Arabian Journal of Chemistry (2022) **15**, 103759

King Saud University

Arabian Journal of Chemistry

www.ksu.edu.sa
www.sciencedirect.com

REVIEW ARTICLE

The ethnobotanical, phytochemistry and pharmacological activities of *Psidium guajava* L.

Eziuche Amadike Ugbogu [a,*], Okezie Emmanuel [a], Miracle Ebubechi Uche [a], Emmanuel Dike Dike [a], Benedict Chukwuebuka Okoro [a], Chibuike Ibe [b], Victor Chibueze Ude [c], Celestine Nwabu Ekweogu [d], Ositadinma Chinyere Ugbogu [b]

[a] *Department of Biochemistry, Abia State University, PMB 2000, Uturu, Abia State, Nigeria*
[b] *Department of Microbiology, Abia State University, Uturu, PMB 2000, Uturu, Abia State, Nigeria*
[c] *Department of Medical Biochemistry, College of Medicine Enugu State University of Science and Technology, PMB 01660 Enugu, Nigeria*
[d] *Department of Medical Biochemistry, Imo State University, PMB 2000, Owerri, Imo State, Nigeria*

Received 8 November 2021; accepted 30 January 2022
Available online 3 February 2022

KEYWORDS

Phytochemistry;
Pharmacological;
Psidium guajava;
Traditional uses;
Toxicity Profile

Abstract *Psidium guajava* L., commonly known as guava is an important tropical food plant with diverse medicinal values. In traditional medicine, it is used in the treatment of various diseases such as diarrhoea, diabetes, rheumatism, ulcers, malaria, cough, and bacterial infections. The aim of this review is to provide up-to-date information on the ethnomedicinal uses, bioactive compounds, and pharmacological activities of *P. guajava* with greater emphasis on its therapeutic potentials. The bioactive constituents extracted from *P. guajava* include phytochemicals (gallic acid, casuariin, catechin, chlorogenic acid, rutin, vanillic acid, quercetin, syringic acid, kaempferol, apigenin, cinnamic acid, luteolin, quercetin-3-O-α-L-arabinopyranoside, morin, ellagic acid, guaijaverin, pedunculoside, asiastic acid, ursolic acid, oleanolic acid, methyl gallate and epicatechin) and essential oils

Abbreviations: *P. guajava*, *Psidium guajava*; HPLC-ESI-QTOF-MS, High-Performance liquid chromatography coupled to electrospray ionization and quadrupole time-of-flight mass spectrometry; GC-FID, Gas Chromatography/Flame Ionization Detector; GC–MS, Gas chromatography/Mass spectrometry; HPLC, High-Performance liquid chromatography; HPLC-DAD, High-Performance Liquid Chromatography with Diode Array Detection.; UPLC-ESI-QTOF-MS, Ultra-Performance liquid chromatography coupled with electrospray ionization tandem quadrupole time-of-flight mass spectrometry; HPLC, High-Performance Liquid Chromatography; HPLC-PDA, High-Performance liquid chromatography photodiode array detection; MIC, Minimum inhibitory concentration; IC_{50}, Half maximal inhibitory concentration; CCl_4, Carbon tetrachloride; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; ALP, Alkaline phosphatase; GGT, Gamma glutamyl transferase; DPPH, 2,2-diphenyl-1-picrylhydrazyl; NIST, National Institute of Science and Technology; MCF-7 cell, Michigan Cancer Foundation-7; HCT116, Human Colorectal carcinoma cell line; HT29, Human Colon cancer cell line

* Corresponding author at: Department of Biochemistry, Faculty of Biological Sciences, PMB 2000, Abia State University, Uturu, Abia, Nigeria.
E-mail address: amasryal@yahoo.com (E. Amadike Ugbogu).

Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

https://doi.org/10.1016/j.arabjc.2022.103759

(limonene, *trans*-caryophyllene, α-humulene, γ-muurolene, selinene, caryophyllene oxide, bisabolol, isocaryophyllene, δ-cadinene, α-copaene, α-cedrene, β-eudesmol, α-pinene, β-pinene, β-myrcene, linalool, α-terpineol and eucalyptol). *In vitro* and *in vivo* studies demonstrated that *P. guajava* possesses pharmacological activities such as antidiabetic, antidiarrhoeal, hepatoprotective, anticancer, antioxidant, anti-inflammatory, antiestrogenic, and antibacterial activities which support its traditional uses. The exhibited pharmacological activities reported may be attributed to the numerous bioactive compounds present in different parts of *P. guajava*. Based on the beneficial effects of *P. guajava* as well as its bioactive constituents, it can be exploited in the development of pharmaceutical products and functional foods. However, there is a need for comprehensive studies in clinical trials to establish the safe doses and efficacy of *P. guajava* for the treatment of several diseases.

Contents

1. Introduction

Globally, medicinal plants and its bioactive constituents are used for the treatment of various diseases. It has been reported that over 80% of the world's population uses medicinal plants or its bioactive compounds for the prevention, management, or treatment of several diseases (Joshi, 2013, Pant, 2014; Ugbogu et al., 2021). Recently, the uses of medicinal plants or their biologically active compounds have attracted the attention of many scientists/researchers because of their use in drug discovery or discovery of natural constituents for therapeutics (Dimmito et al., 2021, Sinan et al., 2021) and in ethnomedicinal uses for the treatment of life-threatening diseases such as cancer, diabetes, and hypertension (Sofowora et al., 2013, WHO, 2019). *Psidium guajava* is one of the plants used in traditional medicine for the treatment of various diseases.

Psidium guajava L. is commonly known as guava. It is a tropical shrub tree and food plant that belongs to the Myrtaceae family (Ravi and Divyashree, 2014). It grows up to 10 m and is widely distributed in many countries. *Psidium guajava* L. is an economically important food plant with diverse medicinal properties. It has a short trunk, patchy, smooth, and peeling bark. The leaves are fleshy dark green with prominent veins (Morais-Braga et al., 2016a; Naseer et al., 2018). It has white flowers, and the fruit contains pulp and small hard seeds (Morais-Braga et al., 2016a) Fig. 1.

In ethnomedicine, the various parts of *P. guajava* – the stem, bark (Beidokhti et al., 2020), fruits, leaves, and roots (Weli et al., 2019) are used in the treatment of diseases such as diarrhea, rheumatism, and diabetes (Gutiérrez et al., 2008, Morais-Braga et al., 2016b, Díaz-de-Cerio et al., 2017), digestive problems, laryngitis, ulcers, malaria, cough, and bacterial infections (Ravi and Divyashree, 2014, Díaz-de-Cerio et al., 2017), wound healing and pain relief (Metwally et al., 2010). Many natives consume decoction, infusion, and/or boiled preparations of *P. guajava* either orally or topically depending on the type of illnesses (Díaz-de-Cerio et al., 2017). For instance, *P. guajava* leaves can be applied on wounds whereas aqueous leaf extract can be orally consumed to lower the blood glucose level in diabetic patients (Gutierrez et al., 2008).

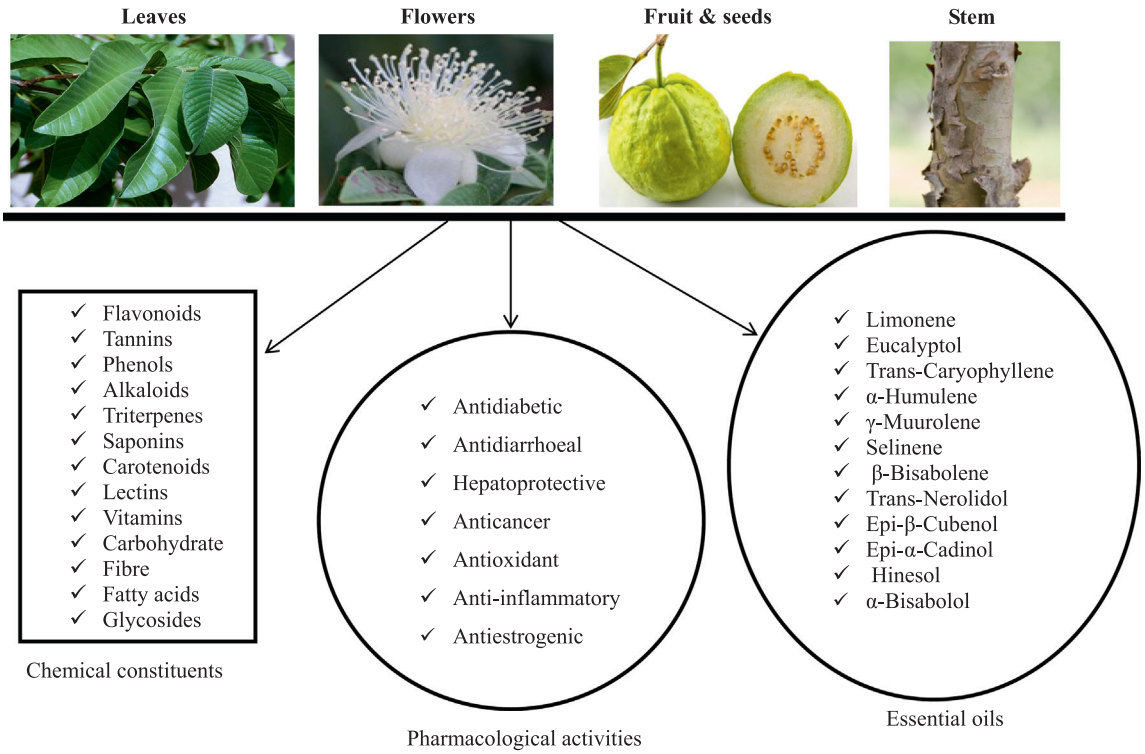


Fig. 1 Various parts of *P. guajava* L., chemical constituents, and pharmacological activities.

Psidium guajava consists of important chemical constituents such as flavonoids, tannins, phenols, alkaloids, triterpenes, saponins, carotenoids, lectins, vitamins, carbohydrate, fiber fatty acids, and glycosides (Gutiérrez et al., 2008, Weli et al., 2019). The leaves have a plethora of beneficial phenolic compounds such as guaijaverin, quercetin, kaempferol, apigenin, catechin, chlorogenic acid, hyperin, gallic acid, epicatechin, myricetin, caffeic acid, and epigallocatechin gallate (Kumar et al., 2021).

Studies have shown the abundance of the following essential oils; β-bisabolene, caryophyllene oxide, β-copanene, farnesene, longicyclene, humlene, selinene, cardinene, curcumene, β-caryophyllene, pinene, caryophyllene oxide, 1,8-cineeole and limonene in the leaves of *P. guajava* (Begum et al., 2004, Gutiérrez et al., 2008, De Souza et al., 2017, Weli et al., 2019) Fig. 1. The fruit is a rich source of dietary fibre (pectin), protein, vitamins (A and C), and minerals (iron, phosphorus, and calcium) (Naseer et al., 2018).

In 2009, *P. guajava* L. was listed in WHO monographs as one of the selected medicinal plants with supported clinical data; however, they reported that there is no information on its uses in pharmacopoeias and internal index components (WHO, 2009).

Pharmacological studies have demonstrated that *P. guajava* extracts possess antimutagenic, lipid-lowering, analgesic, anti-hyperglycemic effect, anti-inflammatory (Vasconcelos et al., 2017), adaptogenic, antidiabetics (Khan et al., 2013, Zhu et al., 2020), antiestodal, antidiarrheal (Koriem et al., 2019), anti-angiogenesis, hepatoprotective (Vijayakumar et al., 2020), antioxidant (Laily et al., 2015, Flores et al., 2015), anticancer (Lin and Lin, 2020), antimicrobial (Silva et al., 2018), cardioprotective, spermatoprotective, antihypertensive, antiparasitic, and anticough activities (Gutiérrez et al., 2008, Ravi and Divyashree, 2014, Kumar et al., 2021) Fig. 1. The pharmacological activities exhibited by *P. guajava* may be attributed to the numerous bioactive compounds present in the plant.

The aim of this study is to comprehensively review past scientific literatures and provide up-to-update information on the ethnomedicinal uses, phytochemical constituents, *in vitro* and *in vivo* pharmacological activities of *P. guajava*.

2. Materials and methods

2.1. Search strategy and study selection

In the search of materials for this study, the following search queries or keywords were used "*Psidium*", "*guajava*", "*Psidium guajava*", "*Psidium guajava* pharmacological", "*Psidium guajava* toxicity" and other related words in combination with words related to botanical description, taxonomical grouping, ethnopharmacological uses, phytochemical constituents, bioactive constituents, essential oils and pharmacological activities to find relevant peer-reviewed journals on four scientific databases, namely: PubMed (https://pubmed.ncbi.nlm.nih.gov/), ScienceDirect (https://www.sciencedirect.com/), Wiley (https://www.wiley.com/en-us) and Springer (https://www.springer.com/gp). Only papers that were published in English language were used for this study. Chemical structures identified from the plant were searched in NIST Chemistry Webbook, ChemSpider, and PubChem databases. The identified structures were drawn using ChemDraw (version 12.0.2).

3. Botanical description

Psidium guajava is a member of the Myrtaceae family. It is a small tree approximately 10 m high with a characteristic thin, smooth, patchy, and peeling bark (Gutiérrez et al., 2008). Guava trees usually have wide-spreading branches (Flores et al., 2015). The leaves have an elliptical and oval shape with a dark green colour and obtuse-type apex (Kumar et al., 2021). The leaves lie opposite each other and possess a short-petiolate with prominent veins. The plant has numerous stamens and showy, whitish petals. Its flowers are between 4 and 6 white

petals and white stamens with yellow anthers (Flores et al., 2015). Guava fruits appear very fleshy. Their shape ranges from a yellowish globose to ovoid berry. Their mesocarp is edible with several small hard white seeds (Gutiérrez et al., 2008). Different cultivars possess varying morphology of the skin of the fruit (Flores et al., 2015).

4. Geographical description and taxonomy

The Guava plant is a tropical plant indigenous to the Colombia, Mexico, Peru and United States of America (Gutiérrez et al., 2008; Hirudkar et al., 2020). It is commonly distributed in the regions like India, Indonesia, Pakistan, Bangladesh (Kumar et al., 2021), Nigeria, South Africa, Malaysia, Bolivia, Cambodia, Cameroon, Philippines, Costa Rica, Senegal, Brazil, Ghana, Haiti, Cuba, Ethiopia, Kenya, Trinidad, Uganda, Namibia, Bangladesh, China and Sri Lanka (Gutierrez et al., 2008; Morais-Braga et al., 2016a; Weli et al., 2019). It is also found in Arabic countries such as Egypt, Oman, Saudi Arabia, Palestine, Sudan, Syria, and Tunisia (Abdelrahim et al., 2002; Qabaha, 2013, Weli et al., 2019) Fig. 2. Aboriginal peoples of the tropical and subtropical regions across the world cultivate the plant as food. It adapts to varying climatic conditions, although it thrives better in dry climates (Gutiérrez et al., 2008).

5. Traditional/ethnomedicinal uses

Different countries have unique applications of the various parts (i.e., roots, leaves, bark, stem, and fruits) of the guava plants for medicinal purposes. These parts have been utilized for treating stomach-related diseases, diabetes, diarrhea, and other forms of disease conditions (Kumar et al., 2021). Asian countries have adopted the use of guava leaves to develop traditional medicines for the treatment of diabetes (Kumar et al., 2021). Indonesians use guava leaves, pulp, and seeds for treating respiratory and gastrointestinal disorders, as well as for increasing blood platelets in dengue fever patients (Laily et al., 2015). Also, guava leaves have been used therapeutically due to their antiamoebic, antispasmodic, antidiarrhoeal antiinflammatory, antihypertension, antiobesity, and antidiabetic properties (Chen and Yen, 2007, Hirudkar et al., 2020).

Digestive disorders can be treated using young leaves of the guava plant. Decoction of the young leaves and shoots of the plant possess febrifuge and spasmolytic properties. Natives employ the flowers to cool the body and treat bronchitis, as well as eye sores. The fruit can also serve as a tonic and laxative. Patients with bleeding gums can also receive treatment with the fruit extract (Begum et al., 2002). South Africans use leaves of *P. guajava* for treating diabetes and hypertension (Oh et al., 2005). In Madagascar, the bark of the plant is used in addition to the leaves for the treatment of diabetes (Beidokhti et al., 2020). Brazilians use *P. guajava* for treating dental and oral diseases. The leaves and bark peels are consumed, either swallowed or mashed whilst still hot, as a tea formulation to combat thrush.

Nigerians employ decoction of the plant for treating microbial infections. In Mexico, Brazil, Philippine, and Nigeria, *P. guajava* is used to prepare a poultice for skin and wound applications (Gutiérrez et al., 2008).

Digestive disorders and severe diarrhoea are treated by natives of Nahuatll and Maya origin, as well as Veracruz,

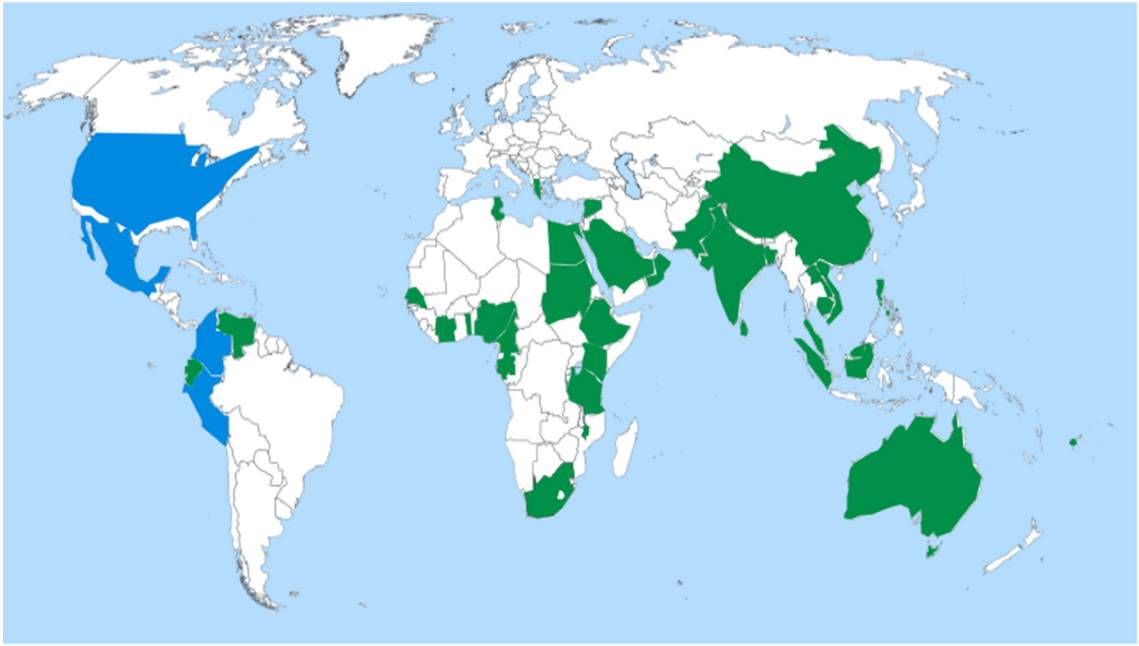


Fig. 2 Map of worldwide distribution of *Psidium guajava* L., the blue colour shows the native regions like Colombia, Mexico, Peru and United States of America, whereas the green colour represents the introduced countries such as Australia, Bangladesh, Brunei, Cambodia, Cameroon, China, Costa Rica, Cote d'Ivoire, Cuba, Dominican Republic, Ecuador, Eritrea, Ethiopia, Fiji, Gabon, Gambia, Greece, Guyana, Haiti, India, Indonesia, Israel, Kenya, Laos, Malawi, Malaysia, Myanmar, Nigeria, Pakistan, Panama, Philippines, Puerto Rico, Samoa, Senegal, South Africa, Sri Lanka, Tanzania, Thailand, Togo, Uganda, Venezuela, Vietnam, Egypt, Oman, Saudi Arabia, Palestine, Sudan, Syria and Tunisia.

using the leaf decoction. Indigenous people of Veracruz use the water leaf extract as a hot tea preparation to control blood glucose level in diabetes patients. Mexicans also handle gastrointestinal and respiratory disturbances using the plant extract– as well as for the treatment of inflammation (Gutiérrez et al., 2008).

Latin Americans and people of the Caribbean use guava for the treatment of diarrhoea and stomach pains (Gutiérrez et al., 2008). In Panama, the guava plant is used for treating dysentery. In Uruguay, formulations are prepared from the decoction of the leaves as a vaginal and uterine wash, especially for cases of leucorrhoea. In Costa Rica, preparations are made from the decoction of the flower buds as therapeutics for inflammation (Gutiérrez et al., 2008).

In Peru, gargles are formulated from the plant for treating gastroenteritis, dysentery, stomach pain, indigestion, inflammations of the mouth and throat. Leaf and bark decoctions of guava plants are also used by Tikuna Indians for treatment of gastrointestinal tract diseases (Gutiérrez et al., 2008). The Indians of the Amazons use decoctions of the plant leaves and bark for treating dysentery, sore throats, vomiting, stomach upsets, vertigo, mouth sores, as well as for regulating menstrual periods (Gutiérrez et al., 2008). West Indians use the leaves and shoots in febrifuge and antispasmodic baths. The Chinese use guava leaves as an antiseptic and anti-diarrhoea agent. Brazilians consume preparations of the plant fruit and leaves for treating anorexia, cholera, diarrhoea, digestive problems, dysentery, gastric insufficiency, inflamed mucous membranes, laryngitis, mouth (swelling), skin problems, sore throat, ulcers, and vaginal discharge (Holetz et al., 2002).

6. Phytochemistry

The study of Díaz-de-cerio et al. (2016) reported the presence of 72 phenolic constituents in guava leaves using high-performance liquid chromatography coupled to electrospray ionization and quadrupole time-of-flight mass spectrometry (HPLC-ESI-QTOF-MS). De Araújo et al., (2014) quantified the polyphenolic content (gallic acid and catechin) of *P. guajava* leaves using high-performance liquid chromatography (HPLC). Results of the study showed the presence of condensed tannins (catechins) and hydrolysable tannins (gallic acid) in *P. guajava* leaves (Table 1). Phytochemical studies of *P. guajava* leaves by Bhagavathy et al. (2018) using gas chromatography and mass spectrometry (GC–MS) confirmed the presence of carotenoids, flavonoids, alkaloids, polyphenols, saponins, tannins, glycosides and sterols. Babatola and Oboh (2021) characterized and quantified the phenolic constituent of guava leaves using HPLC-DAD, the major compounds identified include: chlorogenic acid, rutin, vanillic acid, quercetin, and p-hydroxyl benzoic acid, syringic acid, kaempferol, myricetin, isoquercetin, and apigenin. Bezerra et al. (2018, 2020) analyzed the chemical constituents of two fractions, viz. flavonoid and tannic fractions extracted from *P. guajava* leaves using UPLC-ESI-QTOF-MS. In the flavonoids fraction, reynoutrina (quercetin-3-O-β-D-xylopyranoside), guajaverina (quercetin-3-O-α-L-arabinopyranoside) and Morin), a condensed tannin (Catechin), and two hydrolysable tannins (ellagic acid and guavinoside B), an acetophenone (myrciaphenone B) were identified, whereas in the tannic fraction two flavonoids (quercetin and 2,6-dihydroxy-3-methyl-4-O-(6″-O-galloyl-β-D-glucopyranosyl)-benzophenone), a condensed tannin (catechin), a hydrolysable tannin (guayinoside C), and an elagotonine (vescalagin/Castalagin isomer, (1S*,5S*)-2,2-bis (biphenyl-4-yl)-5- indian-1-yltetrahydrofuran (IV-81)). Hseih et al. (2007) reported the presence of the following phenolic compounds; gallic acid, ferulic acid, and quercetin, in *P. guajava* leaves. Eidenberger et al. (2013) demonstrated that ethanolic extract of guava leaves contain seven main flavonol-glycosides through semipreparative HPLC analysis. They include; peltatoside quercetin-3-O-arabinoglucoside, hyperoside, quercetin-3-β-O-arabinoglucoside, isoquercetrin, quercetin-3-O-β-glucoside, guaijaverin, and quercetin-3-O-α-L-arabinopyranoside (Table 1). Flores et al. (2015) identified the following chemical compounds; delphinidin-3-O-glucoside and cyanidin-3-O-glucoside, myricetin-3-O-arabinoside, myricetin-3-O-xyloside, isorhamnetin-3-O-galac topyranoside, myricetin-3-O-glucoside, gallocatechin-(4α-8)-g allocatechol, gallocatechin-(4α-8)-catechin, abscisic acid, turpinionoside A, pinfaensin, pedunculoside, guavenoic acid, madecassiac acid and asiastic acid from guava cultivars (Table 1).

The chemical constituents present in the essential oil of *P. guajava* include; α-pinene, β-pinene, β-myrcene, linalool, α-terpineol, δ-3-carene, limonene, eucalyptol, *trans*-caryophyllene, α-humulene, γ-muurolene, β-selinene, α-selinene, α-bisabolene β-bisabolene, *trans*-nerolidol, epi-β-cubenol, epi-α-cadinol, hinesol, 14-hydroxy-9-epi-(e)-caryo phyllene, β-bisabolol, α-bisabolol, *iso*-caryophyllene, veridiflorene, β-caryophyllene, farnesene, dl-limonene, δ-cadinene, α-copaene, β-copaene, aromadendene, elemol, scadinol, 1,8-cineole, *trans*-calamenene, junipene, α-gurjunene, *cis*-ocimene, β-ocimene, aromadendene, α-muurolene, *δ*-cadinol, β-eudesmol, γ-eudesmol, α-cedrene, Ɗ-Limoene, globulol, viridiflorol, cubenol, tau-muurolol, *cis*-lanceol, α-acorenol, epiglobulol, spathulenol, ledol and caryophyllene oxide (De Souza et al., 2018; Weli et al., 2019; Hassan et al., 2020) (Table 2).

7. Pharmacological activities of *P. guajava*

7.1. Antidiabetic activity

Several researchers have investigated the antidiabetic potential of *P. guajava* (Huang et al., 2011, Khan et al., 2013, Luo et al., 2019, Zhu et al., 2020; Uuh-Narvaez et al., 2021). Rai et al. (2009, 2010) reported that raw fruit peels and aqueous unripe fruit peels extracts of *P. guajava* exhibited hypoglycaemic effect in streptozotocin-induced diabetic rats. Supplementation of 125 and 250 mg/kg of guava fruit for 4 weeks in streptozotocin (STZ)-induced diabetic rats reduced blood glucose levels (Huang et al., 2011). Ojewole (2005) observed that the aqueous *P. guajava* leaf extracts have a hypoglycaemic effect in diabetic rats (Table 3). Rajpat and Kumar (2021) revealed that 200 mg/kg ethanolic extract of *P. guajava* leaves extract reduced blood glucose levels in diabetic mice. Shen et al. (2008) posited that guava leaf aqueous extract reduces blood glucose level and accelerates plasma insulin level. Oral administration of 300 mg/kg body weight/day of *P. guajava* leaf extract for 30 days to STZ-induced diabetes rats decreased blood glucose levels (Subramanian et al., 2009).

Table 1 Bioactive phytochemicals present in various parts of *Psidium guajava* plant.

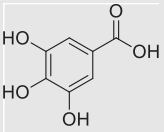
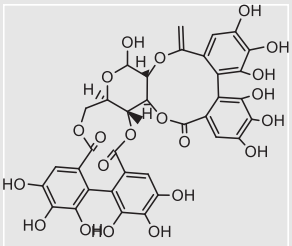
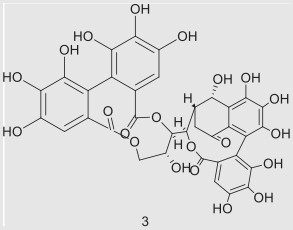
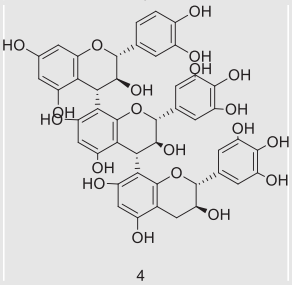
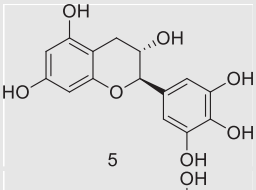
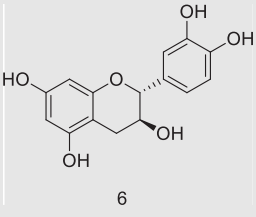
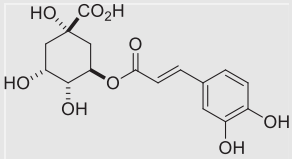
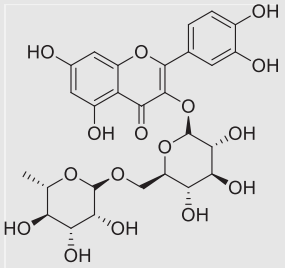
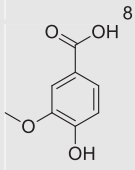
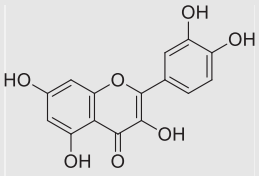
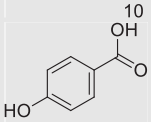
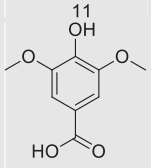
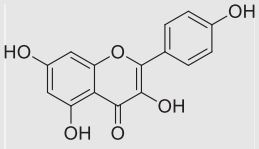
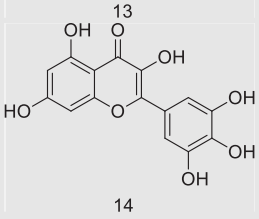
Name of compound	Chemical structure	Method of identification	Pharmacological activity	References
Gallic acid	 1	High-Performance Liquid Chromatography with diode-array detection coupled to electrospray ionization quadrupole time-of-flight mass spectrometry (HPLC-DAD-ESI-QTOF-MS) analysis of phenolic fraction of *P. guajava* leaves using an ultrasound bath and a mixture of ethanol:water 80/20 (v/v) (Díaz-de-cerio et al., 2016)	Anti-inflammatory, Antifungal activities	Alves et al. (2014); De Araújo et al. (2014)
Pedunculagin	 2	HPLC-DAD-ESI-QTOF-MS analysis of phenolic fraction of *P. guajava* leaves using an ultrasound bath and a mixture of ethanol:water 80/20 (v/v) (Díaz-de-cerio et al., 2016)	Anti-diabetic activity	Eidenberger et al. (2013)
Casuariin	 3	HPLC-DAD-ESI-QTOF-MS analysis of phenolic fraction of *P. guajava* leaves using an ultrasound bath and a mixture of ethanol:water 80/20 (v/v) (Díaz-de-cerio et al., 2016)	Anticoagulant, Anti-hypertensive activities	Dong et al. (1998); Xie et al. (2007)
Prodelphinidin dimer isomer	 4	HPLC-DAD-ESI-QTOF-MS analysis of phenolic fraction of *P. guajava* leaves using an ultrasound bath and a mixture of ethanol:water 80/20 (v/v) (Díaz-de-cerio et al., 2016)	Antioxidant activity	Ma et al. (2019)
Gallocatechin	 5	HPLC-DAD-ESI-QTOF-MS analysis of phenolic fraction of *P. guajava* leaves using an ultrasound bath and a mixture of ethanol:water 80/20 (v/v) (Díaz-de-cerio et al., 2016)	Anti-aggregation activity	Sohail et al. (2018)
Catechin	 6	HPLC-DAD-ESI-QTOF-MS analysis of phenolic fraction of *P. guajava* leaves using an ultrasound bath and a mixture of ethanol:water 80/20 (v/v) (Díaz-de-cerio et al., 2016)	Anti-inflammatory, Antifungal activities	De Araújo et al. (2014); Bezerra et al. (2018)

Table 1 (*continued*)

Name of compound	Chemical structure	Method of identification	Pharmacological activity	References
Chlorogenic acid	 7	HPLC-DAD analysis using phenolic fraction of guava leaves (Babatola and Oboh, 2021)	Potential anti-inflammatory activity	Bhandarkar et al. (2019)
Rutin		HPLC-DAD analysis using phenolic fraction of guava leaves (Babatola and Oboh, 2021)	Antitumor, Antimicrobial, Antidiabetic activities	Budzynska et al. (2019); Ghorbani (2017)
Vanillic acid	 8 9	HPLC-DAD analysis using phenolic fraction of guava leaves (Babatola and Oboh, 2021)	Antioxidative activity	Yao et al. (2020)
Quercetin		HPLC-DAD analysis using phenolic fraction of guava leaves (Babatola and Oboh, 2021)	Anti-hypertensive, Antimicrobial, Antioxidant, Antidiarrhea activities	Alves et al. (2014); Hirudkar et al. (2020); Marunaka et al. (2017)
p-hydroxyl benzoic acid	 10 11	HPLC-DAD analysis using phenolic fraction of guava leaves (Babatola and Oboh, 2021)	Anti-inflammatory activity	Banti et al. (2021)
Syringic acid	 12	HPLC-DAD analysis using phenolic fraction of guava leaves (Babatola and Oboh, 2021)	Anti-inflammatory, Anti-microbial activities	Liu et al. (2020)
Kaempferol		HPLC-DAD analysis using phenolic fraction of guava leaves (Babatola and Oboh, 2021)	Anti-inflammatory, Antimicrobial, Antioxidant activities	Alam et al. (2020); Bezerra et al. (2018)
Myricetin	 13 14	HPLC-DAD analysis using phenolic fraction of guava leaves (Babatola and Oboh, 2021)	Cardioprotective activities	Wang et al. (2019)

(*continued on next page*)

Table 1 (*continued*)

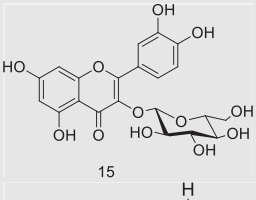
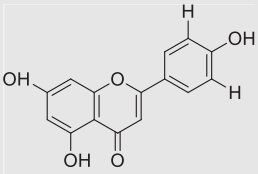
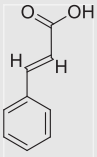
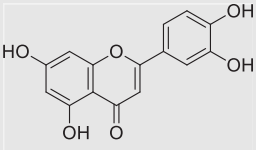
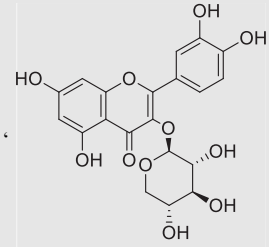
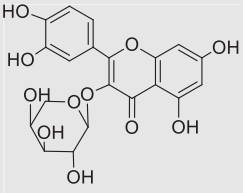
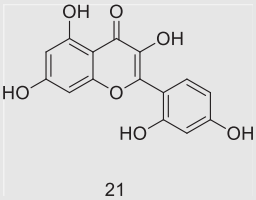
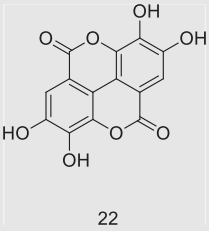
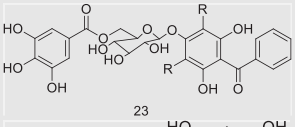
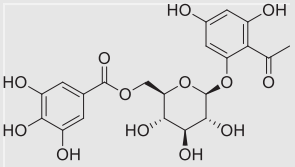
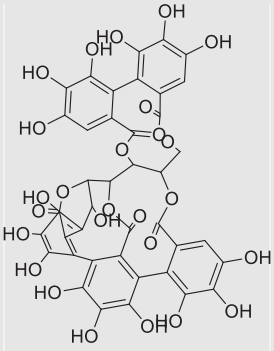
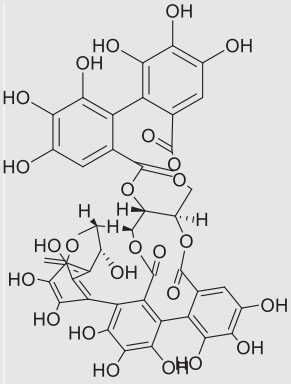
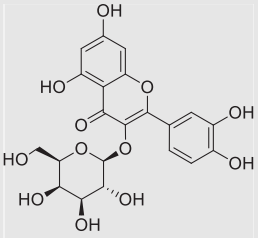
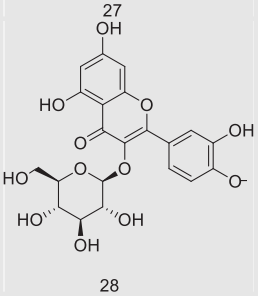
Name of compound	Chemical structure	Method of identification	Pharmacological activity	References
Isoquercetin	 15	HPLC-DAD analysis using phenolic fraction of guava leaves (Babatola and Oboh, 2021)	Neuroprotective activities	Dai et al. (2018)
Apigenin	 16	HPLC-DAD analysis using phenolic fraction of guava leaves (Babatola and Oboh, 2021)	Anticancer activities	Imran et al. (2020)
Cinnamic acid	 17	HPLC-DAD analysis using phenolic fraction of guava leaves (Babatola and Oboh, 2021)	Anti-inflammatory activities	Karatas et al. (2020)
Luteolin	 18	HPLC-DAD analysis using phenolic fraction of guava leaves (Babatola and Oboh, 2021)	Anti-inflammatory, Antifungal activities	Zhang et al. (2018)
Reynoutrina (quercetin-3-O-β-D-xylopyranoside)	 19	Ultrafine liquid chromatography coupled to quadruple time-of-flight (UPLC-QTOF) analysis flavonoid fraction of guava leaves (Bezerra et al., 2018)	Anti-inflammatory activities	Yang et al. (2021)
Guajaverina (quercetin-3-O-α-L-arabinopyranoside)	 20	UPLC-QTOF analysis flavonoid fraction of guava leaves (Bezerra et al., 2018)	Antifungal, Antibacterial activities	Ukwueze et al. (2015)
Morin	 21	UPLC-QTOF analysis flavonoid fraction of guava leaves (Bezerra et al., 2018)	Anti-mastitis, Antimicrobial, Antioxidant activities	Jiang et al. (2020)
Ellagic acid	 22	UPLC-QTOF analysis flavonoid fraction of guava leaves (Bezerra et al., 2018)	Anti-inflammatory activities	Bensaad et al. (2017)

Table 1 (*continued*)

Name of compound	Chemical structure	Method of identification	Pharmacological activity	References
Guavinoside B	 23	UPLC-QTOF analysis flavonoid fraction of guava leaves (Bezerra et al., 2018)	Hepatoprotective activity	Li et al. (2020)
Myrciaphenone B	 24	UPLC-QTOF analysis flavonoid fraction of guava leaves (Bezerra et al., 2018)	Anti-fungal activities	De Leo et al. (2004)
Vescalagin	 25	UPLC-QTOF analysis flavonoid fraction of guava leaves (Bezerra et al., 2018)	Anticancer activities	Kamada et al. (2018)
Castalagin Isomer	 26	UPLC-QTOF analysis flavonoid fraction of guava leaves (Bezerra et al., 2018)	Anticancer activity	Kamada et al. (2018)
Hyperoside	 27	High-Performance Liquid Chromatography coupled to Ultraviolet light and Mass spectrometry (HPLC/UV/MS) analysis of 80% ethanolic extract of guava leaves (Eidenberger et al., 2013)	Anticancer activity	Qiu et al. (2019)
Quercetin-3-O-β-glucoside	 28	HPLC/UV/MS analysis of 80% ethanolic extract of guava leaves (Eidenberger et al., 2013)	Neuroprotective activities	Magalingam et al. (2016)

(*continued on next page*)

Table 1 (*continued*)

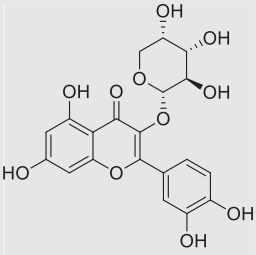
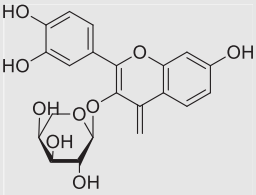
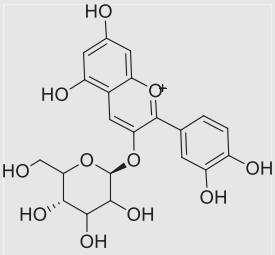
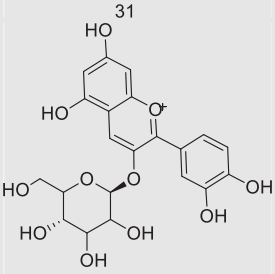
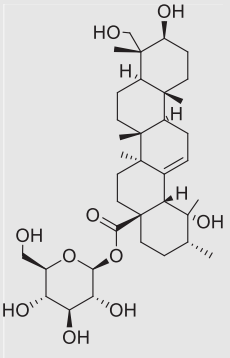
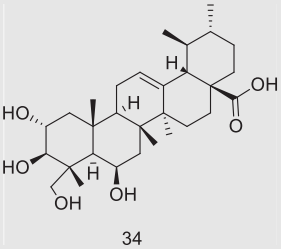
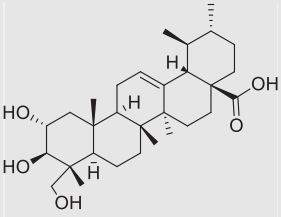
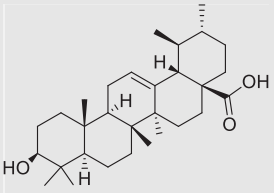
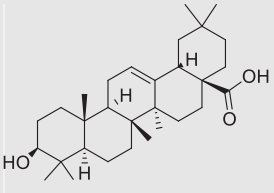
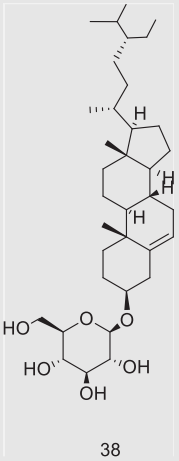
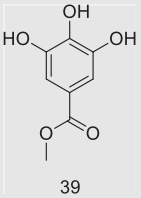
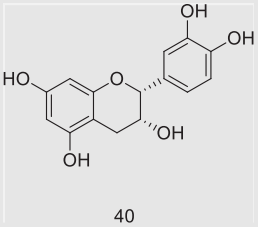
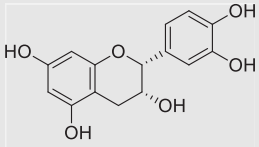
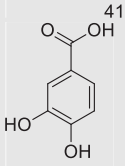
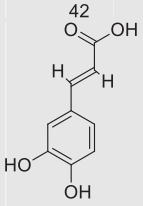
Name of compound	Chemical structure	Method of identification	Pharmacological activity	References
Guaijaverin	 29	HPLC/UV/MS analysis of 80% ethanolic extract of guava leaves (Eidenberger et al., 2013)	Antimicrobial activities	Prabu et al. (2006)
Quercetin-3-O-α-L-arabinopyranoside	 30	HPLC/UV/MS analysis of 80% ethanolic extract of guava leaves (Eidenberger et al., 2013)	Anti-inflammatory activity	Kim et al. (2018)
Delphinidin-3-O-glucoside	 31	High-Performance Liquid Chromatography coupled to Photodiode-Array Detection (HPLC-PDA) analysis of guava pulp extracted using CH_3OH/H_20/formic acid (Flores et al., 2015)	Anticancer activity	Mazewski et al. (2019)
Cyanidin-3-O-glucoside	 32	HPLC-PDA analysis of guava pulp extracted using CH_3OH/H_20/formic acid (Flores et al., 2015)	Anti-obesity activity	Molonia et al. (2020)
Pedunculoside	 33	HPLC-PDA analysis of guava pulp extracted using CH_3OH/H_20/formic acid (Flores et al., 2015)	Antihyperlipidemic activities	Liu et al. (2018)
Madecassiac acid	 34	HPLC-PDA analysis of guava pulp extracted using CH_3OH/H_20/formic acid (Flores et al., 2015)	Anticancer activities	Valdeira et al. (2019)

Table 1 (*continued*)

Name of compound	Chemical structure	Method of identification	Pharmacological activity	References
Asiastic acid	 35	HPLC-PDA analysis of guava pulp extracted using CH_3OH/H_20/formic acid (Flores et al., 2015)	Anti-inflammatory activities	Hao et al. (2017)
Ursolic acid	 36	Thin layer chromatography (TLC) analysis of fresh ethanol leaf extract of *P. guajava* (Begum et al., 2004)	Anti-inflammatory, anticancer, antidiabetic, antioxidant, and antibacterial activities	Hsieh et al. (2007); Mlala et al. (2019)
Oleanolic acid	 37	Thin layer chromatography (TLC) analysis of fresh ethanol leaf extract of *P. guajava* (Begum et al., 2004)	Antitumor, Anti-diabetic, Antimicrobial, Hepatoprotective actiivities	Hsieh et al. (2007); Ayeleso et al. (2017)
Beta-sitosterol glucoside	 38	Thin layer chromatography (TLC) analysis of ethanol leaf extract of *P. guajava* (Begum et al., 2002)	Anticancer, apoptogenic activity	Vo et al. (2020); Dolai et al. (2016)
Methyl gallate	 39	HPLC-UV analysis of leaf extract of *P. guajava* (Farag et al., 2020)	Antileishmanial, antioxidant, anti-inflammatory, antimicrobial and anti-tumor activities	Dias et al. (2020); Anzoise et al. (2018)
Epicatechin	 40	HPLC–DAD of hydroethanolic or aqueous extract of *P. guajava* leaves (Morais-Braga et al., 2017)	Anticoagulant, Pro-fibrinolytic, enzyme-inhibitory activities	Sinegre et al. (2019); Wu et al. (2019)

(*continued on next page*)

Table 1 (*continued*)

Name of compound	Chemical structure	Method of identification	Pharmacological activity	References
Procyanidin		HPLC-DAD-ESI-QTOF-MS analysis of phenolic fraction of *P. guajava* leaves using an ultrasound bath and a mixture of ethanol:water 80/20 (v/v) (Díaz-de-cerio et al., 2016)	Antioxidant activity	Hsieh et al. (2007); Ma et al. (2019)
Protocatechuic acid		LC-HRMS-MS with the OLE Ultra-High-Performance Liquid Chromatography (UHPLC) analysis of *P. guajava* leaf decoction (Lorena et al., 2022)	Antioxidative, Neuroprotective, Anti-atherosclerotic activities	Krzysztoforska et al. (2019); Zheng et al. (2020)
Caffeic acid		HPLC–DAD of hydroethanolic or aqueous extract of *P. guajava* leaves (Morais-Braga et al., 2017)	Neuroprotective, enzyme-inhibitory activities	Habtemariam (2017); Zhang et al. (2019); Maruyama et al. (2018)

Uuh-Narvaez et al. (2021) posited that 10 mg/kg of edible parts *P. guajava* administered to diabetic rodents demonstrated high antihyperglycemic activity. Mazumdar et al. (2015) showed that ethanolic extracts of *P. guajava* administered to alloxan-induced diabetic rats reduced the blood glucose concentration. Jayachandran et al. (2020) investigated the activity of 200 mg/kg b.w of *P. guajava* extract against the insulin signalling proteins of streptozotocin-induced diabetic rats and reported antidiabetic activity of *P. guajava* because of its regulation of insulin signalling pathway genes.

Beidokhti et al. (2020) stated that leaf and bark extracts of *P. guajava* effectively improved glucose uptake in muscle cells and inhibited α-amylase, respectively. Yang et al. (2020) reported that guava leaf extract reduced fasting plasma glucose, fasting insulin, and insulin resistance in KK-Ay diabetic mice. *P guajava* leaves extract decreased fasting blood glucose, lipid level, and altered glucose metabolism in STZ-induced diabetic rats (Khan et al., 2013, Xu et al., 2020) (Table 3).

Supplementation of flavonoids extracted from *P. guajava* markedly reduced fasting plasma glucose, glucose tolerance, and insulin resistance in diabetic mice (Zhu et al., 2020). Luo et al. (2019) opined that polysaccharide from guava leave exhibited anti-diabetic effects in STZ-induced diabetic mice. Shabbir et al. (2020) reported blood glucose level reduction potential of polyphenol extracted from guava pulp, seeds, and leaves in diabetic mice. These antidiabetic activities could be due to the ability of *P. guajava* to increase levels of glycogen synthase and decrease in the activity of the enzyme; glycogen phosphorylase (Tella et al., 2019).

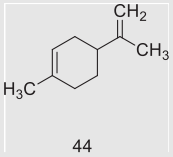
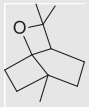
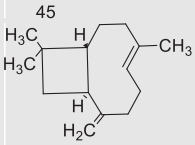
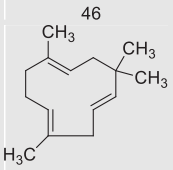
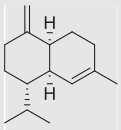
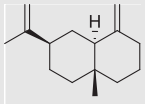
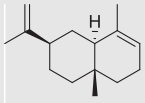
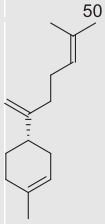
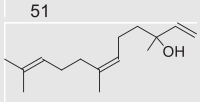
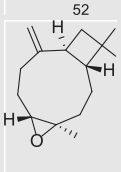
7.2. Hepatoprotective activity

Vijayakumar et al. (2020) assessed the hepatoprotective effect of *P. guajava* against carbon tetrachloride-induced damage in rats. Hepatotoxicity was induced in the liver by the administration of 1.5 mL/kg of carbon tetrachloride (CCl_4) in rats. Daily oral administration of the extract for 21 days decreased the CCl_4 induced increase in serum levels of liver biomarkers (ALT, AST, ALP, and GGT). A similar result was observed by Roy and Das (2010). Saber et al. (2018) studied the effects of *P. guajava* in combination with *P. cattleianum* against paracetamol-induced toxicity in rats. The pre-administration of the extract at 250 and 500 mg/kg reduced elevated levels of liver enzymes ameliorating hepatotoxicity. The hepatoprotective effects of aqueous unripe *P. guajava* fruit peel extract in STZ-induced diabetic rats were evaluated by Rai et al. (2010). They observed a significant decrease in ALP, AST, ALT, indicating hepatoprotective effects of unripe *P. guajava* fruit peel. *P. guajava* extract treatment at the doses of 100, 200, and 300 mg/kg, bw and 20 mg/kg of quercetin fraction decreased lipid metabolism in CCl_4-induced hepatotoxic rats (Vijayakumar et al., 2018). Li et al. (2021) reported that triterpenoid-enriched guava leaf extract reduced serum ALT and AST levels, and hepatic ROS and MDA in acetaminophen-exposed C57BL/6 male mice. Li et al. (2020) posited that 100 mg/kg/day of Guavinoside B extracted from guava fruit markedly improved serum and hepatic biochemical parameters in acetaminophen-induced liver injury in mice (Table 3).

7.3. Antioxidant activity

Scientific studies have reported the antioxidant activities of *P. guajava* (Laily et al., 2015, Flores et al., 2015, Li et al., 2015; Ashraf et al., 2016). Tan et al., (2020) investigated the antioxidative properties of extracts derived from red and white *P. guajava* fruits through different drying processes. Findings from this study revealed maximum antioxidant activity in

Table 2 Chemical structures and pharmacological activities of essential oils identified in *Psidium guajava* plant.

Name of compound	Chemical structure	Method of identification	Pharamacological activity	References
Limonene	 44	Gas chromatography coupled to Flame ionized detector or Gas chromatography coupled to mass spectrometry (GC-FID/GC–MS) of *P. guajava* leaves hydrolate (De Souza et al., 2018)	Antitumor, antiviral, anti-inflammatory, antibacterial, anticancer activities	De Souza et al. (2017); Mukhtar et al. (2018)
Eucalyptol		GC-FID/GC–MS of *P. guajava* leaves hydrolate (De Souza et al., 2018)	Retinoprotective activity	Kim et al. (2020); Hassan et al. (2020)
Trans-Caryophyllene	 45	GC-FID/GC–MS) of *P. guajava* leaves hydrolate (De Souza et al., 2018)	Antileishmanial, antischistosomal, antifungal activities	De Souza et al. (2017)
α-Humulene	 46	GC-FID/GC–MS of *P. guajava* leaves hydrolate (De Souza et al., 2018)	Antiinflammatory	De Souza et al. (2017); Hassan et al. (2020)
γ-Muurolene	 47	GC-FID/GC–MS of *P. guajava* leaves hydrolate (De Souza et al., 2018)	Antifungal, antimicrobial, and anticancer activities	Doan et al. (2021)
β-Selinene	 48	GC-FID/GC–MS of *P. guajava* leaves hydrolate (De Souza et al., 2018)	Trypanocidal activity	De Souza et al. (2017); Fernandes et al. (2021); Hassan et al. (2020)
α-Selinene	 49	GC-FID/GC–MS of *P. guajava* leaves hydrolate (De Souza et al., 2018)	Antifungal activity	De Souza et al. (2017); Oladeji et al. (2020)
β-Bisabolene	 50	GC-FID/GC–MS of *P. guajava* leaves hydrolate (De Souza et al., 2018)	Cytotoxic activity	Yeo et al. (2016); Hassan et al. (2020)
Trans-Nerolidol	 51	GC-FID/GC–MS of *P. guajava* leaves hydrolate (De Souza et al., 2018)	Antifungal activity	De Souza et al. (2017); Hassan et al. (2020)
Caryophyllene oxide	 52 53	GC-FID/GC–MS of *P. guajava* leaves hydrolate (De Souza et al., 2018)	Antifungal and antibacterial activity	Policegoudra et al. (2012); Hassan et al. (2020)

(*continued on next page*)

Table 2 (*continued*)

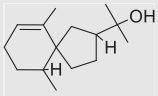
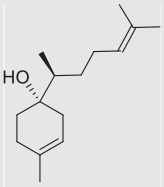
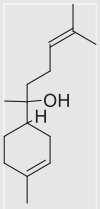
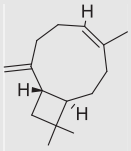
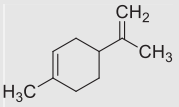
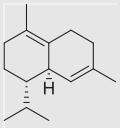
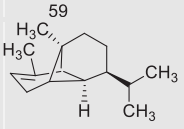
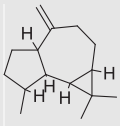
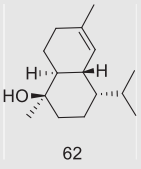
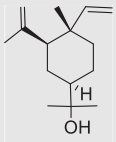
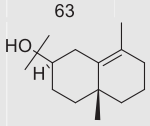
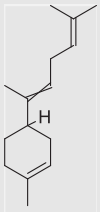
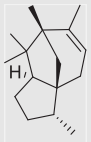
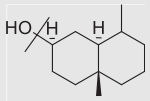
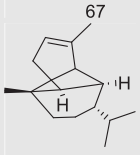
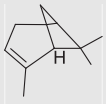
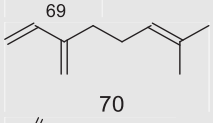
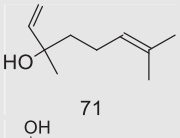
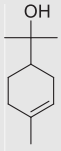
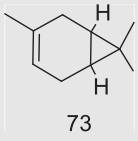
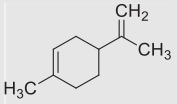
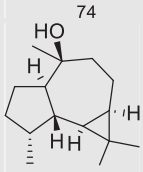
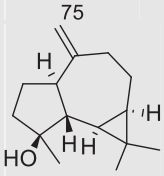
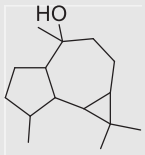
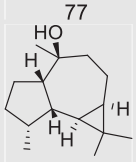
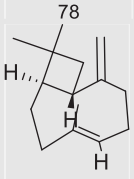
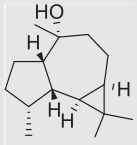
Name of compound	Chemical structure	Method of identification	Pharamacological activity	References
Hinesol	 54	GC-FID/GC–MS of *P. guajava* leaves hydrolate (De Souza et al., 2018)	Antitumor activity	De Souza et al. (2017); Guo et al. (2019)
β-Bisabolol	 55	GC-FID/GC–MS of *P. guajava* leaves hydrolate (De Souza et al., 2018)	Antimicrobial, antitumor activities	De Souza et al. (2017)
α-Bisabolol	 56	GC-FID/GC–MS of *P. guajava* leaves hydrolate (De Souza et al., 2018)	Antimicrobial, antitumor activities	De Souza et al. (2017)
Isocaryophyllene	 57	Gas chromatography coupled to mass spectrometry (GC–MS) analysis of *P. guajava* leaves hydrolate (Weli et al., 2019)	Anticancer	Legault and Pichette (2010)
dl-limonene	 58	GC–MS analysis of *P. guajava* leaves hydrolate (Weli et al., 2019)	Antiaflatoxigenic activity	Singh et al. (2010)
δ-cadinene	 59	GC–MS analysis of *P. guajava* leaves hydrolate (Weli et al., 2019)	Larvicidal, Anticancer activities	Govindarajan et al. (2016); Hui et al. (2015);
α-copaene	 60	GC–MS analysis of *P. guajava* leaves hydrolate (Weli et al., 2019)	Attractant activity	Kendra et al. (2017); Hassan et al. (2020)
Aromadendrene	 61	GC–MS analysis of *P. guajava* leaves hydrolate (Weli et al., 2019)	Insecticidal activity	Hassan et al. (2020); Giuliani et al. (2020)
δ-cadinol	 62	GC–MS analysis of *P. guajava* leaves hydrolate (Weli et al., 2019)	Anti-mildew	Su et al. (2015); Hassan et al. (2020)

Table 2 (*continued*)

Name of compound	Chemical structure	Method of identification	Pharamacological activity	References
Elemol	 63	GC-FID/GC–MS of *P. guajava* hydrolate (De Souza et al., 2018)	Immunosuppressive activity	Yang et al. (2015)
γ-Eudesmol	 64	GC-FID/GC–MS of *P. guajava* hydrolate (De Souza et al., 2018)	Cytotoxic activity	Britto et al. (2012); Hassan et al. (2020)
α-Bisabolene	 65	GC-FID/GC–MS) of *P. guajava* hydrolate (De Souza et al., 2018)	Anti-cancer	Yeo et al. (2016)
α-Cedrene	 66	GC-FID/GC–MS) of *P. guajava* hydrolate (De Souza et al., 2018)	Potential anti-obesity activity	Kim et al. (2015)
β-Eudesmol	 67	GC-FID/GC–MS) of *P. guajava* hydrolate (De Souza et al., 2018)	Anti-allergic, anticancer, anti-angiogenic activities	Han et al. (2017); Narahara et al. (2020); Acharya et al. (2021)
Copaene	 68	GC–MS analysis of methanolic extract of *P. guajava* leaves (Bhagavathy et al., 2018)	Cytotoxic activity	Türkez et al. (2014)
α-Pinene	 69	GC–MS analysis of *P. guajava* leaves hydrolate extracted with hexane (Hassan et al., 2020)	Antioxodant, anti-inflamatory, anticancer, pro-osteogenic activities	Zhao et al. (2018); Min et al. (2020);
β-Myrcene	 70	GC–MS analysis of *P. guajava* leaves hydrolate extracted with hexane (Hassan et al., 2020)	Anxiolytic, antioxidant, anti-ageing, anti-inflammatory, analgesic, genotoxic activities	Surendran et al. (2021); Orlando et al. (2019)
Linalool	 71	GC–MS analysis of *P. guajava* leaves hydrolate extracted with hexane (Hassan et al., 2020)	Antibacterial, anti-inflammatory, anticancer, anti-hyperlipidemic, antinoceptive, analgesic, anxiolytic activities	Sabogal-Guáqueta et al. (2019)
α-Terpineol	 72	GC–MS analysis of *P. guajava* leaves hydrolate extracted with hexane (Hassan et al., 2020)	Cytotoxic, antitumor, antidiarrheal,	Negreiros et al. (2021); Dos Santos Negreiros et al. (2019)
δ-3 carene	 73	GC–MS analysis of *P. guajava* leaves hydrolate extracted with hexane (Hassan et al., 2020)	Sleep-enhancing, anti-inflammatory, antimicrobial, anxiolytic activities	Woo et al. (2019); Shu et al. (2019)

(*continued on next page*)

Table 2 (*continued*)

Name of compound	Chemical structure	Method of identification	Pharamacological activity	References
D-Limoene		GC–MS analysis of *P. guajava* leaves hydrolate extracted with hexane (Hassan et al., 2020)	Antioxidant, antidiabetic, anticancer, anti-inflammatory	Anandakumar et al. (2021); Seo et al. (2020)
Epiglobulol	74 	GC–MS analysis of *P. guajava* leaves hydrolate extracted with hexane (Hassan et al., 2020)	Antimicrobial activity	Kim and Shin (2004)
Spathulenol	75 	GC–MS analysis of *P. guajava* leaves hydrolate extracted with hexane (Hassan et al., 2020)	Antioxidant, anti-inflammatory, antiproliferative activities	do Nascimento et al. (2018); Ziaei et al. (2011); Lou et al. (2019)
Globulol	76 	GC–MS analysis of *P. guajava* leaves hydrolate extracted with hexane (Hassan et al., 2020)	Potential antimicrobial activity	Tan et al. (2008)
Viridiflorol	77 	GC–MS analysis of *P. guajava* leaves hydrolate extracted with hexane (Hassan et al., 2020)	Anti-inflammatory, antioxidant, antibacterial activities	Trevizan et al. (2016)
β-Caryophyllene	78 	GC–MS analysis of *P. guajava* leaves hydrolate extracted with hexane (Hassan et al., 2020)	Neuroprotective, anticancer, analgesic, anti-inflammatory, wound-healing, antimicrobial activities	Scandiffio et al. (2020); Koyama et al. (2019); Yoo and Jwa (2018)
Ledol	79  80	GC–MS analysis of *P. guajava* leaves hydrolate extracted with hexane (Hassan et al., 2020)	Antitumor activity	Cianfaglione et al. (2017)

red *P. guajava* powders extracted by vacuum drying compared to other drying methods. Sobral-Souza et al. (2018) reported the antioxidative ability of flavonoids extracted from extracts of *P. guajava*.

Luo et al. (2019) opined that polysaccharide from guava leaves exhibited antioxidant activities by increasing the total antioxidant activity and superoxide dismutase (SOD) enzyme and lower MDA activities in STZ-induced diabetic mice. Methanolic leaf extract of *P. guajava* fraction showed antioxidant activity (Khedr et al., 2021).

Zahin et al. (2017) revealed that *P. guajava* fractionated in methanol possesses maximum antioxidant activity compared to other solvents; petrol, benzene, acetone, and ethyl acetate. Kim et al. (2016) evaluated the antioxidative properties of polysaccharides extracted from *P. guajava* using hydroxyl radical and 2,2-diphenyl-1-picrylhydrazyl (DPPH). Results from the study of Kim et al. (2016) showed that the extract possesses strong antioxidant activity against hydroxyl radicals. Wang et al. (2018) observed strong antioxidant ability of silver nanoparticles extracted from *P. guajava*. Lee et al. (2012)

Table 3 Pharmacological activities of *Psidium guajava* plant.

Doses	Experimental models	Observation	Effects	References
Psidium guajava dissolved in 125 µL tryptic soy broth	*Streptococcus salivarius, Streptococcus mutans, Streptococcus mitis, Streptococcus sanguinis* and *Streptococcus sobrinus*	Inhibitory activity (500–100 µg/mL) against all *Streptococcus* species used.	Antibacterial activity	Silva et al. (2018)
1000, 500, 250 and 125 µg/ml of essential oils extracted from *Psidium guajava*	*Enterococcus faecalis*, *S. aureus, Streptococcus aureus*, *E. coli, Haemophilus influenzae* and *P. aeruginosa*	Inhibitory activity against *Enterococcus faecalis* and *Streptococcus aureus.*	Antibacterial activity	Weli et al. (2019)
25, 50, 100 and 150 μgml^{-1}	*E. coli, Klebsiella pneumoniae and Salmonella typhimurium*	40 µgml−1 induced a 90% inhibition of *Klebsiella spp*. and 30% inhibition of *Proteus spp*.	Antibacterial activity	Pelegrini et al. (2008)
1024 µg/mL of *Psidium guajava* extracts	*E. coli, P. aeruginosa* and *S. aureus*	Extract produced an MIC value of 256 µg/mL against *S. aureus*	Antibacterial activity	Morais-Braga et al. (2016a,b)
Chemical constituents isolated from *Psidium guajava*	*S. aureus, S. epidermidis, and Mycobacterium Smegmatis*	Psidinone extracted showed inhibitory activity with MIC values of 16, 8, and 0.5 µM respectively.	Antibacterial activity	Huang et al. (2021)
Dilutions of methanol, chloroform and hexane extracts of *Psidium guajava*	*Agrobacterium tumefaciens*	IC_{50} values; 65.02 µg/mL, 160.7 µg/mL and 337.4 µg/mL for hexane, chloroform and methanol extracts	Antitumor activity	Ashraf et al. (2016)
0.5 mL dilutions of methanol, chloroform and hexane extracts of*Psidium guajava*	Brine shrimp; *Artemia salina* nauplii	IC_{50} values of 32.18 µg/mL, 41.05 µg/mL 63.81 µg/mL for hexane, chloroform and methanol extracts	Anticancer activity	Ashraf et al. (2016)
16,384 µg/mL of *Psidium guajava*	Fungal strains of *C. albicans* and *C. tropicals*	IC_{50} value of 3235.94 µg/mL	Antifungal activity	Morais-Braga et al. (2015)
1000 to 5 µg mL^{-1} of concentrated *Psidium guajava*	*C. albicans, C. krusei, C. glabrata*	Antifungal activity against *C. glabrata* with MIC value of 80 µg/mL	Antifungal activity	Fernandes et al. (2014)
250, 500 and 1000 µg/mL of *Psidium guajava*	3×10^4 per millilitre of *Trypanosoma cruzi epimastigote*	Hydroethanolic extract of *Psidium guajava* led to death of mammalian cells at 76.30%	Antiparasitic activity	Machado et al. (2018)
75 mg/kg of ethanolic extract of *Psidium guajava*	$2x10^5$ *Giardia lamblia* cysts /0.1 mL intraesophageally in rats	Extract produced a percentage reduction in trophozoite count	Antiparasitic activity	Khedr et al. (2021)
8, 40 and 200 µg/ml of guava seed polysaccharides	2×10^5 cells/ml of MCF-7 cells	Extracts at the concentration (40 and 200 µg/mL) inhibited MCF-7 cell viability.	Anticancer activity	Lin and Lin (2020)
800 to 6.25 µg/mL of lycopene extracted from *Psidium guajava.*	2×10^5 cells/ml of MCF-7 cells	Extract at the concentration (5.964 µg/mL) inhibited MCF-7 cell viability.	Anticancer activity	dos Santos et al. (2017)
20 to 100 µM of compounds separated from *Psidium guajava*	HCT116 and HT29 cells	After 72 h of administration compound extracted inhibited growth of cells at 81.4% with IC_{50} value of 60 µM	Anticancer activity	Zhu et al. (2020)
10 to 100 mg/mL of methanol, hexane and chloroform of *Psidium guajava* extracts	KBM5, SCC4 and U266	Hexane extract showed maximum inhibitory activity against cancer cells with IC_{50} value less than 30 mg/mL	Anticancer activity	Ashraf et al. (2016)
50 mg/kg of water and fractionated extracts of *Psidium guajava*	0.3 mol L^{-1} of Citric acid aerosol in cognizant guinea pigs	After 30mins of administration antitussive activity becomes prominent with suppression of cough	Antitussive activity	Khawas et al. (2018)
1,2,5 g/kg of *Psidium guajava* leaf extract	30 µmol of capsaicin induced in rats and guinea pigs	Doses suppressed cough by 16%, 35% and 54% respectively after 10 mins	Anticough activity	Jaiarj et al. (1999)
12.5, 25 and 50 mg/kg of extracts fractionated from *P. guajava*	0.3 mg/kg of 17 β-estradiol in female Wistar rats	Administration of extracts inhibited the proliferative effect of 17 β-estradiol on the uterus.	Anti-estrogenic activity	Bazioli et al. (2020)
125 and 250 mg/kg of *P. guajava*	55 mg/kg of STZ in male Sprague–Dawley rats	Reduction of blood glucose levels and amelioration of STZ-induced weight loss	Anti-diabetic activity	Huang et al. (2011)
300 mg/kg of *P. guajava* extracts	50 mg/kg of STZ in rats	Increase in levels of glycosylated hemoglobin, insulin, glucose and restoration of normal hexokinase activity	Anti-diabetic activity	Khan et al. (2013)

(*continued on next page*)

Table 3 (*continued*)

Doses	Experimental models	Observation	Effects	References
Doses of flavonoids extracted from guava leaves	40 mg/kg of STZ in rats	Regulation of fasting blood glucose levels	Anti-diabetic activity	Zhu et al. (2020)
25, 50 mg/kg of *P. guajava* extract	55 mg/kg of STZ in female Sprague–Dawley rats	Reduction of blood glucose levels	Anti-diabetic activity	Soman et al. (2013)
200 mg/kg of *P. guajava* extract	70 mg/kg of STZ in rats	Reduction of blood glucose levels	Anti-diabetic activity	Rajpat and Kumar (2021)
1.00, 0.50 and 0.75 g/kg of ethanolic *P. guajava* extract	100 mg/kg of alloxan tetrahydrate in Wistar rats	Reduction of blood glucose levels	Anti-diabetic activity	Mazumdar et al. (2015)
200 mg/kg of guava leaf extracts	40 mg/kg of STZ in rats	Increase in levels of antioxidants and insulin signalling genes	Anti-diabetic activity	Jayachandran et al. (2020)
300 mg/kg of ethanolic extract of *P. guajava*	1.5 mL/kg of carbon tetrachloride (CCl_4)	Decrease in serum levels of ALT, AST, and ALP	Hepatoprotective activity	Vijayakumar et al. (2020)
250 and 500 mg/kg of *Psidium guajava* and *P. cattleianum* extracts	Single dose of paracetamol (600 mg/kg)	Decrease in serum levels of AST, ALT, and ALP	Hepatoprotective activity	Saber et al. (2018)
0.2 mL of guava leaf solution	1 mL of 0.2mM 2,2-diphenyl-1-picrylhydrazyl (DPPH) ethanolic solution	Production of an antioxidant content value of 201.71 mg BHA eqv $\cdot g^{-1}$	Antioxidant activity	Laily et al. (2015)
50 µL aliquot of *P. guajava* sample	150 µL of 400µM DPPH	High antioxidant activity in DPPH and ABTS assays	Antioxidant activity	Flores et al. (2015)
1 mL of chloroform, methanolic and hexane extracts of *P. guajava*	4 mL of 0.1 mM DPPH	High antioxidative activity of methanolic extract	Antioxidant activity	Ashraf et al. (2016)
200 µL of essential oils derived from *P. guajava*	50 µL of 1 mM DPPH	Reduction of DPPH radical.	Antioxidant activity	Lee et al. (2012)
100 µL of solution silver nanoparticles from *P. guajava*	200 µL of 100 µM DPPH methanol solution	Antioxidant activity increased in dose dependent manner	Antioxidant activity	Wang et al. (2018)
100 µL guava extract solution	100 µL of 0.5 mmo1/L DPPH solution	Presence of poly phenols induced good antioxidant activity	Antioxidant activity	Tan et al. (2020)
90 µL of 1000–50 µg/mL *P. guajava*extracts and fractions	2.7 mL of Ferric reducing antioxidant power (FRAP) reagent	Flavonoid fraction showed highest antioxidant with lowest EC_{50} value	Antioxidant activity	Sobral-Souza et al. (2018)
50 µL of *P. guajava* leaf fractions	1 mL of 0.1 mM DPPH	Methanolic extract showed the most antioxidant activity	Antioxidant activity	Zahin et al. (2017)
Water extract (WE-PGL) and sulfate polysaccharide (PS-PGL) fraction of *P. guajava*	DPPH radicals	PS-PGL produced IC_{50} value of 0.02 mg/mL whilst WE-PGL produced 0.11 mg/mL against hydroxyl radical	Antioxidant activity	Kim et al. (2016)
25, 50 and 100 mg/kg of lycopene extracted from guava leaves	50 µL of a Carrageenan suspension in Swiss mice	Extract at high doses inhibited formation of edema	Anti-inflammatory activity	Vasconcelos et al. (2017)
50–200 mg/kg of *P. guajava* extract	0.1 mL of a carrageenan suspension in rats	Inhibition of edema	Anti-inflammatory activity	Olajide et al. (1999)
50 and 100 mg/kg of *P. guajava* extracts	Lactose containing diet in mice	Reversal of abnormalities in serum electrolytes and urine levels	Antidiarrheal activity	Koriem et al. (2019)
100, 200, 400 mg/kg of *P. guajava* extracts	1 mL of 3.29×10^9 CFU/ml of *Escherichia coli* in rats	Reduction in number and weight of stools	Antidiarrheal activity	Hirudkar et al. (2020)
250 mg/kg, 500 mg/kg and 750 mg/kg of *P. guajava* extracts	2 mL of castor oil in rats	Reduced number of wetted feaces and drop in frequency of stooling	Antidiarrheal activity	Mazumdar et al. (2015)

reported moderate antioxidant activities of essential oil (EO) extracted from guava leaves. Feng et al. (2015) examined the antioxidative effects of compounds isolated from *P. guajava*. Results from this study revealed guavinoside C, guavinoside F, quercetin, quercetin-3-O-a-L-arabinofuranoside and quercetin-3-O-a-L-arabinopyranoside showed strong antioxidant activity using DPPH assay. The antioxidant activity of *P. guajava* extracts might be due to the presence of high phenolic compounds (Hartati et al., 2020) (Table 3).

7.4. Anti-inflammatory activity

Vasconcelos et al. (2017) investigated the anti-inflammatory activity of lycopene extracted from guava and lycopene puri-

fied from guava against carrageenan-induced paw edema. Edema in experimental rats was induced using a single injection of 50 μL of a carrageenan suspension. 25, 50, and 100 mg/kg of lycopene extracted from guava were administered alongside indomethacin. Findings from this study revealed the inhibition of edema by extract at a high dose (50 mg/kg). Olajide et al. (1999) evaluated the anti-inflammatory activity of rats against Carrageenan-induced rat paw edema. Rats were pre-administered *P. guajava* extracts at doses between 50 and 200 mg/kg. Results revealed the significant inhibitory activity of *P. guajava* on edema formation processes (Table 3).

7.5. Antidiarrhoeal activity

Koriem et al. (2019) assessed the antidiarrhoeal activity of *P. guajava* extracts against lactose-containing diet-induced osmotic diarrhoea in rats (Table 3). Rats in treatment groups were administered 50 and 100 mg/kg of *P. guajava* extracts daily for 1 month. Desmopressin was used as the standard drug. Administration of extract revealed a return to normal volume of urine excretion and serum electrolytes. Lipid peroxidation was reduced, emphasizing the extract's antidiarrheal activity. Hirudkar et al. (2020) evaluated the antidiarrhoeal effect of *P. guajava* extracts against enteropathogenic *Escherichia coli* in rats. Diarrhoea was induced in rats by administration of 1 mL of 3.29×10^9 CFU/ml of enteropathogenic *Escherichia coli*. Findings from this study revealed the administration of the extract at 100, 200, 400 mg/kg induced a reduction in the total number of diarrhoeal stools, a decline in the weight of stools, and reduced mean defecation rate of stools in treatment groups. A reversal in declined values of WBC, Hb, and platelets also indicated the antidiarrhoeal ability of the extract. Mazumdar et al. (2015) examined the effect of ethanolic extract of *P. guajava* on castor oil-induced diarrhoea in rats. Doses of 250 mg/kg, 500 mg/kg, and 750 mg/kg of the plant's extract were administered and 2 mg/kg of loperamide was used as a standard drug. Mazumdar et al. (2015) reported that the administration of extract induced a reduction in defecation frequency and the number of wetted faeces. Lutterodt (1992) assessed the propulsion rates in the small intestine of microlax induced diarrhoea in rats. Leaf extract of *P. guajava* at doses ranging from 50 to 400 mg/kg *p.o.* produced anti-diarrhoeal effect against castor oil-induced diarrhoea in rats and mice (Ojewole et al., 2008). *P. guajava* exhibited anti-inflammatory activity (Jang et al., 2014). El-Ahmady et al. (2013) reported that *P. guajava* leaf oil has anti-inflammatory activity. Results showed the extract exhibits a similar inhibition rate compared to the standard drug, morphine sulphate injection used (Table 3).

7.6. Antibacterial activity

Abdelrahim et al. (2002) stated that the aqueous bark and methanolic extracts of *P. guajava* possess anti-bacterial activity. Dutta et al. (2020) reported that benzyl isocyanate obtained from methanol extract of *P. guajava* leaves inhibited *S. aureus*. *P. guajava* leaves extract reduced virulence of *P. aeruginosa*, *C. violaceum*, *S. aureus* and *S. marcescens* (Patel et al. 2019) (Table 3). Essential oil of the senescent leaves of *P. guajava* inhibited human pathogenic bacteria and plant pathogenic fungi, namely *C. lunata* and *F. chlamydosporum* (Chaturvedi et al., 2021).

Silva et al. (2018) showed that extracts of *P. guajava* exhibited antibacterial activity against bacterial species; *Streptococcus salivarius, Streptococcus mutans, Streptococcus mitis, Streptococcus sanguinis,* and *Streptococcus sobrinus*. Weli et al. (2019) studied the antibacterial activity of essential oils derived from *P. guajava* against; *Enterococcus faecalis* and *Staphylococcus aureus*. Findings revealed *P. guajava* possesses significant antibacterial activity at all tested doses; 125, 250, 500 and 1000 μg/ml against tested doses. Pelegrini et al. (2008) revealed that the extracts of *P. guajava* inhibited the growth of *Klebsiella pneumoniae*. Morais-Braga et al. (2016b) showed strong activity against *Escherichia coli, Pseudomonas aeruginosa, Staphyloccocus aureus*. The extract showed strong activity against *Staphyloccocus aureus* exhibiting a MIC value of 256 μg/mL. Huang et al. (2021) showed that chemical constituents isolated from *P. guajava* inhibited *Staphylococcus aureus, Staphylococcus epidermidis* and *Mycobacterium Smegmatis* (Table 3).

7.7. Anticough activity

Jaiarj et al. (1999) investigated the anticough mechanism of *P. guajava* leaf extracts in rats and guinea pigs. A dose of 30 μmol of capsaicin was used to induce cough in rats and guinea pigs (Table 3). Animals in treatment groups were intraperitoneally administered extracts at 1, 2 and 5 g/kg. Findings from this study revealed the suppression of cough in a dose-dependent manner by the extracts. This result emphasizes the therapeutic effect of *P. guajava* on this disorder.

7.8. Anticancer activity

Lin and Lin (2020) evaluated the anticancer activity of guava seed polysaccharides on MCF-7 cells. Findings from this study revealed the inhibition of MCF-7 cell viability significantly in a dose-dependent manner. dos Santos et al. (2017) investigated the anticancer activity of extracts obtained from red *P. guajava*. dos Santos et al. (2017) revealed the inhibitory activity of lycopene-rich extract of *P. guajava* with IC50 value of 29.85 at 5.964 μg/mL. In another study, Zhu et al. (2019) identified compounds exhibiting anticancer activity against HCT116 and HT29 cells. Ashraf et al. (2016) showed the maximum inhibitory activity of *P. guajava* against cancer cells with IC_{50} value of less than 30 mg/mL (Table 3). The anticancer activity of *P. guajava* might be due to the presence of bioactive components; tetracosane, vitamin E, and g-sitosterol (Ryu et al., 2021) (Table 3).

7.9. Antiestrogenic activity

Bazioli et al. (2020) investigated the antiestrogenic effects of extracts fractionated from *P. guajava*. *In vitro* and *in vivo* studies were carried out on 17-β-estradiol inoculated in MCF7 BUS cells and female Wistar rats respectively. 1×10^4 cell mL^{-1} of MCF7 BUS cells in the presence of 10^{-9}M 17 β-estradiol were treated with 0.3, 0.6, 1.25, and 2.5 μg/mL of fractionated *P. guajava* extracts. Experimental rats were inoculated with 0.3 mg/kg of 17-β-estradiol and treated with 12.5,

25, and 50 mg/kg of extracts fractionated from *P. guajava* for 3 days. Results from both *in vitro* and *in vivo* assays revealed inhibition of the proliferative activity of 17-β-estradiol upon administration of extracts suggesting its antiproliferative activity (Table 3).

7.10. Toxicological evaluation

Legba et al. (2019) reported that *P. guajava* does not have any toxic effect on the liver and kidney of Wistar rats. Manekeng et al. (2019) evaluated the possible toxicological effects of methanolic extracts of *P. guajava*. Findings from this study revealed no mortality from the administration of extracts at 5000 mg/kg on experimental rats (Table 3). Evaluations of haematological parameters showed no significant differences in levels of white blood cells, lymphocytes, monocytes, granulocytes, haemoglobin, haematocrit, mean corpuscular hemoglobin concentration and mean corpuscular haemoglobin except platelet levels in experimental male rats at 1000 mg/kg. Observation of serum biochemical parameters showed a significant decrease in total protein levels, alanine aminotransferase, aspartate aminotransferase, total cholesterol, and low-density lipoprotein cholesterol levels. Manekeng et al. (2019) also reported no significant injuries observed from histopathological evaluations of kidneys of male experimental rats. Information gathered from this study emphasizes the low-toxic nature of *P. guajava*.

8. Conclusion

This study revealed that many researchers have conducted in-depth *in vivo* and *in vitro* studies to validate the acclaimed use of *P. guajava* in disease prevention, management, and treatment. In their studies, they reported that *P. guajava* has antioxidant and heptoprotective activities and can be used in the treatment of plethora of health abnormalities such as cough, cancer, bacterial infection, diarrhoea, inflammation, and diabetes. The health-promoting capacity of *P. guajava* has been linked to the presence of vital phytochemicals, essential oils, and biological active components present in the plant. Based on the beneficial effects of *P. guajava* as well as its bioactive constituents, it can be exploited in the development of pharmaceutical products and functional foods. However, there is need for comprehensive studies in clinical trials to establish the safe doses and efficacy of *P. guajava* for the treatment of several diseases.

Funding

No specific funding was provided for this work.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Abdelrahim, S.I., Almagboul, A.Z., Omer, M.E., Elegami, A., 2002. Antimicrobial activity of Psidium guajava L. Fitoterapia 73 (7–8), 713–715. https://doi.org/10.1016/s0367-326x(02)00243-5.

Acharya, B., Chaijaroenkul, W., Na-Bangchang, K., 2021. Therapeutic potential and pharmacological activities of β-eudesmol. Chem Biol Drug Des. 97 (4), 984–996. https://doi.org/10.1111/cbdd.13823.

Alam, W., Khan, H., Shah, M.A., Cauli, O., Saso, L., 2020. Kaempferol as a Dietary Anti-Inflammatory Agent: Current Therapeutic Standing. Molecules 25 (18), 4073. https://doi.org/10.3390/molecules25184073.

Alves, C.T., Ferreira, I.C., Barros, L., Silva, S., Azeredo, J., Henriques, M., 2014. Antifungal activity of phenolic compounds identified in flowers from North Eastern Portugal against Candida species. Future Microbiol. 9 (2), 139–146. https://doi.org/10.2217/fmb.13.147.

Anandakumar, P., Kamaraj, S., Vanitha, M.K., 2021. D-limonene: A multifunctional compound with potent therapeutic effects. J Food Biochem. 45, (1). https://doi.org/10.1111/jfbc.13566 e13566.

Anzoise, M.L., Basso, A.R., Del Mauro, J.S., Carranza, A., Ordieres, G.L., Gorzalczany, S., 2018. Potential usefulness of methyl gallate in the treatment of experimental colitis. Inflammopharmacology. 26 (3), 839–849. https://doi.org/10.1007/s10787-017-0412-6.

Ashraf, A., Sarfraz, R.A., Rashid, M.A., Mahmood, A., Shahid, M., Noor, N., 2016. Chemical composition, antioxidant, antitumor, anticancer and cytotoxic effects of *Psidium guajava* leaf extracts. Pharm. Biol. 54 (10), 1971–1981. https://doi.org/10.3109/13880209.2015.1137604.

Ayeleso, T.B., Matumba, M.G., Mukwevho, E., 2017. Oleanolic Acid and Its Derivatives: Biological Activities and Therapeutic Potential in Chronic Diseases. Molecules 22 (11), 1915. https://doi.org/10.3390/molecules22111915.

Babatola, J.L., Oboh, G., 2021. Extract of varieties of guava (Psidium guajava L.) leaf modulate angiotensin-1-converting enzyme gene expression in cyclosporine-induced hypertensive rats. Phytomed. Plus. 1, (4). https://doi.org/10.1016/j.phyplu.2021.100045 100045.

Banti, C.N., Giannoulis, A.D., Kourkoumelis, N., Owczarzak, A.M., Kubicki, M., Hadjikakou, 2021. S.K. Silver(I) compounds of the anti-inflammatory agents salicylic acid and p-hydroxyl-benzoic acid which modulate cell function. J. Inorg. Biochem. 142,132-144. doi: 10.1016/j.jinorgbio.2014.10.005.

Bazioli, J.M., Costa, J.H., Shiozawa, L., Ruiz, A.L.T.G., Foglio, M. A., Carvalho, J.E., 2020. Anti-estrogenic activity of guajadial fraction, from guava leaves (*Psidium guajava* L.). Molecules 25 (7), 1525. https://doi.org/10.3390/molecules25071525.

Begum, S., Hassan, S.I., Siddiqui, B.S., Shaheen, F., Ghayur, M.N., Gilani, A.H., 2002. Triterpenoids from the leaves of Psidium guajava. Phytochemistry 61 (4), 399–403. https://doi.org/10.1016/s0031-9422(02)00190-5.

Begum, S., Hassan, S.I., Ali, S.N., Siddiqui, B.S., 2004. Chemical constituents from the leaves of Psidium guajava. Nat. Prod. Res. 18 (2), 135–140.

Beidokhti, M.N., Eid, H.M., Villavicencio, M.L.S., Jäger, A.K., Lobbens, E.S., Rasoanaivo, P.R., McNair, L.M., Haddad, P.S., Staerk, D., 2020. Evaluation of the antidiabetic potential of Psidium guajava L. (Myrtaceae) using assays for α-glucosidase, α-amylase, muscle glucose uptake, liver glucose production, and triglyceride accumulation in adipocytes. J. Ethnopharmacol. 257, 1–8. https://doi.org/10.1016/j.jep.2020.112877.

BenSaad, L.A., Kim, K.H., Quah, C.C., Kim, W.R., Shahimi, M., 2017. Anti-inflammatory potential of ellagic acid, gallic acid and punicalagin A&B isolated from Punica granatum. BMC Compl. Altern. Med. 17 (1), 47. https://doi.org/10.1186/s12906-017-1555-0.

Bezerra, C. F., Rocha, J. E., Do Nascimento Silva, M. K., De Freitas, T. S., De Sousa, A. K., Carneiro, J. N. P., Leal, A. L. A. B., Lucas Dos Santos, A. T., Da Cruz, R. P., Rodrigues, A. S., Sales, D. L., Coutinho, H. D. M., Ribeiro, P. R. V., De Brito, E. S., Da Costa, J. G. M., De Menezes, I. R. A., Almeida, W. D. O., Morais-Braga, M. F. B., 2020. UPLC-MS-ESI-QTOF analysis and anti-candida activity of fractions from Psidium guajava L. South Afr. J. Bot., 131, 421-427.

Bezerra, C.F., Rocha, J.E., Nascimento Silva, M.K.D., de Freitas, T. S., de Sousa, A.K., Dos Santos, A.T.L., da Cruz, R.P., Ferreira, M.

H., da Silva, J.C.P., Machado, A.J.T., Carneiro, J.N.P., Sales, D. L., Coutinho, H.D.M., Ribeiro, P.R.V., de Brito, E.S., Morais-Braga, M.F.B., 2018. Analysis by UPLC-MS-QTOF and antifungal activity of guava (Psidium guajava L.). Food. Chem. Toxicol. 119, 122–132. https://doi.org/10.1016/j.fct.2018.05.021.

Bhagavathy, S., Mahendiran, C., Kanchana, R., 2018. Identification of glucosyl transferase inhibitors from Psidium guajava against Streptococcus mutans in dental caries. J. Trad. Comp. Med. 1–14. https://doi.org/10.1016/j.jtcme.2017.09.003.

Bhandarkar, N.S., Brown, L., Panchal, S.K., 2019. Chlorogenic acid attenuates high-carbohydrate, high-fat diet–induced cardiovascular, liver, and metabolic changes in rats. Nutr. Res. 1–40. https://doi.org/10.1016/j.nutres.2018.11.002.

Britto, A.C.S., De Oliveira, A.C.A., Henriques, R.M., Cardoso, G. M.B., Bomfim, D.S., Carvalho, A.A., Moraes, M.O., Pessoa, C., Pinheiro, M.L.B., Costa, E.V., Bezerra, D.P., 2012. In vitro and in vivo antitumor effects of the essential oil from the leaves of Guatteria friesiana. Planta Med. 78 (5), 409–414. https://doi.org/10.1055/s-0031-1298173.

Budzynska, B., Faggio, C., Kruk-Slomka, M., Samec, D., Nabavi, S. F., Sureda, A., Devi, K.P., Nabavi, S.M., 2019. Rutin as neuroprotective agent: from bench to bedside. Curr. Med. Chem. 26 (27), 5152–5164. https://doi.org/10.2174/0929867324666171003114154.

Chaturvedi, T., Singh, S., Nishad, I., Kumar, A., Tiwari, N., Tandon, S., Saikia, D., Verma, R.S., 2021. Chemical composition and antimicrobial activity of the essential oil of senescent leaves of guava (Psidium guajava L.). Nat. Prod. Res. 35 (8), 1393–1397. https://doi.org/10.1080/14786419.2019.1648462.

Chen, H., Yen, G.-C., 2007. Antioxidant activity and free radical-scavenging capacity of extracts from guava (Psidium guajava L.) leaves. Food Chem. 101, 686–694. https://doi.org/10.1016/j.foodchem.2006.02.047.

Cianfaglione, K., Blomme, E.E., Quassinti, L., Bramucci, M., Lupidi, G., Dall'Acqua, S., Maggi, F., 2017. Cytotoxic essential oils from Eryngium campestre and Eryngium amethystinum (Apiaceae) growing in central Italy. Chem Biodivers. 14 (7). https://doi.org/10.1002/cbdv.201700096.

Dai, Y., Zhang, H., Zhang, J., Yan, M., 2018. Isoquercetin attenuates oxidative stress and neuronal apoptosis after ischemia/reperfusion injury via Nrf2-mediated inhibition of the NOX4/ROS/NF-κB pathway. Chem. Biol. Interact. 284, 32–40. https://doi.org/10.1016/j.cbi.2018.02.017.

de Araújo, A.A., Soares, L.A., Assunção Ferreira, M.R., de Souza Neto, M.A., da Silva, G.R., de Araújo, R.F., Jr, G.G.C., de Melo, M.C., 2014. Quantification of polyphenols and evaluation of antimicrobial, analgesic and anti-inflammatory activities of aqueous and acetone-water extracts of Libidibia ferrea, Parapiptadenia rigida and Psidium guajava. J. Ethnopharmacol. 28 (156), 88–96. https://doi.org/10.1016/j.jep.2014.07.031.

De Leo, M., Braca, A., De Tommasi, N., Norscia, I., Morelli, I., Battinelli, L., Mazzanti, G., 2004. Phenolic compounds from Baseonema acuminatum leaves: isolation and antimicrobial activity. Planta. Med. 70 (9), 841–846. https://doi.org/10.1055/s-2004-827233.

De Souza, T.S., Ferreira, M.F.S., Menini, L., Souza, J.R.C.L., Parreira, L.A., Cecon, P.R., Ferreira, A., 2017. Essential oil of Psidium guajava: Influence of genotypes and environment. Sci. Hortic. 216, 38–44. https://doi.org/10.1016/j.scienta.2016.12.026.

De Souza, T.S., Ferreira, M.F.S., Menini, L., Souza, J.R.C.L., Bernardes, C.O., Ferreira, A., 2018. Chemotype diversity of Psidium guajava L. Phytochemistry 129–137. https://doi.org/10.1016/j.phytochem.2018.06.006.

Dias, N.C., Nunes, T.A.L., Sousa, J.M.S., Costa, L.H., Rodrigues, R.R.L., Araújo, A.J., Marinho Filho, J.D.B., da Silva, M.V., Oliveira, M.R., Carvalho, F.A.A., Rodrigues, K.A.D.F., 2020. Methyl gallate: Selective antileishmanial activity correlates with host-cell directed effects. Chem. Biol. Interact. 320,. https://doi.org/10.1016/j.cbi.2020.109026 109026.

Díaz-de-Cerio, E., Verardo, V., Gómez-Caravaca, A.M., Fernández-Gutiérrez, A., Segura-Carretero, A., 2017. Health effects of Psidium guajava L. leaves: An overview of the Last Decade. Int. J. Mol. Sci. 18(4):897. https://doi.org/10.3390/ijms18040897.

Díaz-de-cerio, E., Gómez-caravaca, A.M., Verardo, V., Fernandez-Gutierrez, A., Segura-Carretero, A., 2016. Determination of guava (Psidium guajava L.) leaf phenolic compounds using HPLC-DAD-QTOF-MS. J. Funct. Foods. 376–388. https://doi.org/10.1016/j.jff.2016.01.040.

Dimmito, M.P., Stefanucci, A., Della Valle, A., Scioli, G., Cichelli, A., Mollica, A., 2021. An overview on plants cannabinoids endorsed with cardiovascular effects. Biomed. Pharmacother. 142,. https://doi.org/10.1016/j.biopha.2021.111963 111963.

do Nascimento, K.F., Moreira, F.M.F., Alencar Santos, J., Kassuya, C.A.L., Croda, J.H.R., Cardoso, C.A.L., Vieira, M.D.C., Góis Ruiz, A.L.T., Ann Foglio, M., de Carvalho, J.E., Formagio, A.S. N., 2018. Antioxidant, anti-inflammatory, antiproliferative and antimycobacterial activities of the essential oil of Psidium guineense Sw. and spathulenol. J Ethnopharmacol. 210, 351-358. doi: 10.1016/j.jep.2017.08.030.

Doan, T.Q., Ho, D.V., Trong Le, N., Le, A.T., Van Phan, K., Nguyen, H.T., Raal, A., 2021. Chemical composition and anti-inflammatory activity of the essential oil from the leaves of *Limnocitrus littoralis* (Miq.) Swingle from Vietnam. Nat. Prod. Res. 35 (9), 1550–1554. https://doi.org/10.1080/14786419.2019.1652286.

Dolai, N., Kumar, A., Islam, A., Haldar, P.K., 2016. Apoptogenic effects of β-sitosterol glucoside from Castanopsis indica leaves. Nat. Prod. Res. 30 (4), 482–485. https://doi.org/10.1080/14786419.2015.1023201.

Dong, H., Chen, S.X., Kini, R.M., Xu, H.X., 1998. Effects of tannins from Geum japonicum on the catalytic activity of thrombin and factor Xa of blood coagulation cascade. J. Nat. Prod. 61 (11), 1356–1360. https://doi.org/10.1021/np9801458.

Dos Santos Negreiros, P., da Costa, D. S., da Silva, V. G., de Carvalho Lima, I. B., Nunes, D. B., de Melo Sousa, F. B., de Souza Lopes Araújo, T., Medeiros, J., Dos Santos, R. F., de Cássia Meneses Oliveira, R., 2019. Antidiarrheal activity of α-terpineol in miceAntidiarrheal activity of α-terpineol in mice. Biomed Pharmacother. 2019 Feb;110:631-640. doi: 10.1016/j.biopha.2018.11.131.

dos Santos, R.C., Ombredane, A.S., Souza, J.M.T., Vasconcelos, A. G., Plácido, A., Amorim, A.D.G.N., Barbosa, E.A., Lima, F.C.D. A., Ropke, C.D., Alves, M.M.M., Arcanjo, D.D.R., Carvalho, F. A.A., Delerue-Matos, C., Joanitti, G.A., Leite, J.R.S.A., 2018. Lycopene-rich extract from red guava (*Psidium guajava* L.) displays cytotoxic effect against human breast adenocarcinoma cell line MCF-7 via an apoptotic-like pathway. Food Res. Int. 105, 184–196. https://doi.org/10.1016/j.foodres.2017.10.045.

Dutta, K., Karmakar, A., Jana, D., Ballav, S., Shityakov, S., Panda, A.K., Ghosh, C., 2020. Benzyl isocyanate isolated from the leaves of Psidium guajava inhibits Staphylococcus aureus biofilm formation. Biofouling 36 (8), 1000–1017. https://doi.org/10.1080/08927014.2020.1842877.

Eidenberger, T., Selg, M., Krennhuber, K., 2013. Inhibition of dipeptidyl peptidase activity by flavonol glycosides of guava (Psidium guajava L.): A key to the beneficial effects of guava in type II diabetes mellitus. Fitoterapia 89 (1), 74–79. https://doi.org/10.1016/j.fitote.2013.05.015.

Farag, R.S., Abdel-Latif, M.S., Abd El Baky, H.H., Tawfeek, L.S., 2020. Phytochemical screening and antioxidant activity of some medicinal plants' crude juices. Biotechnol. Reports 28,. https://doi.org/10.1016/j.btre.2020.e00536 e00536.

Feng, X.H., Wang, Z.H., Meng, D.L., Li, X., 2015. Cytotoxic and antioxidant constituents from the leaves of *Psidium guajava*. Bioorg. Med. Chem. Lett. 25 (10), 2193–2198. https://doi.org/10.1016/j.bmcl.2015.03.058.

Fernandes, C.C., Rezende, J.L., Silva, E.A.J., Silva, F.G., Stenico, L., Crotti, A.E.M., Esperandim, V.R., Santiago, M.B., Martins, C.H. G., Miranda, M.L.D., 2021. Chemical composition and biological activities of essential oil from flowers of Psidium guajava (Myrtaceae). Braz. J. Biol. 81 (3), 728–736.

Fernandes, M.R.V., Dias, A.L.T., Carvalho, R.R., Souza, C.R.F., Oliveira, W.P., 2014. Antioxidant and antimicrobial activities of Psidium guajava L. spray dried extracts. Ind. Crops Prod. 60, 39–44. https://doi.org/10.1016/j.indcrop.2014.05.049.

Flores, G., Wu, S.B., Negrin, A., Kennelly, E.J., 2015. Chemical composition and antioxidant activity of seven cultivars of guava (Psidium guajava) fruits. Food Chem. 170, 327–335. https://doi.org/10.1016/j.foodchem.2014.08.076.

Ghorbani, A., 2017. Mechanisms of antidiabetic effects of flavonoid rutin. Biomed. Pharmacother 96, 305–312. https://doi.org/10.1016/j.biopha.2017.10.001.

Giuliani, C., Pieraccini, G., Santilli, C., Tani, C., Bottoni, M., Schiff, S., Fico, G., Papini, A., Falsini, S., 2020. Anatomical investigation and GC/MS analysis of 'Coco de Mer', Lodoicea maldivica (Arecaceae). Chem Biodivers. 17, (11). https://doi.org/10.1002/cbdv.202000707 e2000707.

Govindarajan, M., Rajeswary, M., Benelli, G., 2016. δ-Cadinene, calarene and δ-4-carene from Kadsura heteroclita essential oil as novel larvicides against malaria, dengue and filariasis mosquitoes. Comb. Chem. High. Throughput Screen 19 (7), 565–571. https://doi.org/10.2174/1386207319666160506123520.

Guo, W., Liu, S., Ju, X., Du, J., Xu, B., Yuan, H., Qin, F., Li, L., 2019. The antitumor effect of hinesol, extract from Atractylodes lancea (Thunb.) DC. by proliferation, inhibition, and apoptosis induction via MEK / ERK and NF - κ B pathway in non – small cell lung cancer cell lines A549 and NCI - H1299. J. Cell. Biochem. 1–8. https://doi.org/10.1002/jcb.28696.

Gutiérrez, R.M.P., Mitchell, S., Solis, R.V., 2008. Psidium guajava: A review of its traditional uses, phytochemistry and pharmacology. J. Ethnopharmacol. 117, 1–27. https://doi.org/10.1016/j.jep.2008.01.025.

Habtemariam, S., 2017. Protective Effects of Caffeic Acid and the Alzheimer's Brain: An Update. Mini Rev. Med. Chem. 17 (8), 667–674. https://doi.org/10.2174/1389557516666161130100947.

Han, N.R., Moon, P.D., Ryu, K.J., Jang, J.B., Kim, H.M., Jeong, H. J., 2017. β-eudesmol suppresses allergic reactions via inhibiting mast cell degranulation. Clin. Exp. Pharmacol. Physiol. 44 (2), 257–265. https://doi.org/10.1111/1440-1681.12698.

Hao, C., Wu, B., Hou, Z., Xie, Q., Liao, T., Wang, T., Ma, D., 2017. Asiatic acid inhibits LPS-induced inflammatory response in human gingival fibroblasts. Int. Immunopharmacol. 50, 313–318. https://doi.org/10.1016/j.intimp.2017.07.005.

Hartati, R., Nadifan, H.I., Fidrianny, I., 2020. Crystal guava (*Psidium guajava* L. "Crystal"): evaluation of *in vitro* antioxidant capacities and phytochemical content. Sci. World J. https://doi.org/10.1155/2020/9413727.

Hassan, E.M., El Gendy, A.E.G., Abd-ElGawad, A.M., Elshamy, A. I., Farag, M.A., Alamery, S.F., Omer, E.A., 2020. Comparative chemical profiles of the essential oils from different varieties of *Psidium guajava* L. Molecules 26 (1), 119. https://doi.org/10.3390/molecules26010119.

Hirudkar, J.R., Parmar, K.M., Prasad, R.S., Sinha, S.K., Lomte, A. D., Itankar, P.R., Prasad, S.K., 2020. The antidiarrhoeal evaluation of *Psidium guajava* L. against enteropathogenic *Escherichia coli* induced infectious diarrhoea. J. Ethnopharmacol. 251 (112561). https://doi.org/10.1016/j.jep.2020.112561.

Holetz, F.B., Pessini, G.L., Sanches, N.R., Cortez, A.G., Nakamura, C.V., Filho, D.P.B., 2002. Screening of Some Plants Used in the Brazilian Folk Medicine for the Treatment of Infectious Diseases. Mem. Inst. Oswaldo Cruz 97 (7), 1027–1031.

Hsieh, C.L., Lin, Y.C., Yen, G.C., Chen, H.Y., 2007. Preventive effects of guava (Psidium guajava L.) leaves and its active compounds against α-dicarbonyl compounds-induced blood coagulation. Food Chem. 103 (2), 528–535. https://doi.org/10.1016/j.foodchem.2006.08.022.

Huang, C.S., Yin, M.C., Chiu, L.C., 2011. Antihyperglycemic and antioxidative potential of Psidium guajava fruit in streptozotocin-induced diabetic rats. Food Chem. Toxicol. 49 (9), 2189–2195. https://doi.org/10.1016/j.fct.2011.05.032.

Huang, J., Li, C., Ma, J., Xu, K., Chen, X., Jiang, J., Zhang, D., 2021. Chemical constituents of *Psidium guajava* leaves and their antibacterial activity. Phytochemistry. 186,. https://doi.org/10.1016/j.phytochem.2021.112746 112746.

Hui, L.M., Zhao, G.D., Zhao, J.J., 2015. δ-Cadinene inhibits the growth of ovarian cancer cells via caspase-dependent apoptosis and cell cycle arrest. Int. J. Clin. Exp. Pathol. 8 (6), 6046–6056.

Imran, M., Aslam, Gondal, T., Atif, M., Shahbaz, M., Batool, Qaisarani, T., Hanif, Mughal, M., Salehi, B., Martorell, M., Sharifi-Rad, J., 2020. Apigenin as an anticancer agent. Phytother. Res. 34(8), 1812-1828. doi: 10.1002/ptr.6647.

Jaiarj, P., Khoohaswan, P., Wongkrajang, Y., Peungvicha, P., Suriyawong, P., Saraya, M.L., Ruangsomboon, O., 1999. Anti-cough and antimicrobial activities of *Psidium guajava* Linn. leaf extract. J. Ethnopharmacol. 67 (2), 203–212. https://doi.org/10.1016/s0378-8741(99)00022-7.

Jang, M., Jeong, S.W., Cho, S.K., Ahn, K.S., Lee, J.H., Yang, D.C., Kim, J.C., 2014. Anti-inflammatory effects of an ethanolic extract of guava (Psidium guajava L.) leaves in vitro and in vivo. J. Med. Food 17 (6), 678–685. https://doi.org/10.1089/jmf.2013.2936.

Jayachandran, M., Vinayagam, R., Xu, B., 2020. Guava leaves extract ameliorates STZ induced diabetes mellitus via activation of PI3K/AKT signaling in skeletal muscle of rats. Mol Biol Rep 47 (4), 2793–2799. https://doi.org/10.1007/s11033-020-05399-2.

Jiang, A., Zhang, Y., Zhang, X., Wu, D., Liu, Z., Li, S., Liu, X., Han, Z., Wang, C., Wang, J., Wei, Z., Guo, C., Yang, Z., 2020. Morin alleviates LPS-induced mastitis by inhibiting the PI3K/AKT, MAPK, NF-κB and NLRP3 signaling pathway and protecting the integrity of blood-milk barrier. Int. Immunopharmacol. 78,. https://doi.org/10.1016/j.intimp.2019.105972 105972.

Joshi, R.K., 2013. Chemical composition, in vitro antimicrobial and antioxidant activities of the essential oils of Ocimum gratissimum, O. Sanctum and their major constituents. Indian J. Pharm. Sci. 75, 457–462. https://doi.org/10.4103/0250-474X.119834.

Kamada, Y., Yakabu, H., Ichiba, T., Tamanaha, A., Shimoji, M., Kato, M., Norimoto, C., Yamashiro, R., Miyagi, I., Sakudo, A., Tanaka, Y., 2018. Castalagin and vescalagin purified from leaves of Syzygium samarangense (Blume) Merrill & L.M. Perry: Dual inhibitory activity against PARP1 and DNA topoisomerase II. Fitoterapia. 129, 94–101. https://doi.org/10.1016/j.fitote.2018.06.015.

Karatas, O., Balci, Yuce, H., Taskan, M.M., Gevrek, F., Alkan, C., Isiker, Kara, G., Temiz, C., 2020. Cinnamic acid decreases periodontal inflammation and alveolar bone loss in experimental periodontitis. J. Periodontal. Res. 55(5), 676-685. doi: 10.1111/jre.12754.

Kendra, P.E., Owens, D., Montgomery, W.S., Narvaez, T.I., Bauchan, G.R., Schnell, E.Q., Tabanca, N., Carrillo, D., 2017. α-Copaene is an attractant, synergistic with quercivorol, for improved detection of Euwallacea nr. fornicatus (Coleoptera: Curculionidae: Scolytinae). PLoS One. 12, (6). https://doi.org/10.1371/journal.pone.0179416 e0179416.

Khan, H.B., Shanmugavalli, R., Rajendran, D., Bai, M.R., Sorimuthu, S., 2013. Protective effect of *Psidium guajava* leaf extract on altered carbohydrate metabolism in streptozotocin-induced diabetic rats. J. Diet Suppl. 10 (4), 335–344. https://doi.org/10.3109/19390211.

Khawas, S., Sivová, V., Anand, N., Bera, K., Ray, B., NosáĽová, G., Ray, S., 2018. Chemical profile of a polysaccharide from Psidium guajava leaves and it's in vivo antitussive activity. Int. J. Biol. Macromol. 109, 681–686. https://doi.org/10.1016/j.ijbiomac.2017.12.098.

Khedr, S.I., Mokhamer, E., Hassan, A., El-Feki, A.S., Elkhodary, G. M., El-Gerbed, M., 2021. Psidium guajava Linn leaf ethanolic extract: In vivo giardicidal potential with ultrastructural damage, anti-inflammatory and antioxidant effects. Saudi J. Biol. Sci. 28 (1), 427–439. https://doi.org/10.1016/j.sjbs.2020.10.026.

Kim, Y.S., Shin, D.H., 2004. Volatile constituents from the leaves of Callicarpa japonica Thunb. and their antibacterial activities. J Agric Food Chem. 52 (4), 781–787. https://doi.org/10.1021/jf034936d.

Kim, D.Y., Kang, M.K., Lee, E., Kim, Y., Oh, H., Kim, S., Oh, S.Y., Na, W., Kang, Y., 2020. Eucalyptol Inhibits Amyloid- β -Induced Barrier Dysfunction in Glucose-Exposed Retinal Pigment Epithelial Cells and Diabetic Eyes. Antioxidants 9 (1000), 1–19.

Kim, J., Jin, H.L., Jang, D.S., Jeong, K.W., Choung, S.Y., 2018. Quercetin-3-O-α-l-arabinopyranoside protects against retinal cell death via blue light-induced damage in human RPE cells and Balb-c mice. Food Funct. 9 (4), 2171–2183. https://doi.org/10.1039/c7fo01958k.

Kim, S.Y., Kim, E.A., Kim, Y.S., Yu, S.K., Choi, C., Lee, J.S., Kim, Y.T., Nah, J.W., Jeon, Y.J., 2016. Protective effects of polysaccharides from *Psidium guajava* leaves against oxidative stresses. Int. J. Biol. Macromol. 91, 804–811. https://doi.org/10.1016/j.ijbiomac.2016.05.111.

Kim, T.H., Yoo, S.D., Lee, H.S., Lee, K.M., Seok, S.H., Kim, M.G., Jung, B.H., Kim, M.G., Shin, B.S., 2015. In vivo absorption and disposition of α-cedrene, a sesquiterpene constituent of cedarwood oil, in female and male rats. Drug Metab. Pharmacokinet. 30 (2), 168–173. https://doi.org/10.1016/j.dmpk.2014.12.003.

Koriem, K.M.M., Arbid, M.S., Saleh, H.N., 2019. Antidiarrheal and protein conservative activities of *Psidium guajava* in diarrheal rats. J. Integr. Med. 17 (1), 57–65. https://doi.org/10.1016/j.joim.2018.12.001.

Koyama, S., Purk, A., Kaur, M., Soini, H.A., Novotny, M.V., Davis, K., Kao, C.C., Matsunami, H., Mescher, A., 2019. Beta-caryophyllene enhances wound healing through multiple routes. PLoS One 14, (12). https://doi.org/10.1371/journal.pone.0216104 e0216104.

Krzysztoforska, K., Mirowska-Guzel, D., Widy-Tyszkiewicz, E., 2019. Pharmacological effects of protocatechuic acid and its therapeutic potential in neurodegenerative diseases: Review on the basis of in vitro and in vivo studies in rodents and humans. Nutr. Neurosci. 22 (2), 72–82. https://doi.org/10.1080/1028415X.2017.1354543.

Kumar, M., Tomar, M., Amarowicz, R., Saurabh, V., Nair, M.S., Maheshwari, C., Sasi, M., Prajapati, U., Hasan, M., Singh, S., Changan, S., Prajapat, R.K., Berwal, M.K., Satankar, V., 2021. Guava (Psidium guajava L.) Leaves : Nutritional composition, phytochemical profile, and health-promoting bioactivities. Foods 10 (752), 1–20.

Laily, N., Kusumaningtyas, R.W., Sukarti, I., Rini, M.R.D.K., 2015. The potency of guava *Psidium Guajava* (L.) leaves as a functional immunostimulatory ingredient. Procedia Chem. 14, 301–307. https://doi.org/10.1016/j.proche.2015.03.042.

Lee, W.C., Mahmud, R., Pillai, S., Perumal, S., Ismail, S., 2012. Antioxidant activities of essential oil of *Psidium Guajava* L. leaves. APCBEE Procedia. 2, 86–91. https://doi.org/10.1016/j.apcbee.2012.06.016.

Legault, J., Pichette, A., 2010. Potentiating effect of β-caryophyllene on anticancer activity of α-humulene, isocaryophyllene and paclitaxel. J. Pharm. Pharmacol. 59 (12), 1643–1647. https://doi.org/10.1211/jpp.59.12.0005.

Legba, B., Dougnon, V., Deguenon, E., Agbankpe, J., Senou, M., Aniambossou, A., Gbaguidi, C., Sintondji, K., Baba-Moussa, L., Dougnon, J., 2019. Toxicological Characterization of Six Plants of the Beninese Pharmacopoeia Used in the Treatment of Salmonellosis. J. Toxicol. 3530659. https://doi.org/10.1155/2019/3530659.

Li, P.Y., Hsu, C.C., Yin, M.C., Kuo, Y.H., Tang, F.Y., Chao, C.Y., 2015. Protective effects of red guava on inflammation and oxidative stress in streptozotocin-induced diabetic mice. Molecules 20 (12), 22341–22350. https://doi.org/10.3390/molecules201219831.

Li, Y., Xu, J., Li, D., Ma, H., Mu, Y., Huang, X., Li, L., 2020. Guavinoside B from *Psidium guajava* alleviates acetaminophen-induced liver injury *via* regulating the Nrf2 and JNK signaling pathways. Food Funct. 11 (9), 8297–8308. https://doi.org/10.1039/d0fo01338b.

Li, Y., Xu, J., Li, D., Ma, H., Mu, Y., Zheng, D., Huang, X., Li, L., 2021. Chemical characterization and hepatoprotective effects of a standardized triterpenoid-enriched guava leaf extract. J. Agric. Food Chem. 69 (12), 3626–3637. https://doi.org/10.1021/acs.jafc.0c07125.

Lin, H.C., Lin, J.Y., 2020. GSF3, a polysaccharide from guava (*Psidium guajava* L.) seeds, inhibits MCF-7 breast cancer cell growth via increasing Bax/Bcl-2 ratio or Fas mRNA expression levels. Int. J. Biol. Macromol. 161, 1261–1271. https://doi.org/10.1016/j.ijbiomac.2020.06.057.

Liu, C., Shen, Y.J., Tu, Q.B., Zhao, Y.R., Guo, H., Wang, J., Zhang, L., Shi, H.W., Sun, Y., 2018. Pedunculoside, a novel triterpene saponin extracted from Ilex rotunda, ameliorates high-fat diet induced hyperlipidemia in rats. Biomed. Pharmacother. 101, 608–616. https://doi.org/10.1016/j.biopha.2018.02.131.

Liu, G., Zhang, B.F., Hu, Q., Liu, X.P., Chen, J., 2020. Syringic acid mitigates myocardial ischemia reperfusion injury by activating the PI3K/Akt/GSK-3β signaling pathway. Biochem. Biophys. Res. Commun. 531 (2), 242–249. https://doi.org/10.1016/j.bbrc.2020.07.047.

Lorena, C., Ressaissi, A., Serralheiro, M.L., 2022. Bioactives from Psidium guajava leaf decoction: LC-HRMS-MS-Qtof identification, bioactivities and bioavailability evaluation. Food Chem. Adv. 1,. https://doi.org/10.1016/j.focha.2021.100003 100003.

Lou, L.L., Li, W., Zhou, B.H., Chen, L., Weng, H.Z., Zou, Y.H., Tang, G.H., Bu, X.Z., Yin, S., 2019. (+)-Isobicyclogermacrenal and spathulenol from Aristolochia yunnanensis alleviate cardiac fibrosis by inhibiting transforming growth factor β/small mother against decapentaplegic signaling pathway. Phytother Res. 33 (1), 214–223. https://doi.org/10.1002/ptr.6219.

Luo, Y., Peng, B., Wei, W., Tian, X., Wu, Z., 2019. Antioxidant and Anti-Diabetic Activities of Polysaccharides from Guava Leaves. Molecules 24 (7), 1343. https://doi.org/10.3390/molecules24071343.

Lutterodt, G.D., 1992. Inhibition of Microlax-induced experimental diarrhoea with narcotic-like extracts of *Psidium guajava* leaf in rats. J. Ethnopharmacol. 37 (2), 151–157. https://doi.org/10.1016/0378-8741(92)90073-z.

Ma, Z., Huang, Y., Huang, W., Feng, X., Yang, F., Li, D., 2019. Separation, Identification, and Antioxidant Activity of Polyphenols from Lotus Seed Epicarp. Molecules 24 (4007), 1–10.

Machado, A.J.T., Santos, A.T.L., Martins, G.M.A.B., Cruz, R.P., Costa, M.D.S., Campina, F.F., Freitas, M.A., Bezerra, C.F., Leal, A.L.A.B., Carneiro, J.N.P., Coronel, C., Rolón, M., Gómez, C.V., Coutinho, H.D.M., Morais-Braga, M.F.B., 2018. Antiparasitic effect of the Psidium guajava L. (guava) and Psidium brownianum MART. EX DC. (araçá-de-veado) extracts. Food Chem. Toxicol. 119, 275–280. https://doi.org/10.1016/j.fct.2018.03.018.

Magalingam, K.B., Radhakrishnan, A., Haleagrahara, N., 2016. Protective effects of quercetin glycosides, rutin, and isoquercetrin against 6-hydroxydopamine (6-OHDA)-induced neurotoxicity in rat pheochromocytoma (PC-12) cells. Int. J. Immunopathol Pharmacol. 29 (1), 30–39. https://doi.org/10.1177/0394632015613039.

Manekeng, H.T., Mbaveng, A.T., Ntyam, Mendo, S.A., Agokeng, A. D., Kuete, V., 2019. Evaluation of acute and subacute toxicities of *psidium guajava* methanolic bark extract: a botanical with in vitro antiproliferative potential. Evid Based Complement Alternat. Med. doi: 10.1155/2019/8306986.

Marunaka, Y., Marunaka, R., Sun, H., Yamamoto, T., Kanamura, N., Inui, T., Taruno, A., 2017. Actions of quercetin, a polyphenol, on blood pressure. Molecules 22 (2), 209. https://doi.org/10.3390/molecules22020209.

Maruyama, H., Kawakami, F., Lwin, T.T., Imai, M., Shamsa, F., 2018. Biochemical Characterization of ferulic acid and caffeic acid which effectively inhibit melanin synthesis via different mechanisms in B16 melanoma cells. Biol. Pharm. Bull. 41 (5), 806–810. https://doi.org/10.1248/bpb.b17-00892.

Mazewski, C., Kim, M.S., Gonzalez de Mejia, E., 2019. Anthocyanins, delphinidin-3-O-glucoside and cyanidin-3-O-glucoside, inhibit immune checkpoints in human colorectal cancer cells in vitro and in silico. Sci. Rep. 9 (1), 11560. https://doi.org/10.1038/s41598-019-47903-0.

Mazumdar, S., Akter, R., Talukder, D., 2015. Antidiabetic and antidiarrhoeal effects on ethanolic extract of *Psidium guajava* (L.) Bat. leaves in Wister rats. Asian Pac. J Trop. Biomed. 5 (1), 10–14. https://doi.org/10.1016/S2221-1691(15)30163-5.

Metwally, A.M., Omar, A.A., Harraz, F.M., El Sohafy, S.M., 2010. Phytochemical investigation and antimicrobial activity of Psidium guajava L. leaves. Pharmacogn. Mag. 6 (23), 212–218. https://doi.org/10.4103/0973-1296.66939.

Min, H.Y., Son, H.E., Jang, W.G., 2020. Alpha-pinene promotes osteoblast differentiation and attenuates TNFα-induced inhibition of differentiation in MC3T3-E1 pre-osteoblasts. Clin Exp Pharmacol Physiol. 47 (5), 831–837. https://doi.org/10.1111/1440-1681.13245.

Mlala, S., Oyedeji, A.O., Gondwe, M., Oyedeji, O.O., 2019. Ursolic acid and its derivatives as bioactive agents. Molecules 24 (15), 2751. https://doi.org/10.3390/molecules24152751.

Molonia, M.S., Occhiuto, C., Muscarà, C., Speciale, A., Bashllari, R., Villarroya, F., Saija, A., Cimino, F., Cristani, M., 2020. Cyanidin-3-O-glucoside restores insulin signaling and reduces inflammation in hypertrophic adipocytes. Arch. Biochem. Biophys. 691,. https://doi.org/10.1016/j.abb.2020.108488 108488.

Morais-Braga, M.F.B., Carneiro, J.N.P., Machado, A.J.T., Sales, D. L., dos Santos, A.T.L., Boligon, A.A., Athayde, M.L., Menezes, I. R.A., Souza, D.S.L., Costa, J.G.M., Coutinho, H.D.M., 2017. Phenolic composition and medicinal usage of Psidium guajava Linn.: Antifungal activity or inhibition of virulence? Saudi. J. Biol. Sci. 24 (2), 302–313. https://doi.org/10.1016/j.sjbs.2015.09.028.

Morais-Braga, M.F.B., Carneiro, J.N.P., Machado, A.J.T., dos Santos, A.T.L., Sales, D.L., Lima, L.F., Figueredo, F.G., Coutinho, H.D.M., 2016a. Psidium guajava L., from ethnobiology to scientific evaluation: Elucidating bioactivity against pathogenic microorganisms. J. Ethnopharmacol. 194, 1140–1152. https://doi.org/10.1016/j.jep.2016.11.017.

Morais-Braga, M.F.B., Sales, D.L., Silva, F.D., Chaves, T.P., Bitu, V.D.N., Avilez, W.M.T., Ribeiro-Filho, J., Coutinho, H.D.M., 2016b. *Psidium guajava* L. and *Psidium brownianum* Mart ex DC. potentiate the effect of antibiotics against Gram-positive and Gram-negative bacteria. Eur. J. Integr. Med. 8 (5), 683–687. https://doi.org/10.1016/j.eujim.2016.07.001.

Mukhtar, Y.M., Adu-frimpong, M., Xu, X., Yu, J., 2018. Biochemical significance of limonene and its metabolites: future prospects for designing and developing highly potent anticancer drugs. Biosci. Rep., 1–12

Narahara, C., Saeheng, T., Chaijaroenkul, W., Dumre, S.P., Na-Bangchang, K., Karbwang, J., 2020. β-Eudesmol induces the expression of apoptosis pathway proteins in cholangiocarcinoma cell lines. J. Res. Med. Sci. 25, 7. https://doi.org/10.4103/jrms.JRMS_291_19.

Naseer, S., Hussain, S., Naeem, N., Pervaiz, M., Rahman, M., 2018. The phytochemistry and medicinal value of *Psidium guajava* (guava). Clin. Phytosci. 4, 32 (2018). https://doi.org/10.1186/s40816-018-0093-8.

Negreiros, H. A., de Moura, K. G., Barreto do Nascimento, M., do Nascimento Rodrigues, D. C., Ferreir, P., Braz, D. C., de Farias, M. G., de Sousa Corrêia, L., Pereira, A., Santos, L., Gonçalves, J., Mendes, A. N., Carneiro da Silva, F. C., Cavalcant, A., de Castro E Sousa, J. M., 2021. Alpha-terpineol as antitumor candidate in pre-clinical studies. Anticancer Agents Med Chem. 21(15):2023-2031. doi: 10.2174/1871520621999210104195820.

Oh, W.K., Lee, C.H., Lee, M.S., Bae, E.Y., Sohn, C.B., Oh, H., Kim, B.Y., Ahn, J.S., 2005. Antidiabetic effects of extracts from Psidium guajava. J. Ethnopharmacol. 96 (3), 411–415. https://doi.org/10.1016/j.jep.2004.09.041.

Ojewole, J.A., 2005. Hypoglycemic and hypotensive effects of Psidium guajava Linn. (Myrtaceae) leaf aqueous extract. Methods Find. Exp. Clin. Pharmacol. 10, 689–695. https://doi.org/10.1358/mf.2005.27.10.948917.

Ojewole, J.A., Awe, E.O., Chiwororo, W.D., 2008. Antidiarrhoeal activity of Psidium guajava Linn. (Myrtaceae) leaf aqueous extract in rodents. J. Smooth Muscle Res. 44 (6), 195–207. https://doi.org/10.1540/jsmr.44.195.

Oladeji, O.S., Adelowo, F.E., Oluyori, A.P., Bankole, D.T., 2020. Ethnobotanical Description and Biological Activities of *Senna alata*. Evid. Based Complement. Alternat. Med. 2020, 2580259. https://doi.org/10.1155/2020/2580259.

Olajide, O.A., Awe, S.O., Makinde, J.M., 1999. Pharmacological studies on the leaf of *Psidium guajava*. Fitoterapia. 70 (1), 25–31. https://doi.org/10.1016/S0367-326X(98)00010-0.

Orlando, J.B., Silva, B.O., Pires-Cunha, C.L., Hiruma-Lima, C.A., Gaivão, I.O.M., Maistro, E.L., 2019. Genotoxic effects induced by beta-myrcene following metabolism by liver HepG2/C3A human cells. J Toxicol Environ Health A. 82 (3), 176–185. https://doi.org/10.1080/15287394.2019.1577195.

Pant, B., 2014. Application of plant cell and tissue culture for the production of phytochemicals in medicinal plants. Adv. Exp. Med. Biol. 808, 25–39. https://doi.org/10.1007/978-81-322-1774-9_3.

Patel, P., Joshi, C., Birdi, T., Kothari, V., 2019. Anti-infective efficacy of Psidium guajava L. leaves against certain pathogenic bacteria. F1000Research 8, 12 https://doi.org/10.12688/f1000research.17500.2.

Pelegrini, P.B., Murad, A.M., Silva, L.P., Dos Santos, R.C., Costa, F.T., Tagliari, P.D., Bloch Jr, C., Noronha, E.F., Miller, R.N., Franco, O.L., 2008. Identification of a novel storage glycine-rich peptide from guava (*Psidium guajava*) seeds with activity against Gram-negative bacteria. Peptides. 29 (8), 1271–1279. https://doi.org/10.1016/j.peptides.2008.03.013.

Policegoudra, R.S., Goswami, S., Aradhya, S.M., Chatterjee, S., Datta, S., Sivaswamy, R., Chattopadhyay, P., Singh, L., 2012. Bioactive constituents of Homalomena aromatica essential oil and its antifungal activity against dermatophytes and yeasts. J. Mycol. Med. 22 (1), 83–87. https://doi.org/10.1016/j.mycmed.2011.10.007.

Prabu, G.R., Gnanamani, A., Sadulla, S., 2006. Guaijaverin – a plant flavonoid as potential antiplaque agent against Streptococcus mutans. J. Appl. Microbiol. 101 (2), 487–495. https://doi.org/10.1111/j.1365-2672.2006.02912.

Qabaha, K.I., 2013. Antimicrobial and free radical scavenging activities of five Palestinian medicinal plants. Afr. J. Trad. Compl. Altern. Med. 10 (4), 101–108. https://doi.org/10.4314/ajtcam.v10i4.17.

Qiu, J., Zhang, T., Zhu, X., Yang, C., Wang, Y., Zhou, N., Ju, B., Zhou, T., Deng, G., Qiu, C., 2019. Hyperoside Induces Breast Cancer Cells Apoptosis via ROS-Mediated NF-κB Signaling Pathway. Int. J. Mol. Sci. 21 (1), 131. https://doi.org/10.3390/ijms21010131.

Rai, P.K., Jaiswal, D., Mehta, S., Watal, G., 2009. Anti-hyperglycaemic potential of Psidium guajava raw fruit peel. Indian J. Med. Res. 129 (5), 561–565.

Rai, P.K., Mehta, S., Watal, G., 2010. Hypolipidaemic & hepatoprotective effects of Psidium guajava raw fruit peel in experimental diabetes. Indian J. Med. Res. 131, 820–824.

Rajpat, R., Kumar, K., 2021. Protective effect of ethanolic extract of guava leaves (*Psidium guajava* L.) in alloxan-induced diabetic mice. Materials Today: Proceedings. https://doi.org/10.1016/j.matpr.2021.04.617.

Ravi, K., Divyashree, P., 2014. Psidium guajava: A review on its potential as an adjunct in treating periodontal disease. Pharma-

cogn. Rev. 8 (16), 96–100. https://doi.org/10.4103/0973-7847.134233.

Roy, C.K., Das, A.K., 2010. Comparative evaluation of different extracts of leaves of Psidium guajava Linn. for hepatoprotective activity. Pak. J. Pharm. Sci. 23 (1), 15–20.

Ryu, B., Cho, H.M., Zhang, M., Lee, B.W., Doan, T.P., Park, E.J., Lee, H.J., Oh, W.K., 2021. Meroterpenoids from the leaves of *Psidium guajava* (guava) cultivated in Korea using MS/MS-based molecular networking. Phytochemistry. 186,. https://doi.org/10.1016/j.phytochem.2021.112723 112723.

Saber, F.R., Abdelbary, G.A., Salama, M.M., Saleh, D.O., Fathy, M. M., Soliman, F.M., 2018. UPLC/QTOF/MS profiling of two *Psidium* species and the in-vivo hepatoprotective activity of their nano-formulated liposomes. Food Res. Int. 105, 1029–1038. https://doi.org/10.1016/j.foodres.2017.12.042.

Sabogal-Guáqueta, A.M., Hobbie, F., Keerthi, A., Oun, A., Kortholt, A., Boddeke, E., Dolga, A., 2019. Linalool attenuates oxidative stress and mitochondrial dysfunction mediated by glutamate and NMDA toxicity. Biomed Pharmacother. 118,. https://doi.org/10.1016/j.biopha.2019.109295 109295.

Scandiffio, R., Geddo, F., Cottone, E., Querio, G., Antoniotti, S., Gallo, M.P., Maffei, M.E., Bovolin, P., 2020. Protective effects of (*E*)-β-Caryophyllene (BCP) in chronic inflammation. Nutrients. 12 (11), 3273. https://doi.org/10.3390/nu12113273.

Seo, S., Song, Y., Gu, S.M., Min, H.K., Hong, J.T., Cha, H.J., Yun, J., 2020. D-limonene inhibits pentylenetetrazole-induced seizure via adenosine A2A receptor modulation on gabaergic neuronal activity. Int. J. Mol. Sci. 21 (23), 9277. https://doi.org/10.3390/ijms21239277.

Shabbir, H., Kausar, T., Noreen, S., Rehman, H.U., Hussain, A., Huang, Q., Gani, A., Su, S., Nawaz, A., 2020. In Vivo Screening and Antidiabetic Potential of Polyphenol Extracts from Guava Pulp. Seeds and Leaves. Animals 10 (9), 1714. https://doi.org/10.3390/ani10091714.

Shen, S.C., Cheng, F.C., Wu, N.J., 2008. Effect of guava (Psidium guajava Linn.) leaf soluble solids on glucose metabolism in type 2 diabetic rats. Phytother. Res. 22 (11), 1458–1464. https://doi.org/10.1002/ptr.2476.

El-Ahmady, S.H., Mohamed, L.A., Michael, W., 2013. Chemical composition and anti-inflammatory activity of the essential oils of Psidium guajava fruits and leaves. J. Essent. Oil Res. 6, 475–481. https://doi.org/10.1080/10412905.2013.796498.

Shu, H., Chen, H., Wang, X., Hu, Y., Yun, Y., Zhong, Q., Chen, W., Chen, W., 2019. Antimicrobial Activity and Proposed Action Mechanism of 3-Carene against *Brochothrix thermosphacta* and *Pseudomonas fluorescens*. Molecules. 24 (18), 3246. https://doi.org/10.3390/molecules24183246.

Silva, E.A.J., Estevam, E.B.B., Silva, T.S., Nicolella, H.D., Furtado, R.A., Alves, C.C.F., Souchie, E.L., Martins, C.H.G., Tavares, D. C., Barbosa, L.C.A., Miranda, M.L.D., 2018. Antibacterial and antiproliferative activities of the fresh leaf essential oil of *Psidium guajava* L. (Myrtaceae). Braz. J. Biol. 79 (4), 697–702. https://doi.org/10.1590/1519-6984.189089.

Sinan, K.I., Dall'Acqua, S., Ferrarese, I., Mollica, A., Stefanucci, A., Glamočlija, J., Sokovic, M., Nenadić, M., Aktumsek, A., Zengin, G., 2021. LC-MS based analysis and biological properties of *Pseudocedrela kotschyi* (Schweinf.) Harms extracts: A valuable source of antioxidant, antifungal, and antibacterial compounds. Antioxidants 10 (10), 1570. https://doi.org/10.3390/antiox10101570.

Sinegre, T., Teissandier, D., Milenkovic, D., Morand, C., Lebreton, A., 2019. Epicatechin influences primary hemostasis, coagulation and fibrinolysis. Food Funct. 10 (11), 7291–7298. https://doi.org/10.1039/c9fo00816k.

Singh, P., Shukla, R., Prakash, B., Kumar, A., Singh, S., Mishra, P. K., Dubey, N.K., 2010. Chemical profile, antifungal, antiaflatoxigenic and antioxidant activity of Citrus maxima Burm. and Citrus sinensis (L.) Osbeck essential oils and their cyclic monoterpene, DL-limonene. Food Chem. Toxicol. 48 (6), 1734–1740. https://doi.org/10.1016/j.fct.2010.04.001.

Sobral-Souza, C.E., Silva, A.R.P., Leite, N.F., Rocha, J.E., Sousa, A. K., Costa, J.G.M., Menezes, I.R.A., Cunha, F.A.B., Rolim, L.A., Coutinho, H.D.M., 2018. *Psidium guajava* bioactive product chemical analysis and heavy metal toxicity reduction. Chemosphere 216, 785–793. https://doi.org/10.1016/j.chemosphere.

Sofowora, A., Ogunbodede, E., Onayade, A., 2013. The role and place of medicinal plants in the strategies for disease prevention. Afr. J. Tradit. Complement. Altern. Med. 10 (5), 210–229. https://doi.org/10.4314/ajtcam.v10i5.2.

Sohail, A., Bhat, W.F., Bhat, S.A., Furkan, M., Shah, A., Bano, B., 2018. Investigating the preventive effects of baicalin and gallocatechin against glyoxal-induced cystatin aggregation. J. Biomol. Struct. Dyn. 36 (14), 3791–3802. https://doi.org/10.1080/07391102.2017.1400470.

Soman, S., Rajamanickam, C., Rauf, A.A., Indira, M., 2013. Beneficial effects of *Psidium guajava* leaf extract on diabetic myocardium. Exp. Toxicol. Pathol. 65 (1–2), 91–95. https://doi.org/10.1016/j.etp.2011.06.005.

Su, Y.C., Hsu, K.P., Wang, E.I., Ho, C.L., 2015. Chemical composition and anti-mildew activities of essential oils from different parts of Michelia compressa var.formosana. Nat. Prod. Commun. 10 (4), 665–668.

Subramanian, S., Banu, H.H., Bai, R.M.R., Shanmugavalli, R., 2009. Biochemical evaluation of antihyperglycemic and antioxidant nature of Psidium guajava leaves extract in streptozotocin-induced experimental diabetes in rats. Pharm. Biol. 47 (4), 298–303.

Surendran, S., Qassadi, F., Surendran, G., Lilley, D., Heinrich, M., 2021. Myrcene-what are the potential health benefits of this flavouring and aroma agent? Front Nutr. 8,. https://doi.org/10.3389/fnut.2021.699666 699666.

Tan, M., Zhou, L., Huang, Y., Wang, Y., Hao, X., Wang, J., 2008. Antimicrobial activity of globulol isolated from the fruits of Eucalyptus globulus Labill. Nat Prod Res. 22 (7), 569–575. https://doi.org/10.1080/14786410701592745.

Tan, S., Wang, Z., Xiang, Y., Deng, T., Zhao, X., Shi, S., Zheng, Q., Gao, X., Li, W., 2020. The effects of drying methods on chemical profiles and antioxidant activities of two cultivars of *Psidium guajava* fruits. L.W.T. 118. https://doi.org/10.1016/j.lwt.2019.108723.

Tella, T., Masola, B., Mukaratirwa, S., 2019. The effect of *Psidium guajava* aqueous leaf extract on liver glycogen enzymes, hormone sensitive lipase and serum lipid profile in diabetic rats. Biomed. Pharmacother. 109, 2441–2446. https://doi.org/10.1016/j.biopha.2018.11.137.

Trevizan, L.N.F., Nascimento, K.F.D., Santos, J.A., Kassuya, C.A. L., Cardoso, C.A.L., Vieira, M.D.C., Moreira, F.M.F., Croda, J., Formagio, A.S.N., 2016. Anti-inflammatory, antioxidant and anti-Mycobacterium tuberculosis activity of viridiflorol: The major constituent of Allophylus edulis (A. St.-Hil., A. Juss. & Cambess.) Radlk. J. Ethnopharmacol. 192, 510–515. https://doi.org/10.1016/j.jep.2016.08.053.

Türkez, H., Celik, K., Toğar, B., 2014. Effects of copaene, a tricyclic sesquiterpene, on human lymphocytes cells in vitro. Cytotechnology. 66 (4), 597–603. https://doi.org/10.1007/s10616-013-9611-1.

Ugbogu, O.C., Emmanuel, O., Agi, G.O., Ibe, C., Ekweogu, C.N., Ude, V.C., Uche, M.E., Nnanna, R.O., Ugbogu, E.A., 2021. A review on the traditional uses, phytochemistry, and pharmacological activities of clove basil (*Ocimum gratissimum* L.). Heliyon 7, (11). https://doi.org/10.1016/j.heliyon.2021.e08404 e08404.

Ukwueze, S.E., Osadebe, P.O., Okoye, F.B., 2015. A new antibacterial benzophenone glycoside from Psidium guajava (Linn.) leaves. Nat. Prod Res. 29 (18), 1728–1734. https://doi.org/10.1080/14786419.2014.1003188.

Uuh-Narvaez, J.J., Negrete-León, E., Acevedo-Fernández, J.J., Segura-Campos, M.R., 2021. Antihyperglycemic and hypoglycemic

activity of Mayan plant foods in rodent models. J. Sci. Food Agric. 101 (10), 4193–4200. https://doi.org/10.1002/jsfa.11057.

Valdeira, A.S.C., Darvishi, E., Woldemichael, G.M., Beutler, J.A., Gustafson, K.R., Salvador, J.A.R., 2019. Madecassic Acid Derivatives as Potential Anticancer Agents: Synthesis and Cytotoxic Evaluation. J. Nat. Prod. 82 (8), 2094–2105. https://doi.org/10.1021/acs.jnatprod.8b00864.

Vasconcelos, A.G., Amorim, A.D.G.N., Dos Santos, R.C., Souza, J. M.T., de Souza, L.K.M., Araújo, T.S.L., Nicolau, L.A.D., de Lima Carvalho, L., de Aquino, P.E.A., da Silva Martins, C., Ropke, C. D., Soares, P.M.G., Kuckelhaus, S.A.S., Medeiros, J.R., Leite, J.R. S.A., 2017. Lycopene rich extract from red guava (*Psidium guajava* L.) displays anti-inflammatory and antioxidant profile by reducing suggestive hallmarks of acute inflammatory response in mice. Food Res. Int. 99 (2), 959–968. https://doi.org/10.1016/j.foodres.2017.01.017.

Vijayakumar, K., Arumugam, V.A., Ramasamy, M., Natesan, M., Palanisamy, S., Thajuddin, N.B., Balasubramanian, B., Meyyazhagan, A., 2020. Hepatoprotective effects of *Psidium guajava* on mitochondrial enzymes and inflammatory markers in carbon tetrachloride-induced hepatotoxicity. Drug Dev. Ind. Pharm. 46 (12), 2041–2050. https://doi.org/10.1080/03639045.2020.1843474.

Vijayakumar, K., Rengarajan, R.L., Radhakrishnan, R., Anand, A. V., 2018. Hypolipidemic Effect of Psidium guajava Leaf Extract Against Hepatotoxicity in Rats. Pharmacogn. Mag. 53, 4–8. https://doi.org/10.4103/pm.pm_167_17.

Vo, T.K., Ta, Q.T.H., Chu, Q.T., Nguyen, T.T., Vo, V.G., 2020. Anti-Hepatocellular-Cancer Activity Exerted by β-Sitosterol and β-Sitosterol-Glucoside from Indigofera zollingeriana Miq. Molecules. 25 (13), 3021. https://doi.org/10.3390/molecules25133021.

Wang, L., Wu, H., Yang, F., Dong, W., 2019. The Protective Effects of Myricetin against Cardiovascular Disease. J. Nutr. Sci. Vitaminol. 65 (6), 470–476. https://doi.org/10.3177/jnsv.65.470.

Wang, L., Wu, Y., Xie, J., Wu, S., Wu, Z., 2018. Characterization, antioxidant and antimicrobial activities of green synthesized silver nanoparticles from *Psidium guajava* L. leaf aqueous extracts. Mater. Sci. Eng. C. Mater. Biol. Appl. 86, 1–8. https://doi.org/10.1016/j.msec.2018.01.003.

Weli, A., Al-Kaabi, A., Al-Sabahi, J., Said, S., Hossai, A., Al-Riyami, S., 2019. Chemical composition and biological activities of the essential oils of Psidium guajava leaf. J. King Saud Univ. Sci. 2–24. https://doi.org/10.1016/j.jksus.2018.07.021.

WHO., 2009. WHO monographs on selected medicinal plants - Volume 4 Number of pages: 448 Publication date: 02 November 2009 Languages: English ISBN: 978 92 4 154705 5. https://www.who.int/medicines/areas/traditional/selecmonv4/en/. (Accessed January 3, 2022).

WHO., 2019. WHO global report on traditional and complementary medicine 2019. ISBN 978-92-4-151543-6. https://www.who.int/traditional-complementary-integrative-medicine/WhoGlobalReportOnTraditionalAndComplementaryMedicine2019.pdf.

Woo, J., Yang, H., Yoon, M., Gadhe, C.G., Pae, A.N., Cho, S., Lee, C.J., 2019. 3-Carene, a Phytoncide from Pine Tree Has a Sleep-enhancing Effect by Targeting the $GABA_A$-benzodiazepine Receptors. Exp Neurobiol. 28 (5), 593–601. https://doi.org/10.5607/en.2019.28.5.593.

Wu, X., Zhang, G., Hu, X., Pan, J., Liao, Y., Ding, H., 2019. Inhibitory effect of epicatechin gallate on protein glycation. Food Res. Int. 122, 230–240. https://doi.org/10.1016/j.foodres.2019.04.023.

Xie, Y., Xu, H., Dong, H., Fiscus, R.R., But, P.P.H., 2007. Role of nitric oxide in the vasorelaxant and hypotensive effects of extracts and purified tannins from Geum japonicum. J. Ethnopharmacol. 109, 128–133. https://doi.org/10.1016/j.jep.2006.07.015.

Xu, C., Li, X., Zeng, D., Liu, Y., Gao, Y., Tsunoda, M., Deng, S., Xie, X., Wang, R., Li, L. S., Song, Y., Zhang, Y., 2020. Amino acid profiling study of Psidium guajava L. leaves as an effective treatment for type 2 diabetic rats. eCAM. 9784382. https://doi.org/10.1155/2020/9784382.

Yang, H., Jung, E.M., Ahn, C., Lee, G.S., Lee, S.Y., Kim, S.H., Choi, I.G., Park, M.J., Lee, S.S., Choi, D.H., Jeung, E.B., 2015. Elemol from Chamaecyparis obtusa ameliorates 2,4-dinitrochlorobenzene-induced atopic dermatitis. Int. J. Mol. Med. 36 (2), 463–472. https://doi.org/10.3892/ijmm.2015.2228.

Yang, Q., Wen, Y.M., Shen, J., Chen, M.M., Wen, J.H., Li, Z.M., Liang, Y.Z., Xia, N., 2020. Guava Leaf Extract Attenuates Insulin Resistance via the PI3K/Akt Signaling Pathway in a Type 2 Diabetic Mouse Model. Diabetes, metabolic syndrome and obesity: targets and therapy 13, 713–718. https://doi.org/10.2147/DMSO.S231979.

Yang, W., Tu, H., Tang, K., Huang, H., Ou, S., Wu, J., 2021. Reynoutrin Improves Ischemic Heart Failure in Rats Via Targeting S100A1. Front Pharmacol. 12,. https://doi.org/10.3389/fphar.2021.703962 703962.

Yao, X., Jiao, S., Qin, M., Hu, W., Yi, B., Liu, D., 2020. Vanillic Acid Alleviates Acute Myocardial Hypoxia/Reoxygenation Injury by Inhibiting Oxidative Stress. Oxid. Med. Cell Longev. 2020, 8348035. https://doi.org/10.1155/2020/8348035.

Yeo, S.K., Ali, A.Y., Hayward, O.A., Turnham, D., Jackson, T., Bowen, I.D., Clarkson, R., 2016. 'β -Bisabolene, a sesquiterpene from the essential oil extract of opoponax (Commiphora guidottii), exhibits cytotoxicity in breast cancer cell lines. Phytother. Res. 30, 418–425.

Yoo, H.J., Jwa, S.K., 2018. Inhibitory effects of β-caryophyllene on Streptococcus mutans biofilm. Arch Oral Biol. 88, 42–46. https://doi.org/10.1016/j.archoralbio.2018.01.009.

Zahin, M., Ahmad, I., Aqil, F., 2017. Antioxidant and antimutagenic potential of *Psidium guajava* leaf extracts. Drug Chem. Toxicol. 40 (2), 146–153. https://doi.org/10.1080/01480545.2016.1188397.

Zhang, Y., Wu, Q., Zhang, L., Wang, Q., Yang, Z., Liu, J., Feng, L., 2019. Caffeic acid reduces A53T α-synuclein by activating JNK/Bcl-2-mediated autophagy in vitro and improves behaviour and protects dopaminergic neurons in a mouse model of Parkinson's disease. Pharmacol. Res. 150,. https://doi.org/10.1016/j.phrs.2019.104538 104538.

Zhang, B.C., Li, Z., Xu, W., Xiang, C.H., Ma, Y.F., 2018. Luteolin alleviates NLRP3 inflammasome activation and directs macrophage polarization in lipopolysaccharide-stimulated RAW264.7 cells. Am. J. Transl. Res. 10 (1), 265–273.

Zhao, Y., Chen, R., Wang, Y., Yang, Y., 2018. α-Pinene Inhibits Human Prostate Cancer Growth in a Mouse Xenograft Model. Chemotherapy. 2018;63(1):1-7. doi: 10.1159/000479863.

Zheng, J., Li, Q., He, L., Weng, H., Su, D., Liu, X., Ling, W., Wang, D., 2020. Protocatechuic acid inhibits vulnerable atherosclerotic lesion progression in older apoe-/- mice. J. Nutr. 150 (5), 1167–1177. https://doi.org/10.1093/jn/nxaa017.

Zhu, X., Ouyang, W., Lan, Y., Xiao, H., Tang, L., Liu, G., Feng, K., Zhang, L., Song, M., Cao, Y., 2020. Anti-hyperglycemic and liver protective effects of flavonoids from *Psidium guajava* L. (guava) leaf in diabetic mice. Food Biosci. https://doi.org/10.1016/j.fbio.2020.100574.

Zhu, X., Ouyang, W., Pan, C., Gao, Z., Han, Y., Song, M., Feng, K., Xiao, H., Cao, Y., 2019. Identification of a new benzophenone from Psidium guajava L. leaves and its antineoplastic effects on human colon cancer cells. Food Funct. 17, 10(7):4189-4198. doi: 10.1039/c9fo00569b.

Ziaei, A., Ramezani, M., Wright, L., Paetz, C., Schneider, B., Amirghofran, Z., 2011. Identification of spathulenol in Salvia mirzayanii and the immunomodulatory effects. Phytother Res. 25 (4), 557–562. https://doi.org/10.1002/ptr.3289.