interest in the bioactive properties of *Eugenia klotzschiana* O.Berg flowers. The leaves and fruits of Myrtaceae species have appealing but little-known and explored pharmacological properties, and this botanical family presents antioxidant activity (Ribeiro, Paula, & Peixoto, 2022).

The selected articles that did not meet the inclusion criteria were ecological studies and narrative, integrative, and systematic literature reviews. No study analyzed the therapeutic and antimicrobial properties of *Eugenia klotzschiana* O.Berg or other related plant species (Figure 3).

Figure 3 – Flowchart of the article selection process



Source: Authors

The research on *Eugenia klotzschiana* O.Berg is pioneering, which can be observed in the abstracts and/or final considerations of the articles, as follows:

Carneiro et al. (2017)^b:

The promising trypanocidal and cytotoxic activities were described for the first time. In summary, our results provide subsidies for future studies of the essential oil of the fresh flowers of *Eugenia klotzschiana* aiming at the isolation of bioactive compounds and investigation of their antiparasitic potentials. (p.1389).

Carneiro et al. (2019):

This study provides information about the fruits of *Eugenia klotzschiana* O.Berg, which are unknown and unexplored in the Brazilian Cerrado. (p.9).

Carneiro et al. (2017)^a:

This is the first report of the chemical composition and antibacterial and antioxidant activities of the essential oils of *Eugenia klotzschiana*. These results suggest that *Eugenia klotzschiana*, a Brazilian plant, provides initial evidence of a new and alternative source of substances with medicinal interest. (p.1907).

Vicente (2020) identified only a few studies on *Eugenia klotzschiana* O.Berg, corroborating our results.

The environmental vulnerability assessment of *Eugenia klotzschiana* O.Berg is of "least concern" on the list of endangered species (CNCFLORA, 2022), but the IUCN (International Union for Conservation of Nature) does not show threatened status records (Corvalán et al., 2017).

The compelling therapeutic properties of the Myrtaceae family, to which the *Eugenia klotzschiana* O.Berg species belongs, stimulate a growing interest in studies seeking to identify promising bioactive compounds with a great variety of polyphenols, terpenes, and other unique compounds (Nicoletti et al., 2018). However, the *Eugenia* genus species presents few related studies (Silveira et al., 2021), as for *Eugenia klotzschiana* O.Berg.

Carneiro et al. (2017)^a, Carneiro et al. (2017)^b and Carneiro et al. (2019), presented

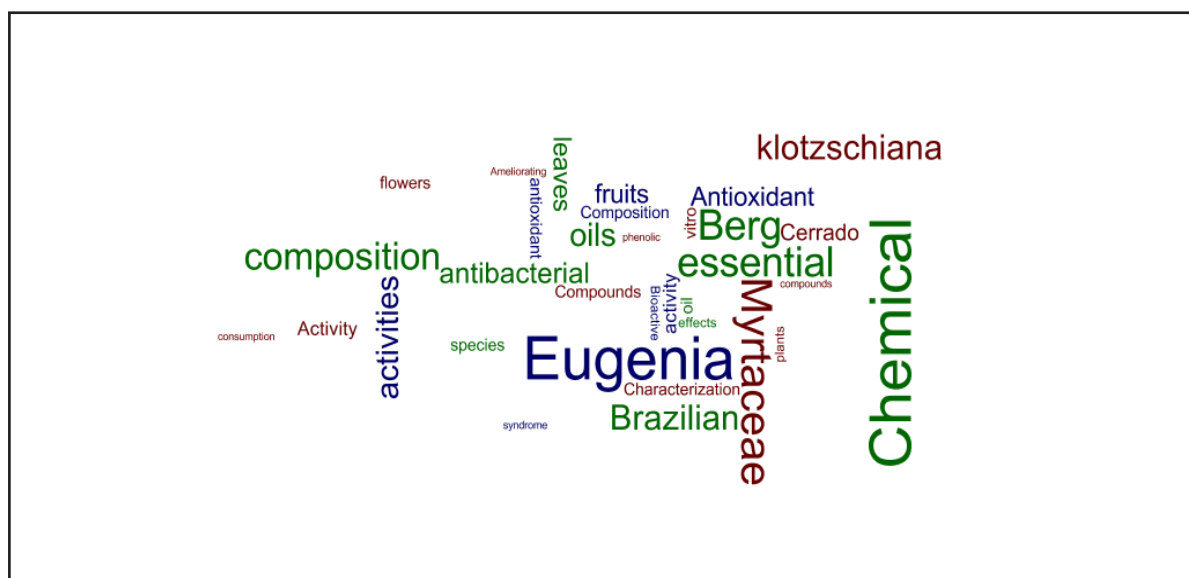
this perspective of expanding studies on *Eugenia klotzschiana* O.Berg to promote sustainability, conservation, and preservation relationships, which is ratified in this review.

Overall, species of the Myrtaceae family, such as *Eugenia klotzschiana* O.Berg, require more studies to elucidate their therapeutic potential, raising the necessity to combine the interest and requirement for new bioactive agents with the preservation and conservation of the Cerrado biome (Ribeiro, Souza, & Peixoto, 2022).

DESCRIBED BIOLOGICAL ACTIVITIES FOR *Eugenia klotzschiana* O.Berg

The scientific literature shows antioxidant and antibacterial activities as therapeutic properties of *Eugenia klotzschiana* O.Berg fruits and leaves (Ribeiro, Souza, & Peixoto, 2022). The articles related to the medicinal properties of *Eugenia klotzschiana* O.Berg address biological relationships and pharmacological potentials, such as anticancer activity (Figure 4).

Figure 4 – Word cloud of contents and topics of the evaluated articles



Source: Authors

ANTIOXIDANT ACTIVITY

The fruit of *Eugenia klotzschiana* O.Berg presents significant iron and fiber levels, antioxidant activity from phenolic compounds, ascorbic acid compositions, flavonoids, and carotenoids, suggesting that this species improves nutrient intake (Carneiro et al., 2019).

The species of the Myrtaceae family were evaluated, and among them, *Eugenia klotzschiana* O.Berg showed a considerable content of phenolic compounds, representing a promising source for new antioxidant agents (Takao, Imatomi, & Gualtieri, 2015).

The ethanolic and aqueous extracts and aqueous infusions of roots, stems, and leaves showed expressive antioxidant activity, focusing on stem extracts (Vicente, 2020). The essential oils from the leaves and flowers showed antioxidant activity and a dominant presence of α -copaene found in the oil of *in natura* leaves, β -bisabolene from the oil of dried leaves, and α -(E)-bergamotene from the oil of flowers (Carneiro et al., 2017^a).

ANTIMICROBIAL ACTIVITY

Essential oils were extracted from leaves and flowers by hydrodistillation in a modified Clevenger apparatus, and chemical characterization occurred with GC-MS. The chemical expression in fresh and dried biological material showed that most compounds were α -copaene, β -bisabolene, and α -(E)-bergamotene. The antimicrobial activity presented a minimum inhibitory concentration (MIC) of 200 μ g/mL against *Streptococcus salivarius* and *Streptococcus mitis* and 50 μ g/mL against *Streptococcus mutans* and *Prevotella nigrescens* (Carneiro et al., 2017^a).

ANTIPARASITIC AND CYTOTOXIC ACTIVITY

The essential oils of flowers showed trypanocidal action, with an inhibitory concentration (IC₅₀) of 20.2 μ g/mL against *Trypanosoma cruzi*, and on fibroblasts with

moderate toxicity at the cytotoxic concentration (CC_{50}) of 220.3 $\mu\text{g/mL}$. The compounds identified in the flowers should be noted: β -caryophyllene (21.1%), spathulenol (20.9%), and bicyclogermacrene (10.2%) (Carneiro et al., 2017^b).

“The essential oil of fresh flowers of *Eugenia klotzschiana* O.Berg can be considered a new source of bioactive compounds for the development of antiparasitic drugs” (Carneiro et al., 2017^b, p.1381).

4 CONCLUSION

There were only a few studies evaluating the therapeutic capabilities of *Eugenia klotzschiana* O.Berg, such as antioxidant, antimicrobial, antiparasitic, and cytotoxic activity in flowers, leaves, and fruits. The latter plant organ was the most prevalent in the identified studies. Research on this species has been increasing over the last five years, but *Eugenia klotzschiana* O.Berg has been cited on lists of endangered species in the past. The present study is pioneering, formatting the knowledge about this species with therapeutic potential, and its protagonism in applied studies can mainly aid the adoption of preservation and conservation measures for the species and the Cerrado biome. Studies on *Eugenia klotzschiana* O.Berg must be expanded, and further investigations can be conducted based on this review.

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