Research, Society and Development, v. 12, n. 1, e7312139161, 2023
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v13i1.39161

Therapeutical potential of *Psidium guajava* L. (guava tree) for the development of pharmaceutical products

Potencial terapêutico da *Psidium guajava* L. (goiabeira) para o desenvolvimento de produtos farmacêuticos

Potencial terapéutico de *Psidium guajava* L. (árbol de guayaba) para el desarrollo de productos farmacéuticos

Received: 12/09/2022 | Revised: 12/29/2022 | Accepted: 12/30/2022 | Published: 01/01/2023

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Abstract

The *Psidium guajava* is a species utilized traditionally to treat many pathologies for presenting a variety of phytochemicals, for: flavonoids, terpenoids, tannins, cineol, β-karyophylene. With the intent of exploring the pharmacological potential of *P.guajava*, its use for the creation of pharmaceutical products, an integrative review of the literature was made, using the guiding question: "How can the guava tree's therapeutic potential contribute to the development of new pharmaceutical products?". The searches ocurred in official documents and cientific articles indexed to the ANVISA data base of Scielo, PubMed and Lilacs, during the months of august and september of 2022. The describers used were: Phytotherapy, complementary therapies, Psidium, Therapeutic Action and Pharmaceutical Products being crossed with the help of operator And. Were considered as criteria of inclusion official documents and complete articles available for access, indexed to the aforementioned platforms, in english and portuguese, between 2012 and 2022, and as criteria of exclusion, duplicated studies, studies with thematic escape and that weren't available for access both free and in full, resulting in an atmosphere of 16 files. The researches has shown that the guava tree presents several therapeutic actions, such as: antioxidant, anti-inflammatory, photoprotective, antibacterial, anticariogenic, anti-tumor, antispasmodic, hypoglycemic, nephroprotective, anti-diarrheal, antinociceptive, healing,

cytotoxic, and acts against dermatitis. Therefore, the bioactive compounds of this vegetable can be used for the development of pharmaceutical products with the purpose of expanding the therapeutic options in the market and optimize the patients' quality of life becoming fundamental to foster cientific researches that discuss about the safety, efficiency and toxicity of the using these metabolites.
Keywords: Phytotherapy; Complementary therapies; Psidium; Therapeutics; Pharmaceutical products.

Resumo

A *Psidium guajava* é uma espécie utilizada tradicionalmente para tratar diversas patologias por apresentar uma variedade de compostos fitoquímicos, como: flavonoides, terpenoides, taninos, cineol, β-cariofileno. Com intuito de explorar o potencial farmacológico da *P.guajava* vislumbrando a criação de produtos farmacêuticos foi realizada uma revisão integrativa da literatura, utilizando a questão norteadora: "Como o potencial terapêutico da goiabeira pode contribuir para o desenvolvimento de novos produtos farmacêuticos?". As buscas ocorreram em documentos oficiais da ANVISA e em artigos científicos indexados nas bases de dados do Scielo, PubMed e Lilacs, durante os meses de agosto e setembro de 2022. Os descritores utilizados foram: Fitoterapia, Terapias Complementares, Psidium, Ação Terapêutica e Produtos Farmacêuticos sendo cruzados com auxílio do operador And. Considerou-se como critérios de inclusão artigos completos disponíveis para acesso e documentos oficiais indexados nas plataformas supracitadas, em inglês e português, entre 2012 a 2022 e como critérios de exclusão estudos duplicatos, com fuga temática, que não estavam disponíveis para acesso livre e na íntegra, resultando numa amostra de 16 arquivos. As pesquisas evidenciaram que a goiabeira apresenta diversas ações terapêuticas como: antioxidante, anti-inflamatória, fotoprotetora, antibacteriana, anticariogênica, anti-tumoral, antiplasmódica, hipoglicemiante, nefroprotetora, antiglicante, antidiarreica, antinociceptiva, cicatrizante, citotóxica e atua frente a dermatite. Portanto, os compostos bioativos desse vegetal podem ser empregados para o desenvolvimento de produtos farmacêuticos com o propósito de ampliar as opções terapêuticas no mercado e otimizar a qualidade de vida dos pacientes tornando-se fundamental o fomento às pesquisas científicas que discorram sobre a segurança, eficácia e toxicidade do uso desses metabólitos.
Palavras-chave: Fitoterapia; Terapias complementares; Psidium; Ação terapêutica; Produtos farmacêuticos.

Resumen

Psidium guajava es una especie tradicionalmente utilizada para tratar diversas patologías debido a que presenta una variedad de compuestos fitoquímicos, tales como: flavonoides, terpenoides, taninos, cineol, β-cariofileno. Con el fin de explorar el potencial farmacológico de *P.guajava*, vislumbrando la creación de productos farmacéuticos, se realizó una revisión integrativa de la literatura, teniendo como pregunta guía: "¿Cómo el potencial terapéutico del árbol de guayaba puede contribuir al desarrollo de nuevos productos farmacéuticos? ?". Las búsquedas se realizaron en documentos oficiales de ANVISA y en artículos científicos indexados en las bases de datos Scielo, PubMed y Lilacs, durante los meses de agosto y septiembre de 2022. Los descriptores utilizados fueron: Fitoterapia, Terapias Complementarias, Psidium, Acción Terapéutica y Productos Farmacéuticos en cruce con la ayuda del operador Y. Fueron criterios de inclusión artículos completos disponibles para acceso y documentos oficiales indexados en las mencionadas plataformas, en inglés y portugués, entre 2012 y 2022, y como criterios de exclusión, estudios duplicados, con fuga temática, que no estuvieran disponibles para libre acceso y en en su totalidad, resultando una muestra de 16 archivos. Las investigaciones han demostrado que el árbol de guayaba tiene varias acciones terapéuticas como: antioxidante, antiinflamatoria, fotoprotectora, antibacteriana, anticariogénica, antitumoral, antiplasmódica, hipoglucemiante, nefroprotectora, antiglicante, antidiarreica, antinociceptiva, cicatrizante, citotóxica y actúa contra la dermatitis. Por lo tanto, los compuestos bioactivos de esta planta pueden ser utilizados para el desarrollo de productos farmacéuticos con el propósito de ampliar las opciones terapéuticas en el mercado y optimizar la calidad de vida de los pacientes, por lo que es fundamental promover la investigación científica que discuta la seguridad, eficacia y toxicidad por el uso de estos metabolitos.
Palabras clave: Fitoterapia; Terapias complementarias; Psidium; Terapéutica; Productos farmacéuticos.

1. Introduction

The use of medicinal plants in the health-disease process is a practice that transcends generations, historical data report that since antiquity, plants have been used with a curative character (Leite et al., 2015). For this use, Western culture created the term Phytotherapy, which consists of the combination of Python meaning "plants" and Therapeia "treatment" (KIiliç et al., 2016). In Brazil, the accumulation of knowledge in the field of herbal medicine is attributed to miscegenation and strengthened by the development of scientific research in the area of natural products, intended for health care (Caetano, 2016).

In view of this, the use of vegetable preparations for cosmetics, beverages, foods and medicines has grown extensively, in which a market growth of preparations with vegetable raw material of around US$ 86.74 billion is projected until 2022 worldwide, with emphasis on the pharmaceutical and nutraceutical industry. Interestingly, the part of the plant most used in

vegetable preparations for the most diverse applications is the leaf, which stands out as the most accumulating part of secondary metabolites (Kumar et al. 2021). This is due to the presence of secretory structures on the surface or inside the leaves, such as nectaries, resinous ducts, secretory vesicles, saline glands, oil cells and secretory trichomes, which are structures responsible for the synthesis and accumulation of bioactive compounds. However, the degree of maturity of the structures influences the yield and quality of medicinal materials (Li et al. 2020).

The guava leaf (*Psidium guajava* L.) it is a rich source for the creation of therapeutic products because its biological constituents trigger various actions such as antioxidant, antidiarrheal, acts against stomach pains and acts as a hypoglycemic. These characteristics are described by popular medicine and proven by scientific studies that used extracts from parts of this plant (Hirudkar et al., 2020; Huang et al., 2022).

It is worth noting that one of the goals defined by the United Nations (UN) is to guarantee access to medicines in a safe, effective way, with quality and at a fair price, in order to promote the well-being and ensure the health of the world's population. From this perspective, the herbal medicine industry is promising, as it has great potential for innovation in health based on the exploitation of the rich plant biodiversity. These actions favor the introduction of new therapeutic options offered to individuals that indirectly optimize health care (Hasenclever et al., 2017).

Herbal products are manufactured using strictly active vegetable raw materials. They must follow efficacy standards, have defined the risks of their use, guarantee reproducibility and quality (Oliveira & Ropke, 2016). A research that was based on the set of records of new Chemical Entities on the planet between the years 1981 to 2010, concluded that 27% were related to natural products, their derivatives and herbal medicines. The same study states that 24% of synthetic medicines were inspired from natural substrates, 2% biological items and 1% related to vaccine development, consolidating that biodiversity is an important source for the emergence of pharmaceuticals (Newman & Cragg, 2012; Pimentel et al., 2015).

In addition, it should be noted that the guava tree is of great economic importance in many countries around the world, due to its high yield and variety of products derived from its fruits. As cultivation is carried out in more than 60 countries, whose world production is estimated at around 40 million tons in 2020. India is the world's largest producer, followed by China and Kenya, also highlighting Brazil and Venezuela, where Mexico ranks fifth in the world with a production of 302,718 tons per year, with an increase of the harvested area of 5%, in which 4% of the total production is exported (Angulo-López et al., 2021).

Given the above, the present work aims to carry out an integrative literature review based on the broad therapeutic potential of P. guajava for the development of pharmaceutical products. Based on the use of the species in popular medicine and proven by scientific studies, it is possible to propose the use of bioactive compounds present in this plant in order to stimulate the development of products for the treatment of various pathologies that contribute to an improvement in the clinical picture and consequent increase in the quality of life of users.

2. Methodology

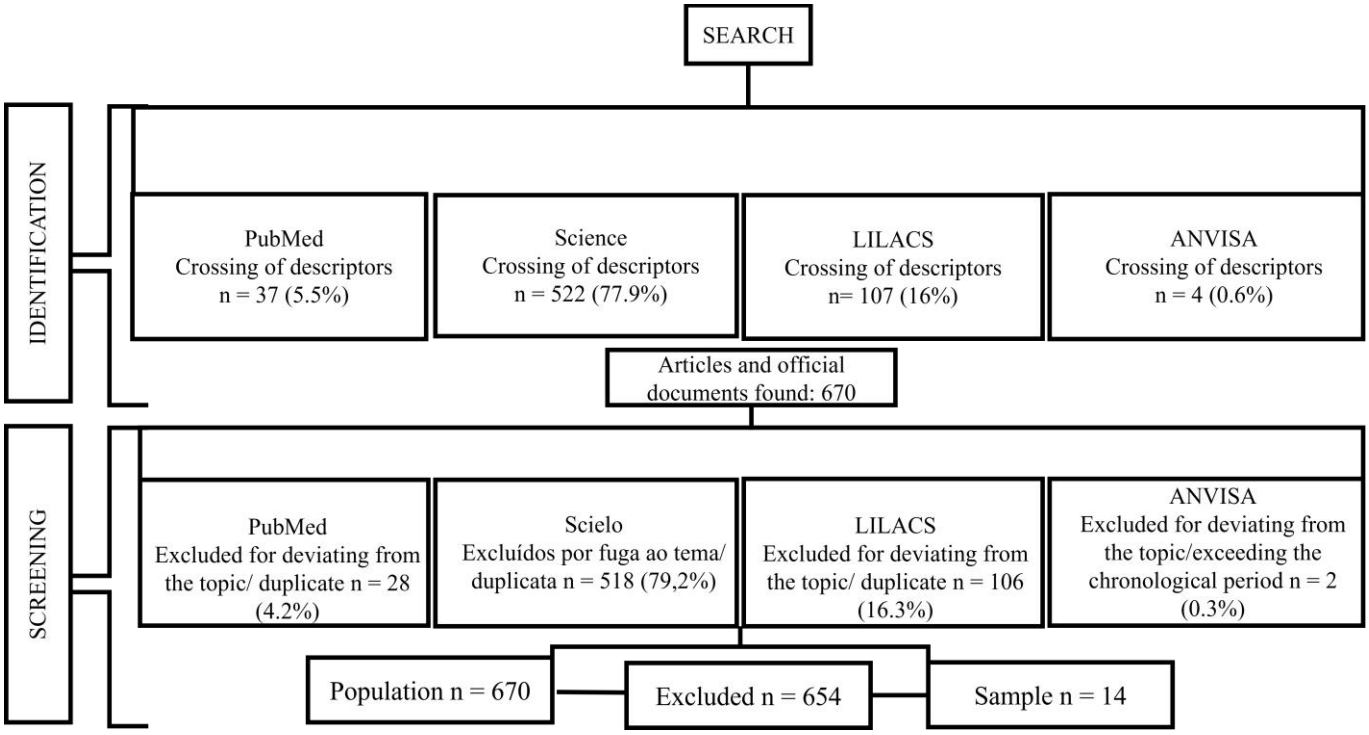
An integrative literature review was carried out to obtain scientific productions, using the following guiding question: “How can the therapeutic potential of *P.guajava* contribute to the development of pharmaceutical products?”. The integrative review is a technique that allows performing the search for data, discussing them through a critical analysis in which it summarizes the main conclusions according to the theme addressed, and its outcome is important to achieve an overview of the subject studied. and, with that, stimulate the implementation of new knowledge that direct future studies and solidify strategies for optimizing the population's health and quality of life, as well as allowing to reduce public health expenses (Mendes et al., 2008).

In view of this, data collection was carried out on the bases: Scientific Electronic Library Online (SciELO), National Library of Medicine (PubMed), Latin American and Caribbean Literature in Health Sciences (LILACS) and on the ANVISA platform, during the August and September 2022. The sample consisted of official documents and scientific articles indexed in the aforementioned databases, identified through the use of descriptors in the vernacular and English: "Phytotherapy", "Complementary Therapies", "Psidium", "Therapeutic Action" and "Pharmaceutical Products" which were based on Health Sciences Descriptors (DeCS). The data collection procedure employed the intersection of the chosen descriptors through the use of the Boolean operator "And". Subsequently, the sample was selected according to the inclusion criteria: documents with full text, available for access, indexed in the aforementioned databases, written in English and Portuguese and published between the years 2012 to 2022. As exclusion criteria, were considered: Research considered duplicates, which did not address the proposed theme, did not have free and full access. For the elaboration of the writing, a qualitative analysis of the content of the selected sample was used, aiming to confirm the possibility of using the chosen species for the elaboration of therapeutic products, through a pre-analysis in which the files were chosen, followed by the exploration of the material and later treatment of the results, allowing the juxtaposition of the listed ideas to reach an understanding about the guiding question of this study (Schiavini & Garrido, 2018).

3. Results and discussion

After applying the selection criteria, the files were descriptively analyzed according to absolute and relative frequency using Microsoft Excel® software. 670 articles were found, of which 37 are located in the PubMed database, 522 in SciELO, 107 in LILACS and 4 documents issued by ANVISA, after sorting, the final sample consisted of 14 articles and 2 official documents (Figure 1).

Figure 1 - Flowchart for searching and selecting official articles and documents.



Source: Prepared by the authors (2022).

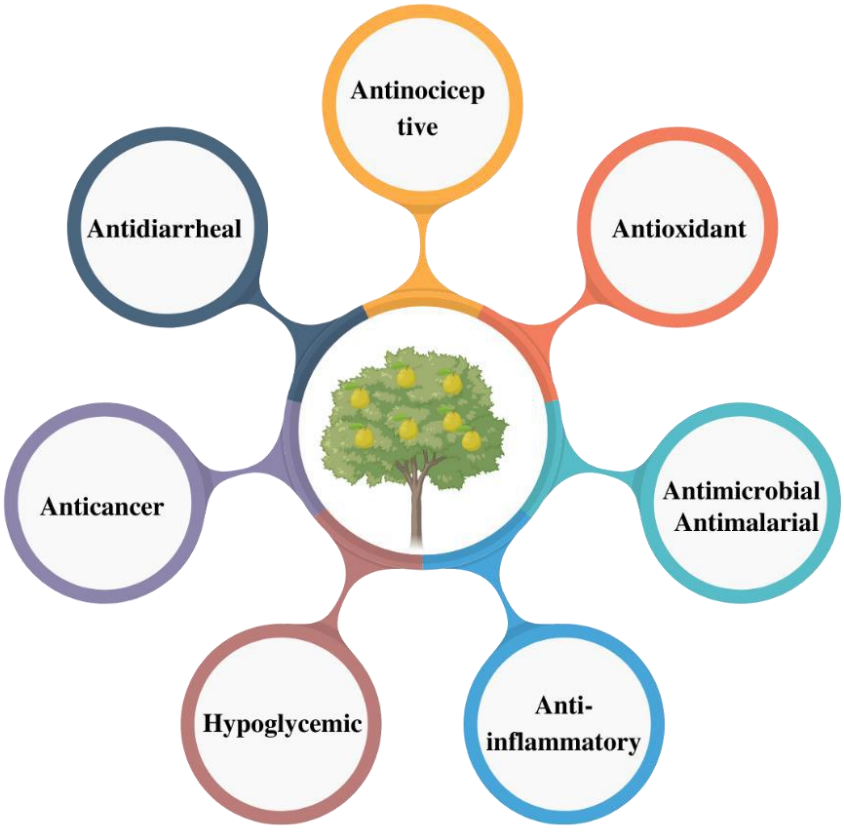
It is important to emphasize through this flowchart that the searches took place on different platforms, allowing the selection of a list of files that were used for discussion and proof of the vast capacity of action of the resources extracted from P. guajava as therapeutic inputs for the creation of pharmaceutical products.

Due to its wide use, *P.guajava* is standardized in several official compendiums such as the National List of Medicinal Plants of Interest of the SUS (RENISUS), in the Brazilian Pharmacopoeia Phytotherapy Form and in the Memento Phytoterapic of the Brazilian Pharmacopoeia. These documents aim to guide the prescription of medicinal species such as guava (bringing therapeutic indications, contraindications, adverse effects, precautions for use and type of pharmaceutical forms in which they can be used) encourage research in the field of herbal medicine, their teaching at universities and institute plants as a basic input for the emergence of new therapeutic tools (Brasil, 2016, 2021; Mazzari & Prieto, 2014).

P. guajava is a member of the *Myrtaceae* family which is widespread throughout the world, especially in the Americas, Asia and Australia. The gender *Psidium* It has approximately 150 types of bushes, among them the guava tree, which is the most popular (Pereira et al., 2017). This plant is distinguished by its arboreal size and can reach up to 8 meters in height., elliptical sheet, leathery, lonely flower and rounded fruits, glabrous, which when they are ripe take on a yellowish color (Tuler et al., 2017).

Guava is chemically constituted by several types of secondary metabolites such as: flavonoids, terpenoids (sesquiterpenes and triterpenes), tannins and its essential oil is composed of cineol, eugenol, kaempferol, malic acid, gallic acid, β-caryophyllene, α-humulene, aromadendrene oxide, δ-selinene and Selin-11-en-4alpha-ol (Brasil, 2016; Shaheena et al., 2019; Silva et al., 2018). These secondary metabolites confer numerous biological activities, as seen in Figure 2.

Figure 2 - Biological activities related to P. guajava extract.



Source: Prepared by the authors (2022).

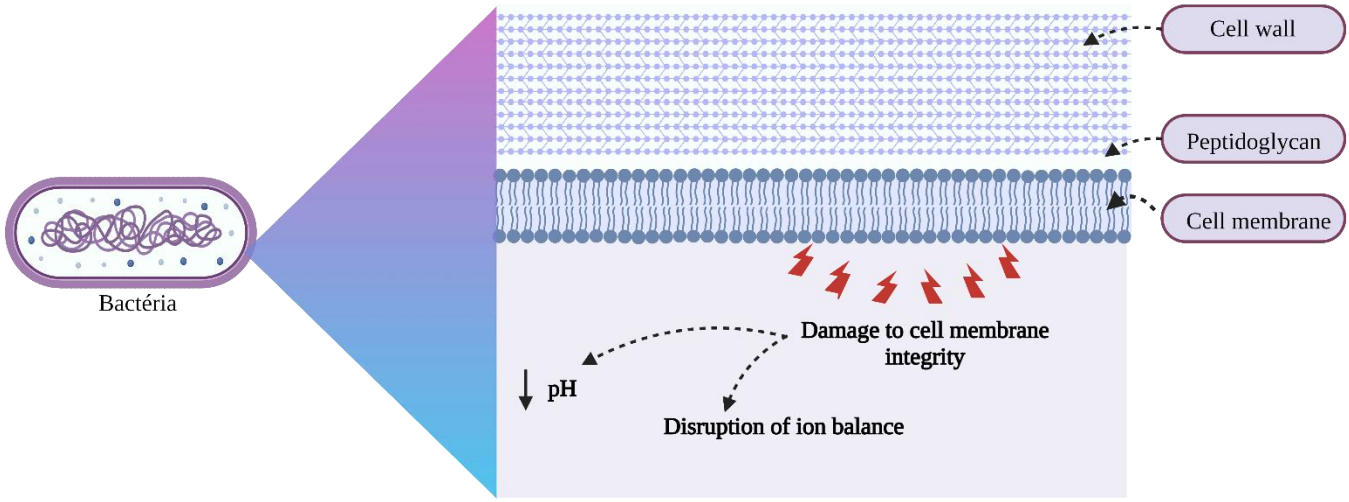
These compounds are responsible for the pharmacological actions of this species, for example, a research evaluated the effect of guava leaf extract in three formulations (F1-10% extract), (F2-15% extract), (F3- 20% extract) of toothpaste containing other excipients (Arabic gum, stevia, salt, extra virgin coconut oil, peppermint oil, distilled water). Criteria related to pH parameters were analyzed, degree of abrasiveness, sparkling capacity, spreading and cleaning action. It was highlighted that the F3 formulation demonstrated antioxidant capacity, antimicrobial, low cytotoxicity, good spreadability and great cleaning ability. Demonstrating an eco-friendly alternative, with therapeutic capacity to promote hygiene and oral care (Shaheena et al., 2019).

P.guajava has in its phytochemical composition a lycopene content and total phenols that are responsible for its antioxidant activity (Zapata et al., 2014). One study showed that an extract rich in lycopene from red guava presented, anti-inflammatory activity by reducing inflammatory markers such as TNFα, IL1B and IL6 in hypertensive and diabetic patients (Londoño et al., 2019). Quercetin, quercetin-3-O-glucopyranoside and morphine are phytochemical compounds that can be isolated from the guava leaf and, that exhibit anti-oxidant activity, by inducing the balance of free radicals, due to the high reducing power (Naseer et al. 2018). However, despite the antioxidant and anti-inflammatory potential being a new therapeutic alternative, the real mechanism involved in the antioxidant activity is still not fully elucidated.

Fresh *P. guajava* leaf essential oil acts as antibacterial *in vitro* against various oral bacteria of the genus *Streptococcus* as *S. salivarius*, *S. mutans*, *S. mitis*, *S. sanguinis* and *S. sobrinus* (Silva et al., 2018). This activity comes from the chemical components of guava, such as β-caryophyllene, α-humulene, aromadendrene oxide, δ-selinene and selin-11-en-4α-ol, which are present in the oil of the aerial parts of this vegetable (Silva et al., 2018). In general, it is described that essential oils act through damage to the integrity of the microorganism cell membrane, which affect microbial growth, deregulating cell pH and homeostasis of inorganic ions (Figure 3) (Oliveira et al., 2016).

Dental caries is a multifactorial disease that is influenced by *S. mutans*, in this perspective, research was carried out with humans in which they were submitted to chewing guava leaves to evaluate the impacts of this practice on caries. The results demonstrated that the treatment decreased the bacterial load through the action of bioactive compounds on sucrose active sites and inhibited the formation of glucan, revealing potential to act as a tool for dental treatments in terms of reducing bacterial plaque (Bhagavathy et al., 2019).

Figure 3 - Mechanism of action of the antibacterial activity of the leaf of *P. guajava*.



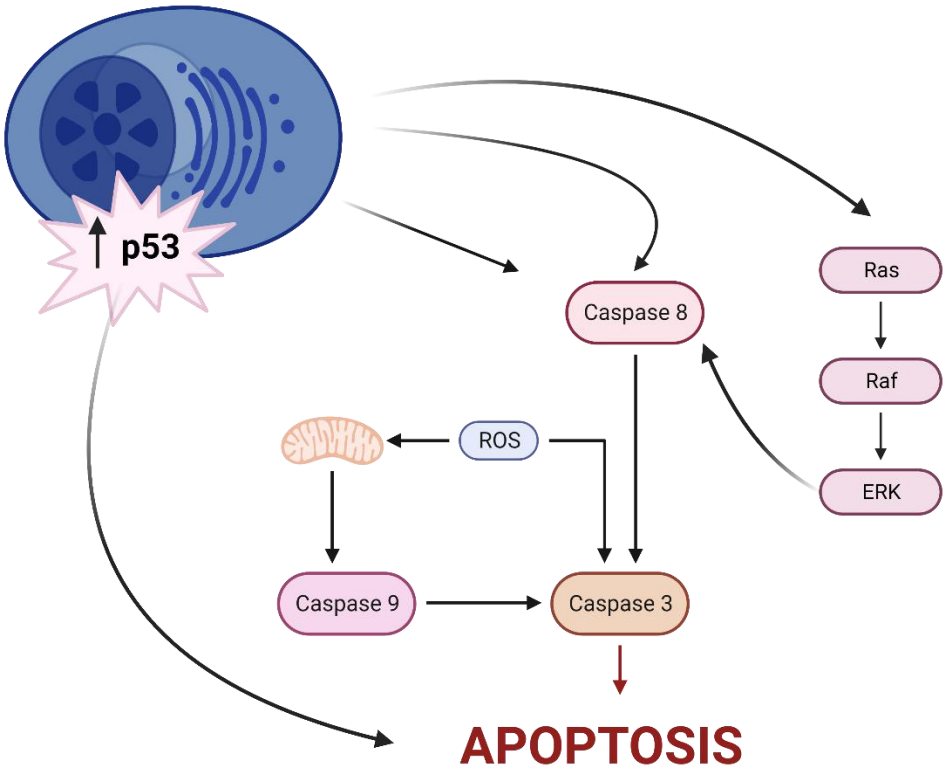
Source: Prepared by the authors (2022).

One study focused on the extraction of three compounds with anticancer action from P. guajava leaves, respectively: guavinoside E, 3,5-dihydroxy-2,4-dimethyl-1-O-(6'-O-galloyl-β-d-glucopyranosyl)-benzophenone and guavinoside B. Cell

viability tests described that the second and third substance were able to inhibit the growth of human colon cancer cells HCT116 in a dose-dependent manner, in which substance 2 was more effective in inducing cell apoptosis compared to active 3. Furthermore, it is worth noting that 3,5-dihydroxy-2,4-dimethyl-1-O-(6'-O-galloyl-β-d-glucopyranosyl)-benzophenone and guavinoside B, were able to control the expression levels of proteins related to cell proliferation and apoptosis signaling. Substance 2 significantly increased levels of p53, p-ERK1/2, p-JNK and cleaved caspases 8 and 9, and compound 3 increased levels of p53 and cleaved caspase 8. This highlights the possibility of using the leaves of this plant to extract chemotherapy substrates with a focus on colon câncer (Zhu et al., 2019).

Guava leaves can also be used as an antimalarial agent due to its inhibitory capacity, an analysis developed with ethyl acetate and methanol extracts derived from the leaves of this plant were tested against *Plasmodium falciparum in vitro* and the results were validated using the fluorescence signal as parameters and based on the Giemsa staining method and it was concluded that this species has a promising antiplasmodic activity (Kaushik et al., 2015).

Figure 4 - Mechanism of action of the anticancer activity of the leaf of *P. guajava*.



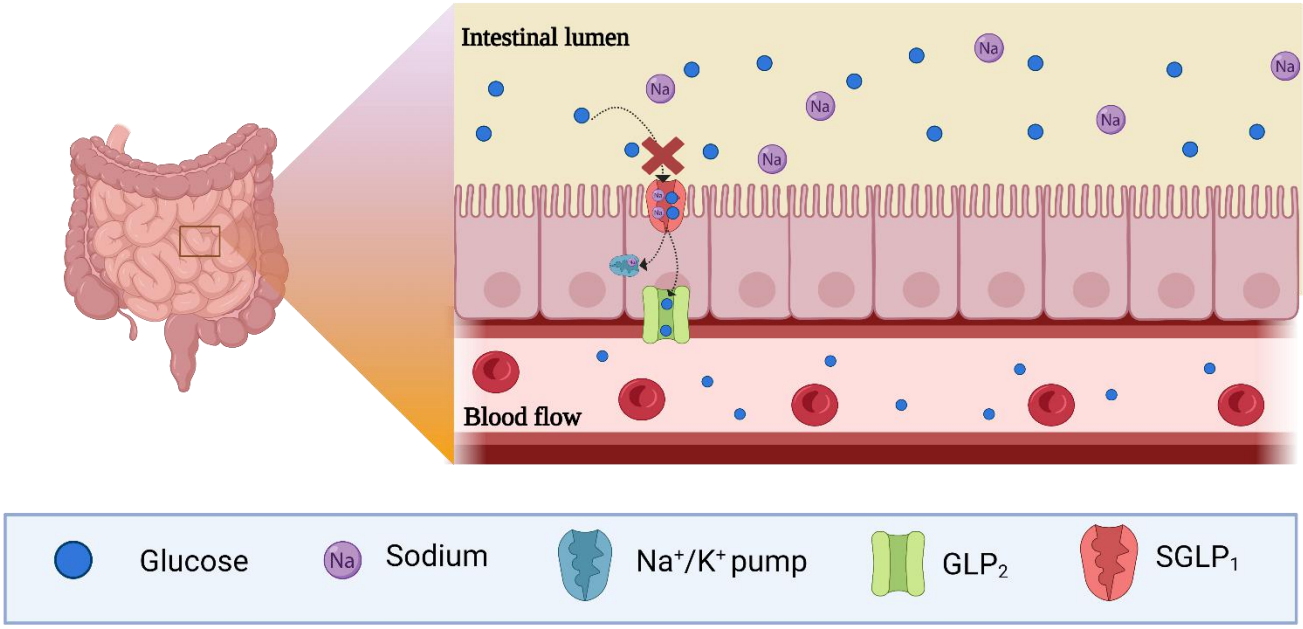
Source: Prepared by the authors (2022).

A study carried out with diabetic mice evaluated the effect of polysaccharides isolated from the guava leaf, this product has *in vitro* antioxidant activity and potentially decreases fasting blood glucose, total cholesterol and triglycerides, fructosamine, creatinine and malondialdehyde *in vivo*. Furthermore, significantly increased the action of the superoxide enzyme and reduced damage to the liver, kidney and pancreas of the animals. Thus, these polysaccharides can be incorporated into functional foods and complementary drugs to explore their antioxidant and hypoglycemic effects (Luo et al., 2019). This was also seen by Díaz-de-Cerio et al. (2017) when conducting a study with obese mice, that when using guava leaf extract at a concentration of 5 mg/kg, showed a reduction of all serum lipid markers, except LDL, which may be associated with reduced insulin resistance.

The aqueous extract prepared from the fruit of *P. guajava* when incorporated into the diet of mice at a concentration of 1% over a period of 12 weeks, it was able to potentially decrease glucose levels, urea in the blood and increase insulin levels in the plasma of these animals. Thus, the fruit has the ability to act by protecting the kidney against diabetic nephropathy through antioxidant, anti-inflammatory and antiglycant actions (Lin & Yin, 2012).

In some recent studies, GLUT2 was found to be associated with the intestinal transport of glucose across the membrane of enterotics. Therefore, the prevention and regulation of hyperglycemia include the use of substances that mimic insulin, direct manipulation of GLUT4, which directly regulates glucose in the bloodstream, as well as reducing glucose uptake in the small intestine through inhibition of SGLT1 transporters. and GLUT2. A study carried out with guava leaf and fruit extract, promotes the hypoglycemic effect through the inhibition of GLUT2 and SGLT1, as well as reduces the intestinal transport of glucose in vitro and in vivo (Müller et al.,2018) (Figure 5).

Figure 5 - Mechanism of action of the hypoglycemic effect of the *P. guajava* leaf.



Source: Prepared by the authors (2022).

Diarrhea is a disease that shows resistance to conventional drugs, being a growing health problem. In view of this, with the aim of discovering therapeutic alternatives for the treatment of this pathology, an *in vivo* research was carried out with the decoction of guava leaves and the results showed that the decoction prepared with 14 leaves, administered three times a day was effective in restoring the body's homeostasis, reducing treatment time by 48 hours and the patients demonstrated normal renal, hepatic and hemoglobin parameters (Birdi et al., 2020).

P. guajava has antinociceptive activity, in a study carried out *in vivo* with guinea pigs, the results showed that the extract of the bark of this vegetable induced an antinociceptive response in all models of mechanical and peripheral nociception through activation of central and peripheral mechanisms compared to the control group that was tested with aspirin and tramadol (Sekhar et al., 2014).

It is pertinent to portray the healing potential of plant extracts for second intention wounds. An analysis performed *in vivo* with mice using a 5% Bepantol® aqueous solution as a positive control (PC), negative control sterile water (NC) and

experimental groups aqueous extract of guava stem bark (10%-GO) and jabuticabeira leaf extract (1 g/mL-JU), demonstrated that in five days after the start of treatment there is a change in the time of wound closure, through accelerated re-epithelialization and lower number of acute inflammatory cells (for CP, GO and JU). With 10 days of treatment, GO was able to stimulate the formation of a smaller scar, with deposition of collagen fibers closer to the skin while for JU there was an advanced repair, with excellent vascularization and low inflammation, but there was no superiority in relation to the group treated with CP. This represents a promising path for the development of further research, since this work points out that there is no standardization in the literature regarding the concentration, route of administration and frequency of use of extracts with healing activity (Faria et al., 2019).

Dermatitis is an inflammatory skin disease that causes eczema and overproduction of immunoglobulin Eneeds pharmacological treatment. That said, to verify the activity of the aqueous extract of *P. guajava* to curb atopic dermatitis, a study was carried out with mice in which skin lesions were induced through the use of 2,4 dinitrochlorobenzene and it was verified that the cream containing the aqueous extract of this vegetable can act as a complementary therapy capable of containing pruritus and effectively controlling this type of lesion (Choi et al., 2012).

A survey in which the Sun Protection Factor was evaluated (SPF) of guava extract standardized in ellagic acid in emulsions for topical use in vitro compared to a synthetic chemical filter in the aspect of photoprotection of guava extract standardized in ellagic acid in emulsions for topical use in vitro compared to a synthetic chemical filter in the aspect of photoprotection, the extract demonstrated synergistic activity in relation to methoxycinnamate sunscreen. Therefore, the phytocosmetic was able to absorb radiation in the ultraviolet range (UVB) and increased the sun protection factor by 17.99% demonstrating that this vegetable is a valuable complementary source for the development of cosmetic products aimed at photoprotection (Milani et al., 2018).

In view of this, in order to provide the information indicated in a more synthetic way, a table was prepared (Table 1) with the arrangement of the articles according to author, year of publication, file title, origin and the main considerations about *P.guajava*.

Table 1 - Distribution of articles according to Year of publication, Title, Origin and Considerations about *P.guajava*.

Year	Title	Origin	Considerations
2014	Capacidad atrapadora de radicales oxígeno (ORAC) y fenoles totales de frutas y hortalizas de Colombia.	Scielo	Antioxidant activity of guava.
2019	Effect of the consumption of a food based on fruits and natural additives in patients with cardiovascular risk.	Scielo	Anti-inflammatory action of red guava extract evidenced in hypertensive and diabetic patients.
2018	Extract from byproduct *Psidium guajava* standardized in ellagic acid: additivation of the in vitro photoprotective efficacy of a cosmetic formulation.	Scielo	Guava extract standardized in ellagic acid and incorporated into emulsions for topical use has *in vitro* photoprotective activity.
2019	Antibacterial and antiproliferative activities of the fresh leaf essential oil of *Psidium guajava* L.(Myrtaceae).	Scielo	Guava leaf essential oil has antibacterial activity against species of the genus *Streptococcus in vitro*.
2019	Identification of glucosyl transferase inhibitors from *Psidium guajava* against *Streptococcus mutans* in dental caries.	PubMed	*P. guajava* leaves show *in vivo* anticariogenic activity.
2019	Identification of a new benzophenone from *Psidium guajava* L. leaves and its antineoplastic effects on human colon cancer cells	PubMed	The extract of the leaves of *P.guajava* in a research demonstrated perspective of acting against colon cancer, since they hold three relevant compounds guavinoside E, 3,5-dihydroxy-2,4-dimethyl-1-O-(6'- O-galloyl-β-d-glucopyranosyl)-benzophenone and guavinoside B.

2015	Evaluation of antiplasmodial activity of medicinal plants from North Indian Buchpora and South Indian Eastern Ghats.	PubMed	Ethyl acetate and methanol extracts derived from *P. guajava* leaves in an in vitro assay demonstrated antiplasmodic activity.
2019	Antioxidant and anti-diabetic activities of polysaccharides from guava leaves.	PubMed	Polysaccharides isolated from guava leaves have antioxidant (*in vitro*) and hypoglycemic (*in vivo*) action.
2012	Renal protective effects of extracts from guava fruit (*Psidium guajava* L.) in diabetic mice.	PubMed	The aqueous extract of guava tree has nephroprotective activity (*in vivo*) due to its antioxidant, anti-inflammatory and antiglycant actions.
2020	A randomized open label efficacy clinical trial of oral guava leaf decoction in patients with acute infectious diarrhoea.	PubMed	The decoction of P. guajava leaves demonstrated *in vivo* antidiarrheal action.
2014	Evaluation of antinociceptive activity of aqueous extract of bark of *Psidium guajava* in albino rats and albino mice.	PubMed	Guava bark extract has *in vivo* antinociceptive activity.
2019	Potencial de cicatrização da *Psidium Guajava* e *Myrciaria cauliflora* em feridas cutâneas: avaliação histológica em estudo de modelo experimental	Lilacs	In a study carried out in vivo, the extracts from the stem bark of the guava tree *Psidium Guajava* and from the leaves of Myrciaria cauliflora showed healing activity for second intention wounds.
2012	Inhibitory effect of *Psidium guajava* water extract in the development of 2, 4-dinitrochlorobenzene-induced atopic dermatitis in NC/Nga mice.	PubMed	The aqueous extract of P. guajava demonstrates effectiveness in combating pruritus and treating atopic dermatitis *in vivo.*
2016	Memento Fitoterápico da Farmacopeia Brasileira	ANVISA	Capsules or tablets containing the plant drug or dry extract, and infusion are for the treatment of acute non-infectious diarrhea and rotavirus enteritis
2021	Formulário de Fitoterápicos da Farmacopéia Brasileira	ANVISA	Infusion of *P. guajava* leaves acts as an aid in the treatment of mild non-infectious diarrhea
2019	Extraction of bioactive compounds from *Psidium guajava* and their application in dentistry	PubMed	*P. guajava* leaf extract demonstrated antioxidant and antimicrobial activity quando incorporado em formulações de pasta dental

Source: Prepared by the authors (2022).

From this table it is possible to observe that *Psidium guajava* is a species with broad therapeutic properties in which all parts of the plant can be explored for the development of pharmaceutical products of commercial interest, promoting the execution of research using this plant.

The study of natural products is closely related to pharmaceutical technology for potential application in the preparation of pharmacological items, in which through the techniques of identification, definition and quantification of plant metabolites it is possible to develop phytopharmaceuticals with safety, efficacy and quality. The progress in research involving herbal medicines allows the creation of a wide arsenal of studies in the fields of pharmacology and toxicology, which represents an area of great therapeutic interest for the exploration of the pharmaceutical industries.

4. Conclusion

It can be concluded that *P.guajava* presents bioactive compounds effective for the treatment of various diseases can be used to formulate new pharmaceutical products that will offer an optimization of the existing therapies generating direct benefits to the quality of life of the patients. It is worth mentioning that as limiting criteria of this review, the deficiency of research demonstrating the side effects, the determination of efficacy in the clinical context and the design of the safe use of these metabolites, signaling the need to develop new studies based on these principles that support the construction of pharmaceutical products with high technological rigor.

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