Galactia glaucescens KUNTH – FABACEAE (Leguminosae): STATE-OF-THE-ART

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Rosimere Farias de Mendonça Florenziano[1], Marcio Galdino dos Santos[2], Letícia Cristina Gonçalves[3], Yoko Oshima-Franco[4]

ABSTRACT

Galactia glaucescens Kunth is a native species from South America whose traditional use is mainly associated with antivenom properties. Recent studies have demonstrated the ability of its extracts to neutralize neurotoxic and myotoxic activities of snake venoms, reinforcing its pharmacological potential. However, despite this growing interest, there is still a lack of information regarding its toxicological, pharmacological, and regulatory aspects. Plants from the Fabaceae family may present secondary metabolites of therapeutic importance but also risks and adverse effects. This duality between benefits and risks highlights the need for more robust scientific approaches, especially through *in vitro* and *in vivo* assays to assess genotoxicity, mutagenicity, and safety under different doses and exposure conditions. In the biotechnological field, *in vitro* culture techniques, micropropagation, and metabolomics represent promising alternatives to standardize plant material and identify bioactive compounds safely. Furthermore, the use of nanotechnology and computational modeling can contribute to enhancing pharmacological efficacy, reducing adverse effects, and predicting relevant molecular interactions. Nevertheless, the absence of rigorous regulation on herbal medicines in Brazil and the persistence of the myth that “natural means harmless” pose additional barriers to the responsible use of the species. It is concluded that G. glaucescens holds attributes of scientific and therapeutic interest, but its safe exploitation will depend on the integration of pharmacology, toxicology, biotechnology, and regulation. Overcoming popular misconceptions and advancing preclinical and clinical studies will be crucial to consolidating its potential in the field of phytotherapy.

Keywords: Biotechnology. *Galactia glaucescens*. Phytotherapy. Toxicity.

[1] Doctoral student in Pharmaceutical Sciences. Universidade de Sorocaba, Uniso.
E-mail: rosiflorenziano@gmail.com Orcid: https://orcid.org/0009-0002-2140-6328
[2] Postdoctoral Research in Chemistry. Colegiado de Ciências Biológicas, Universidade Federal do Tocantins (UFT). E-mail: galdino@mail.uft.edu.br Orcid: https://orcid.org/0000-0002-2570-9425
[3] Postdoctoral Research in Cell and Molecular Biology. Hermínio Ometto Foundation University Center (FHO).
E-mail: leticiagoncalves@fho.edu.br Orcid: https://orcid.org/0000-0002-7362-7774
[4] Research in Natural Products. Universidade de Sorocaba. Uniso (Pós-Graduação em Ciências Farmacêuticas). E-mail: yoko.franco@prof.uniso.br Orcid: https://orcid.org/0000-0002-4972-8444

RESUMO

A *Galactia glaucescens* Kunth é uma espécie nativa da América do Sul cujo uso popular está associado principalmente a propriedades antiofídicas. Estudos recentes têm demonstrado a capacidade de seus extratos em neutralizar atividades neurotóxica e miotóxica de venenos ofídicos, reforçando seu potencial farmacológico. Entretanto, apesar desse interesse crescente, ainda há escassez de informações sobre seus aspectos toxicológicos, farmacológicos e regulatórios. Plantas da família Fabaceae podem apresentar metabólitos secundários de importância terapêutica, mas também riscos associados à toxicidade e efeitos adversos. Essa dualidade entre benefícios e riscos impõe a necessidade de abordagens científicas mais robustas, especialmente por meio de ensaios *n vitro* e *in vivo* que avaliem genotoxicidade, mutagenicidade e segurança em diferentes doses e condições de exposição. No campo biotecnológico, técnicas de cultivo *in vitro*, micropropagação e metabolômica representam alternativas promissoras para padronizar o material vegetal e identificar compostos bioativos de forma segura. Além disso, o uso da nanotecnologia e de modelagens computacionais pode contribuir para ampliar a eficácia farmacológica, reduzir efeitos adversos e prever interações moleculares relevantes. Contudo, a ausência de regulamentação rigorosa sobre fitoterápicos no Brasil e a persistência do mito de que “natural não faz mal” constituem barreiras adicionais para o uso responsável da espécie. Conclui-se que *G. glaucescens* reúne atributos de interesse do seu potencial no campo da fitoterapia.

Palavras-chave: Biotecnologia. Fitoterapia. *Galactia glaucescens*. Toxicidade.

RESUMEN

Galactia glaucescens Kunth es una especie nativa de América del Sur cuyo uso tradicional se asocia principalmente con propiedades antivenenosas. Estudios recientes han demostrado la capacidad de sus extractos para neutralizar las actividades neurotóxica y miotóxica de los venenos de serpiente, lo que refuerza su potencial farmacológico. Sin embargo, a pesar de este creciente interés, sigue habiendo una falta de información sobre sus aspectos toxicológicos, farmacológicos y normativos. Plantas de la familia Fabaceae pueden presentar metabolitos secundarios de importancia terapéutica, pero también riesgos y efectos adversos. Esta dualidad entre beneficios y riesgos pone de relieve la necesidad de enfoques científicos más sólidos, especialmente mediante ensayos *in vitro* e *in vivo* para evaluar la genotoxicidad, la mutagenicidad y la seguridad en diferentes dosis y condiciones de exposición. En el campo biotecnológico, las técnicas de cultivo *in vitro*, la micropropagación y la metabolómica representan alternativas prometedoras para estandarizar el material vegetal e identificar compuestos bioactivos de forma segura. Además, el uso de la nanotecnología y los modelos computacionales puede contribuir a mejorar la eficacia farmacológica, reducir los efectos adversos y predecir las interacciones moleculares relevantes. No obstante, la ausencia de una regulación rigurosa sobre los medicamentos a base de hierbas en Brasil y la persistencia del mito de que «natural significa inocuo» suponen obstáculos adicionales para el uso responsable de las especies. Se concluye que *G. glaucescens* posee atributos de interés científico y terapéutico, pero su explotación segura dependerá de la integración de la farmacología, la toxicología, la biotecnología y la regulación. Superar los conceptos erróneos populares y avanzar en los estudios preclínicos y clínicos será crucial para consolidar su potencial en el campo de la fitoterapia.

Palabras clave: Biotecnología. Fitoterapia. *Galactia glaucescens*. Toxicidad.

1 INTRODUCTION

Scientific interest in medicinal plants has grown exponentially in recent decades, due to the search for safe, effective and low-cost therapeutic alternatives. In this context, species of the Leguminosae family (=Fabaceae) have been highlighted for their phytochemical diversity and pharmacological potential demonstrated in different experimental models. Among them, (Barros; Silva; Porto, 2014) *Galactia glaucescens* (Kunth) has emerged as a subject of investigations due to its pharmacological properties, especially in the management of snake envenomations and inflammatory disorders. (Dal Belo et al., 2008)

G. glaucescens has bioactive compounds with recognized antioxidant, anti-inflammatory and antineurotoxic activity, being considered a promising candidate for the development of new herbal medicines. Experimental results indicate that fractions of the plant are able to neutralize the effects of the venom of (Dos Santos et al., 2019) *Crotalus durissus terrificus,* expanding the perspective of its use as an adjuvant in serum therapies. Despite this therapeutic potential, the use of plant species is still surrounded by misperceptions, such as the belief that "natural does not cause harm". This paradigm has been questioned by recent studies demonstrating potential adverse effects of plant compounds, including hepatotoxicity, genotoxicity, and mutagenicity. Thus, it is essential to critically evaluate the safety of plants such as (Dal Belo et al., 2008) (Chan, 2003; Ekor, 2014) *G. glaucescens,* whose traditional use can hide important toxicological risks.

The presence of complex secondary metabolites gives the species both its pharmacological properties and its toxic potential. Flavonoids and alkaloids, although widely investigated as bioactive molecules, can, under certain conditions, induce oxidative stress, chromosomal instability, and DNA damage. The absence of systematic toxicogenomic studies on (Cardoso, 2017) *G. glaucescens* becomes, therefore, a relevant gap to be explored.

Recent studies in pharmacognosy have reinforced the need to investigate not only the beneficial effects of medicinal plants, but also their potential genotoxic risks. Reviews published between 2020 and 2025 highlight that the indiscriminate consumption of herbal medicines may be related to mutagenic effects that are still poorly recognized clinically. These data alert to the importance of integrating molecular toxicology methodologies into pharmacological studies of the species. (Chan, 2003; Posadzki; Watson; Ernst, 2013)

In the field of experimental pharmacology, the investigation of toxicological effects is essential to validate the safety of potential herbal medicines. Assays such as comet test, micronucleus, and chromosomal aberrations have been widely used to evaluate the genotoxic

impacts of plant extracts. Applying these methodologies to (Hartmann, 2003) *G. glaucescens* would represent an advance in the understanding of its risk profile.

In addition to the pharmacological approach, it is necessary to consider the ecological aspects associated with the use of this species. *G. glaucescens* plays an important role in tropical ecosystems, particularly due to its nitrogen fixation capacity, contributing to soil fertility and environmental restoration. However, indiscriminate exploitation for medicinal purposes can negatively impact biodiversity conservation. (Sprent ; Gehlot , 2010)

Another critical point is the accelerated growth of the global herbal medicine market, which often anticipates the scientific validation of many plant species. This expansion, associated with the popularization of natural medicine, exposes populations to the risk of consuming extracts without proof of toxicological safety. The case of (Bent, 2008; Ekor, 2014) *G. glaucescens* illustrates the need for stricter regulations.

In parallel, international regulatory bodies such as the European Medicines Agency (EMA) and the Food and Drug Administration (FDA) have strengthened requirements for preclinical genotoxicity and mutagenicity analyses before the approval of plant-derived compounds for therapeutic use. The adequacy of research on (European Medicines Agency, 2026) *G. glaucescens* to these guidelines is an essential condition for future validation of the species in clinical contexts.

In Brazil and other Latin American countries, where the traditional use of the species is reported, it is urgent to promote investigations that reconcile popular knowledge with modern scientific approaches. The rescue of ethnopharmacology needs to be linked to toxicological tests that guarantee consumer safety. This strengthens rational use and avoids risks associated with empiricism. (Bent, 2008; Posadzki; Watson; Ernst, 2013)

When analyzing the state of the art on *G. glaucescens*, it is observed a concentration of studies on its pharmacological effects, but still a significant lack of data on toxicity. This asymmetry between efficacy and safety constitutes a challenge to be overcome by the scientific community, especially in the face of the growing demands for safe and validated herbal medicines. (Chan, 2003; Dos Santos et al., 2019)

Thus, the aim of this study was to present a critical and comprehensive review of *Galactia glaucescens* (Kunth), highlighting its therapeutic properties, but also emphasizing the potential risks related to toxicity, genotoxicity and mutagenicity. It is intended, therefore, to offer subsidies for the advancement of future research and for the consolidation of the safe and rational use of this species in the contemporary pharmacological context.

2 METHODOLOGY

The present study consists of a literature review with a systematic approach and narrative character, aimed at identifying, critically analyzing, and synthesizing the scientific knowledge published between the years 2015 and 2025 on the species *Galactia glaucescens* (Kunth). The objective was to map evidence related to morphology, ecology, phytochemistry, pharmacological potential and, especially, the toxicological risks associated with its use, including aspects of toxicity, genotoxicity and mutagenicity.

The searches were carried out between August and September 2025 in widely recognized international databases, including PubMed/MEDLINE, Scopus, Web of Science, ScienceDirect, and SciELO. In order to broaden the scope and reduce publication biases, the searches were complemented with queries to Google Scholar, repositories of theses and dissertations, and technical documents available in Brazilian and international digital libraries.

To ensure terminological coverage, controlled and uncontrolled descriptors were used in Portuguese and English, according to the MeSH (Medical Subject Headings) and DeCS (Health Sciences Descriptors) vocabularies. The combinations included terms such as "*Galactia glaucescens*", "Fabaceae", "Leguminosae", "medicinal plants", "toxicity", "genotoxicity", "mutagenicity", "pharmacological potential", "natural products", "ecology" and "distribution", using Boolean operators to refine the search.

Original articles, reviews, brief communications, and book chapters published from January 2015 to May 2025, available in English, Portuguese, or Spanish, that presented specific data on *G. glaucescens* in botanical, pharmacological, toxicological, or ethnobotanical aspects, were included. Studies published before 2015, those without access to the full text, studies that mentioned only the genus *Galactia sp* without directly addressing the target species, as well as editorials, case reports, abstracts in annals of events, and gray literature without peer review were excluded.

The selection of articles followed a process in three successive stages. Initially, titles and abstracts were evaluated for relevance and adherence to the theme. Then, the full texts of potentially eligible studies were examined in depth. Finally, two independent reviewers applied the inclusion and exclusion criteria rigorously, and any divergences were resolved by consensus.

The extracted data were systematized in a standardized spreadsheet, including information such as author, year of publication, country of origin, indexing base, methodological design, objectives, main results and conclusions. The organization of the information allowed the categorization of the findings into five main axes: botany and morphology; geographic

distribution and ecology; phytochemistry and secondary metabolites; pharmacological potential, including studies on antivenom, antioxidant and anti-inflammatory effects; and toxicity, with emphasis on genotoxicity and mutagenicity analyses.

The synthesis of the data was carried out in a narrative and integrative way, seeking to relate trends, advances and gaps in the recent literature. Priority was given to studies published in the period from 2015 to 2025, although some previous works were mentioned punctually for historical and complementary contextualization.

3 LITERATURE REVIEW

3.1 BOTANICAL AND TAXONOMIC ASPECTS

The genus *Galactia* groups approximately 50 species described in tropical regions. Of these, about 45 species are distributed in Tropical America. According to

Beyra Matos et al. (2005) little is known about the economic applications of the species belonging to this genus. The species *Galactia glaucescens* belongs to the class Dicotyledoneae, which includes angiosperms that are characterized by developing two cotyledon leaves in the seed embryo; family Leguminosae (=Fabaceae), which comprises one of the largest families among the dicots with more than 600 genera. The plant stands out for its pharmacological potential and the complexity of its botanical characterization. Floristic studies in the state of São Paulo have shown the occurrence of different species of the genus (J oly , 2005) *Galactia,* but have not recorded the presence of *G. glaucescens*, pointing to gaps in knowledge about its geographic distribution. This absence in regional surveys highlights the need to expand taxonomic and ecological investigations, especially to support future therapeutic uses in a responsible manner. (Portal Plantas do Brasil, 2026)

In Brazil, the species *Galactia glaucescens* is found in the cerrado and is distributed mainly in ecotonal areas of this biome, as in the state of Tocantins. According to the BIOTA program developed by the Foundation for Research Support of the State of São Paulo and according to a resolution of the Department of the Environment of the same state, the plant ("BIOTA-FAPESP Program", *[Undated]*) (Legislation , 2022) *G. glaucescens* is on the list of species of flora in the state of São Paulo threatened with extinction.

In the state of Tocantins there is no study on the population density of this species. However, in an ethnobotanical survey carried out by Barra D'Aroeira, the use of G (S Antos ; Lolis; Dal Belo , 2006) . *glaucescens* leaves (vernacular Three Leaves) by healers belonging to the community of black remnants Barra D'Aroeira, located in the municipality of Santa Tereza, Tocantins, in the treatment of snakebite envenomation was identified. The

vernacular "three leaves" was attributed by the healers of this community due to the plant having a leaf blade divided into three independent leaflets.

Its taxonomic classification is supported by international databases such as the NCBI Taxonomy Browser, which places the species in the group of Papilionoideae, highlighting its relationship with legumes of ecological importance. Despite the consolidated systematic positioning, there are still challenges in the chemical and pharmacological characterization of the species. This reality reinforces the maxim that botanical identification, although essential, does not ensure safety of use, and it is essential to deepen toxicological studies. (NCBI Taxonomy Browser, 2026)

3.2 ANATOMY AND HISTOCHEMISTRY

Anatomy and histochemistry surveys of vegetative organs of *G. glaucescens* demonstrated the presence of specialized secretory structures and phenolic compounds distributed in different tissues, confirming its pharmacological potential. Such findings corroborate the interest in the species as a source of bioactive metabolites. However, the production of these substances must be analyzed from a critical perspective, since natural compounds can also trigger adverse effects on biological systems. (Barros; Silva; Porto, 2014)

The histochemical characterization showed a predominance of flavonoids, alkaloids and phenolic derivatives, which are often associated with antioxidant and cellular protective effects. Despite these potential benefits, there is evidence in the literature that these same chemical groups can exert genotoxic activities, especially at high doses or in prolonged exposures. Thus, the study of histochemistry not only provides support for therapeutic uses, but also warns of risks intrinsic to the indiscriminate use of the species.(Barros; Silva; Porto, 2014)

3.3 PHARMACOLOGICAL PROPERTIES AND ETHNOBOTANICAL USES

The pharmacological potential of *G. glaucescens* includes antivenom activities, with promising results against certain effects of the venom of the snake *Crotalus durissus terrificus* (Dal Belo et al., 2008; Gómez-Murillo; Arellano-Martín, 2021 ; Sumedh et al., 20 18) . These effects strengthen the perspective of using the plant as a complementary therapeutic resource in endemic regions, where snakebites represent a serious public health problem. However, studies remain incipient and lack further study on safety and clinical applicability.

From the ethnobotanical point of view, records in the Pantanal region point to the use of plants of the genus *Galactia* in traditional practices. These reports, although relevant to

ethnopharmacology, should be interpreted with caution, since popular knowledge tends to reinforce the mistaken notion that "natural does no harm". Without robust investigations into toxicity, genotoxicity and mutagenicity, the consumption of these plants may imply silent health risks. (P ott ; P ott , 1995)

3.4 DIVERSITY, CONSERVATION AND GAPS

Broader studies on legume diversity in the Gran Chaco highlight the importance of legumes as a whole and the existence of several endemic species, but do not include specific data on *G. glaucescens*, underscoring the paucity of detailed research on the species. This lack of data reinforces the urgency of systematic studies that consider both the pharmacological potential and the toxicological risks associated with the species. (C Eolin ; M iotto , 2013)

Although the genus *Galactia,* as well as other Fabaceae, has potential for the discovery of bioactive compounds, there are still no studies directed to *G. glaucescens* — highlighting a gap in knowledge (Carvalho et al., 2008) However, more general research shows the complexity of these species, which can concentrate biologically active molecules with effects that are not only beneficial, but also potentially harmful. The balance between benefit and risk, therefore, needs to be investigated with greater scientific rigor.

3.5 POLLEN MORPHOLOGY AND TOXICOLOGICAL IMPLICATIONS

The analysis of the pollen morphology of the genus *Galactia sp*, including Brazilian representatives, provides subsidies to understand its diversification and phylogenetic relationship with other legumes. This type of characterization, in addition to having taxonomic implications, can help in understanding the biosynthetic pathways responsible for the production of secondary metabolites. Such pathways are precisely the ones that determine the bioactivity and toxicity profile of compounds present in (Roubik; Moreno, 1991 ; Bishop of the Santos, 2014) *G. glaucescens.*

Analysis of the pollen morphology of representatives of the genus *Galactia,* including *G. glaucescens*, reveals features—such as perforated murus—that may be useful for distinguishing this species from others and inferring phylogenetic relationships and potential metabolic correlations. The characterization of these structures contributes to identifying potential correlations with the synthesis of molecules that, while having therapeutic properties, can trigger genotoxic or mutagenic effects. In this sense, morphological and biochemical analysis must be interpreted in an integrated way, reinforcing the central debate about the risks

embedded in the belief that natural substances are harmless. (Roubik; Moreno, 1991 ; Bishop of the Santos, 2014)

3.6 ECOLOGY AND GEOGRAPHICAL DISTRIBUTION OF *GALACTIA GLAUCESCENS*

Recent taxonomic studies, such as that of Ceolin & Miotto (2013), provide a synthesis of the genus *Galactia* in Brazil and present relevant data for *G. glaucescens*, such as its synonymy and distribution. In addition, the formal description of the species in the Plazi TreatmentBank provides essential information about its typification, morphological variation, and relationship with other species of the genus. (Ceolin; Miotto, 2013) (“ *Galactia glaucescen s* , Prefix Match - Plazi TreatmentBank", *[Undated]*)

The absence of consistent data on the geographic range of the species has a direct impact on the risk analyses associated with its use. Plants of restricted distribution tend to accumulate secondary metabolites at differentiated concentrations, a result of local environmental pressures. Such chemical changes can ultimately modify its toxicological profile. The ethnobotanical literature indicates that traditional populations often use species of the genus (Gobbo-Neto; Lopes, 2007) *Galactia* without clear taxonomic distinction, which can lead to the misuse of plants with potential adverse effects. This overlap in popular knowledge reinforces the urgency of detailed investigations into the identity and risks of (De Albuquerque et al., 2007) *G. glaucescens.*

From an ecological point of view, it is notable that Fabaceae species, when occupying marginal niches, often synthesize bioactive compounds as a defense strategy against herbivory. In (Wink, 2013) *G. glaucescens*, this characteristic can be interpreted as a pharmacological advantage, but also a warning of genotoxic risks. In addition, anthropogenic changes in ecosystems, such as deforestation and fragmentation, may be further restricting the distribution of *G. glaucescens*. Such environmental pressures often intensify the production of defense metabolites, increasing the need for toxicity monitoring. This interface between ecology and pharmacology cannot be neglected. (Bravo-Monzón et al., 2022)

Pollination ecology is also related to the availability of the species. Studies on pollen morphology indicate that *Galactia* has specific patterns that influence its dispersion. Alterations in this process can compromise natural reproduction and reduce genetic variability, a relevant factor for biochemical and toxicological potential. Finally, the restricted distribution and ecological challenges faced by the species reinforce the need for multidisciplinary approaches. Without robust data on its occurrence, it becomes impossible to accurately assess both the therapeutic potential and the risks associated with indiscriminate use. This reinforces the

centrality of the debate about the myth that natural products are necessarily safe. (Veasey et al., 1999) (“ *Galactia glaucescens* Kunth | Plants of the World Online | Kew Science", 2026)

The ecology of *G. glaucescens*, therefore, should not be seen only as a field of botanical interest. It is an essential element for understanding its pharmacological safety and for the formulation of public policies that reconcile conservation and sustainable use. The integration of ecological, taxonomic and toxicological data is, in this sense, an indispensable path. (Clement et al., 2010)

3.7 POTENTIAL HERBAL MEDICINES AND SAFETY LIMITATIONS

The use of *Galactia glaucescens* in traditional healing practices in Brazil is documented by communities that employ it mainly in disorders related to inflammatory processes and snakebites. The reported pharmacological potential is in line with the presence of bioactive metabolites that act on neuronal and enzymatic receptors. While this ethnobotanical knowledge is valuable, its transposition into clinical settings requires rigorous toxicological studies. (Calixto, 2000)

Preclinical trials have demonstrated antineurotoxic activity of plant extracts against the venom of *Crotalus durissus terrificus*, suggesting its application as an adjuvant in snakebite treatments. This result, however, should not be interpreted as a guarantee of safety, since pharmacological efficacy may coexist with risks of systemic toxicity and genotoxicity. (Dal Belo et al. , 2008)

The appreciation of native flora as a therapeutic resource is growing, driven by the global movement in favor of phytotherapy. However, this scenario favors the spread of the mistaken belief that natural is free of adverse effects. In the case of (Ekor, 2014) *G. glaucescens*, this perception can induce consumption without adequate scientific support, exposing users to potential risks of mutagenicity.

The concept of "relative safety" in herbal medicines is particularly sensitive, as different methods of preparation — infusion, decoction or alcoholic extracts — can substantially modify the concentration of active and toxic compounds. Thus, the same plant material may have divergent profiles in terms of efficacy and risk. Recent pharmacological research highlights the importance of isolating and characterizing the compounds responsible for the effects attributed to the plant. In (Firenzuoli; Gori, 2007) *G. glaucescens*, flavonoids and alkaloids are among the leading candidates. Even so, many of these chemical groups have reports in the literature

of potential genotoxic effects, which reinforces the need for careful evaluation. (P ott ; P ott , 1995)

The risk of popular use of plant species is not restricted to the intrinsic toxicity of the metabolites. External factors, such as contamination by heavy metals, pesticides, or microorganisms during collection and processing, can further increase the deleterious effects. This indicates that the issue of safety goes beyond the species itself, encompassing the entire production and use chain. (Street, 2012)

Another central point is the absence of specific regulations on the commercialization of products derived from *G. glaucescens*. Without official quality control protocols, variability in extracts compromises both therapeutic efficacy and toxicological evaluation. Such regulatory fragility reinforces the urgency of standardized studies. The literature on herbal medicines highlights that plants with recognized therapeutic potential also have reports of adverse effects in cell and animal models, including DNA damage and chromosomal instability. In this context, (World Health Organization, 2007) (Wagner; Ulrich-Merzenich, 2009) *G. glaucescens* should be studied from the same perspective, aiming to identify genotoxic risks early.

In addition to direct toxicity, the possibility of drug interactions is an aspect that is often overlooked. Bioactive compounds of *G. glaucescens* may interfere with metabolic pathways of conventional drugs, increasing clinical risks. This pharmacological dimension should be incorporated into future research protocols. Therefore, although the herbal potential of (Williamson, 2003) *G. glaucescens* is promising, it cannot be dissociated from the need for scientific rigor. The popular discourse that "natural does no harm" lacks support when confronted with the growing evidence of toxicological, mutagenic and genotoxic risks. The consolidation of safe use will depend on the integration between pharmacology, toxicology and regulatory policies. (Efferth; Koch, 2011)

3.8 TOXICOLOGICAL RISKS: GENOTOXICITY AND MUTAGENICITY

The safety of the use of *Galactia glaucescens* requires special attention in the field of toxicology. Plants of the Fabaceae family are known for the production of compounds with relevant pharmacological activity, but may also contain potential adverse effects. In the case of (Susilawati et al., 2023) *G. glaucescens*, the scarcity of specific studies on safety reinforces the need for systematic investigations that consider cellular and molecular parameters. The genotoxic risk associated with secondary metabolites is widely documented in plant species. Flavonoids, for example, have antioxidant activity, but under certain conditions they can induce DNA damage and generate genomic instability. This duality requires caution in interpreting the

benefits attributed (López-Lázaro, 2007) *to G. glaucescens*, since positive and adverse effects can coexist.

In vitro *experimental models* represent a valuable tool to evaluate genotoxicity and mutagenicity of plant extracts. However, in the case of (Pfuhler et al., 2009) *G. glaucescens*, such studies are still incipient, limiting the understanding of the real risk potential. The absence of micronucleus assays, comet testing, or chromosomal aberrations represents a relevant gap that must be filled.

Popular use without scientific backing exposes individuals to invisible risks. The mutagenic effects of plant compounds may not manifest immediately, but accumulate over time, increasing the likelihood of developing chronic diseases, including cancer. This dimension reinforces the urgency of breaking the paradigm that medicinal plants are inherently safe. (Stich; Rosin, 1984)

Another critical point refers to reproductive toxicity. Some legumes have compounds capable of interfering with fertility and embryonic development. Considering the phytochemical similarity between species of the genus (Hughes Jr, 1988) *Galactia*, it is plausible that *G. glaucescens* shares characteristics that require experimental evaluation. Toxicity should not be analysed solely from the perspective of high doses. Recent studies highlight that even subtherapeutic concentrations of some herbal medicines can induce mutations when exposure is chronic. This perspective magnifies the challenges in defining safe limits for long-term use of (European Food Safety Authority, 2010) *G. glaucescens extracts.*

The risk of genotoxic interactions also extends to the environmental context. Bioactive compounds released by plant species can interfere with soil microorganisms and, in the long term, affect food chains. This relationship between ecotoxicology and human safety has not yet been explored for (Duke; Dayan, 2011) *G. glaucescens,* but it should be considered in multidisciplinary approaches. It is also necessary to highlight the absence of regulatory protocols that require mutagenicity tests before the commercialization of herbal medicines in Brazil. This gap opens space for the circulation of potentially harmful products, without robust evidence of safety. In the case of (Mattei et al., 1998) *G. glaucescens,* the risk is amplified by the lack of standardization in preparation and dosage methods.

In parallel, recent reviews on medicinal plants highlight that the underreporting of adverse events compromises the real safety assessment. Often, genotoxicity-related side effects are not directly attributed to plant consumption, making epidemiological screening difficult. This phenomenon may be hiding the impacts of the indiscriminate use of (De Sousa , 2023) *G. glaucescens.*

Thus, the discussion about the toxicological risks associated with any herbal compound, such as *G. glaucescens,* needs to be broadened, integrating molecular biology, regulatory toxicology and pharmacovigilance methods. Only in this way will it be possible to counteract in a reasoned way the popular argument that "natural does not hurt" and build solid foundations for the responsible use of this species. (Rodrigues; Barnes, 2013)

3.9 FUTURE PHARMACOLOGICAL PERSPECTIVES AND BIOTECHNOLOGY

Biotechnology has expanded the possibilities for safe exploitation of medicinal plants, including *Galactia glaucescens*. Modern techniques of *in vitro* cultivation and micropropagation allow the achievement of standardized plant biomass, reducing phytochemical variability and favoring more consistent pharmacological studies. This advance may contribute to isolating compounds of therapeutic interest with greater safety. In addition to standardization, biotechnology enables the genetic manipulation of plant species in order to reduce potentially toxic compounds, maintaining the production of relevant bioactive metabolites. For (Fazili et al., 2022) (Georgiev et al., 2012) *G. glaucescens,* this represents a promising path, since the coexistence of therapeutic properties and genotoxic risks limits its full use.

Nanotechnology emerges as another strategic tool for plant pharmacology. The encapsulation of plant extracts in nanoparticles can reduce adverse effects, control the release of active ingredients and increase bioavailability. These approaches would demonstrate efficacy in other Fabaceae, which reinforces their potential application. (Srinivasan, 2023)

Still, pharmacological development requires strict safety protocols. Preclinical and clinical trials should be conducted to verify toxicity in cellular and animal systems prior to transposition to human therapies The absence of such studies for (Martins et al., 2011). *G. glaucescens* highlights a barrier that must be overcome. Another emerging field is metabolomics, which enables the global analysis of the compounds present in the plant. Applied to *G. glaucescens,* this technique would make it possible to identify both molecules with therapeutic potential and those associated with genotoxicity. This systemic view is essential to advance in the balance between benefits and risks. (Wolfender et al., 2015)

Bioprospecting for natural compounds faces ethical challenges, especially when it involves traditional knowledge from local communities. The use of this knowledge must respect the principle of fair sharing of benefits, avoiding undue exploitation of ancestral knowledge. This ethical dimension is inseparable from pharmacological advances. On the other hand, the growing demand for natural products in the global market increases the pressure for rapid scientific validation of new species. This scenario can favor methodological shortcuts that

compromise security. For (Singh; Pathak; Rai, 2022) (Tilburt, 2008) *G. glaucescens*, it is essential that the commercial rush does not supplant the need for robust toxicological tests.

The integration between pharmacology and bioinformatics also opens horizons for the species. Molecular modeling can predict interactions of *G. glaucescens* compounds with biological targets, anticipating potential therapeutic and adverse effects. This approach allows prioritizing safer molecules for future assays. The biotechnological perspective should not be seen as a substitute for traditional studies, but as a necessary complement. Technological advancement can optimize the investigation of (Sliwoski et al. , 2014) *G. glaucescens*, as long as it is accompanied by appropriate toxicological evaluations. This synergy is indispensable to transform the plant's potential into safe clinical applications. (Atanasov et al., 2021)

In short, the pharmacological prospects of *G. glaucescens* are promising, but the future of the species in the field of phytotherapy will depend on the ability to reconcile biotechnological innovation and scientific rigor. Without this, there is a risk of perpetuating the cycle of exploitation of medicinal plants with proclaimed benefits, but invisible risks. (Newman; Cragg, 2020)

3.10 THE SCIENTIFIC DEBATE ABOUT "NATURAL DOES NOT HURT"

The discourse that natural products are risk-free remains rooted in the popular imagination, but the scientific literature increasingly demonstrates that this belief is mistaken. In the case of *Galactia glaucescens*, the therapeutic potential is accompanied by uncertainties regarding toxicity and genotoxicity. This duality needs to be clearly communicated to society. (Veiga Junior; Pinto; Maciel, 2005)

The popularization of herbal medicines often relies on arguments of cultural tradition and historical use, without considering that long-term adverse effects have rarely been systematically documented in traditional contexts. This perception bias contributes to the perpetuation of the idea of absolute security. (De Smet, 2002)

The precautionary principle should guide the exploitation of *G. glaucescens.* The absence of conclusive studies is not equivalent to proof of harmlessness. On the contrary, the lack of evidence should be understood as a warning of the risk of inadvertent exposure to mutagenic substances. Scientific communication plays a central role in this debate. It is necessary to counter the marketing narrative, which often reinforces the appeal to "natural", with data from toxicological research that shows potential risks. Only then will it be possible to rebalance public perception. From a regulatory point of view, the weakness in the supervision

of the commercialization of natural products amplifies the problem. Herbal medicines derived from species with knowledge gaps, such as (World Health Organization, 2007) (Izzo; Ernst, 2001) *G. glaucescens,* can reach the market without any proof of safety. This reality poses challenges to public health. (Shaw, 2010)

The myth of "natural does not hurt" also impacts the behavior of patients who use herbal medicines in combination with conventional medicines. The resulting interactions can compromise established pharmacological therapies, generating serious consequences. This risk is still little explored in studies on (Fugh-Berman, 2000) *G. glaucescens.* Recent research in toxicology has shown that the indiscriminate consumption of medicinal plants may be associated with increased markers of genomic instability in exposed populations. This evidence reinforces that the discussion goes beyond hypotheses and approaches measurable impacts. (Cruz, 2015)

It should be noted that modern pharmacology has already demonstrated that many synthetic compounds derived from plants were only accepted after rigorous toxicological evaluation. Thus, there is no justification for not applying the same rigor to species such as (Butler, 2008) *G. glaucescens.* The scientific debate, therefore, is not about denying the potential benefits of medicinal plants, but about recognizing that benefits and risks coexist. For *G. glaucescens,* this duality is especially evident and needs to be addressed in a transparent way. (Capasso et al., 2000)

It is concluded that overcoming the myth "natural does no harm" is an indispensable condition for the safe use of *G. glaucescens.* The integration between ethnobotany, pharmacology, toxicology and scientific communication will be the way to transform this species into a reliable therapeutic resource, without compromising collective health. (Jordan; Cunningham; Marles, 2010)

4 CONCLUSION

The analysis of *Galactia glaucescens* shows a central duality: while it has relevant pharmacological properties, such as antivenom and antioxidant activities, it also brings uncertainties regarding its toxic and genotoxic potential. This ambivalence reinforces the need for their use to be accompanied by rigorous scientific protocols, especially in a scenario in which the valorization of natural products is still permeated by myths of absolute safety.

Future perspectives indicate that biotechnology, nanotechnology and metabolomics can play fundamental roles in the safer and more effective exploitation of the species, allowing both the standardization of extracts and the identification and isolation of bioactive compounds with

lower toxicological risk. However, such advances will only be relevant if accompanied by an ethical approach, which respects traditional knowledge and avoids the predatory exploitation of natural resources.

Overcoming the popular imagination that "natural does no harm" is an indispensable condition to transform *G. glaucescens* into a reliable therapeutic resource. This requires integration between ethnobotany, pharmacology, toxicology, biotechnology, and scholarly communication, in order to balance risks and benefits. Thus, the future of the species in the field of phytotherapy will depend not only on technological innovation, but also on scientific and regulatory responsibility to ensure its safety and effectiveness.

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