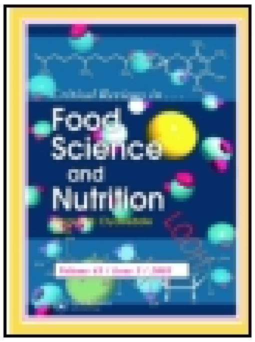

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REVIEW

Family Myrtaceae: The treasure hidden in the complex/diverse composition

Fatema R. Saber[a], Paulo E. S. Munekata[b], Komal Rizwan[c], Heba A. S. El-Nashar[d], Nouran M. Fahmy[d], Shaza H. Aly[e], Mohamed El-Shazly[d], Abdelhakim Bouyahya[f] and Jose M. Lorenzo[b,g]

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ABSTRACT

Myrtaceae is one of the most important plants families, being regarded as the eighth largest flowering plant family. It includes many genera of utmost ecological and economical importance distributed all over the world. This review aimed to report the latest studies on this family focusing on certain widely used plants including *Eucalyptus* sp., *Eugenia* sp. (*Eugenia uniflora, Eugenia sulcata)*, *Syzygium* sp. (*Syzygium aromaticum* and *Syzygium cumini)*, *Psidium* sp., *Pimenta dioica*, *Myrtus* sp. (*Myrtus communis*), *Myrciaria* sp. and *Melaleuca alternifolia*. The extraction of bioactive compounds has been evolving through the optimization of conventional methods and the use of emerging technologies. Supercritical CO_2 was applied for essential oils and ultrasound for polyphenols leading to extracts and essential oils rich in bioactive compounds. Advances in the field of encapsulation and delivery systems showed promising results in the production of stable essential oils nanoemulsions and liposomes and the production of plant extracts in the form of nanoparticles. Moreover, a significant increase in the number of patents was noticed especially the application of Myrtaceae extracts in the pharrmacuetucal field. The applications of ceratin plants (*Pimenta dioica*, *Melaleuca alternifolia*, *Syzygium aromaticum* essential oils or *Myrciaria cauliflora* peel extract) in food area (either as a free or encapsulated form) also showed interesting results in limiting microbial spoilage of fresh meat and fish, slowing oxidative degradation in meat products, and inhibiting aflatoxin production in maize. Despite the massive literature on Myrtaceae plants, advances are still necessary to optimize the extraction with environmentally friendly technologies and carry out risk assessment studies should be accomplished to harness the full potential in food, industrial and pharmaceutical applications.

KEYWORDS
Myrtaceae; bioactive phytochemicals; phloroglucinols; phenolic acids and flavonoids; Response surface methodology; nanoemulsions; food applications

Introduction

Plants, thanks to their ability to carry out photosynthesis, constitute an indispensable source of nutritious, bioactive and cosmetic compounds for humanity (Dildora Iskandarovna 2021). Thousands of medicinal and edible plants belong to certain plant families and these families are of special interest to nutritional, pharmaceutical and cosmotic industries (Bondam et al. 2022; Bouyahya et al., 2021). The Myrtaceae family is a large family of dicotyledonous woody plants, taxonomically belonging to the order Myrtales. It comprises about 5800 species representing 130 to 150 genera. It is regarded as the eighth largest flowering plant family. It includes many genera of utmost ecological and economical importance distributed all over the world. Myrtaceae plants grow in South America, Australia, tropical Asia, Africa and Europe (de Paulo Farias et al. 2020; Govaerts et al. 2008).

Medicinal and aromatic plants belonging to family Myrtaceae are endowed with valuable medicinal properties and are highly enriched sources of plants' bioactive volatiles. The large number of plants belonging to this family, encouraged us to focus in this review on certain plants with interesting pharmaceutical, food and industrial applications including *Eucalyptus* sp., *Eugenia* sp. (*Eugenia uniflora, Eugenia sulcata)*, *Syzygium* sp. (*Syzygium aromaticum* and *Syzygium cumini)*, *Psidium* sp., *Pimenta dioica*, *Myrtus* sp. (*Myrtus communis*), *Myrciaria* sp. and *Melaleuca alternifolia.* These species contain several phytochemicals belonging to different chemical classes such as phenolic acids, flavonoids, phloroglucinols, terpenoids, condensed and non-condensed tannins (Vuolo, Lima, and Maróstica Junior 2019). Several factors are responsible for the quantitative and qualitative differences in the chemical composition of Myrtaceae plants. These factors include the genus, species, geographical origin, climate, part used and phenological stage of the collected plants (Padovan et al. 2014).

Phenolic acids and flavonoids are mainly localized in the fruits, seeds, leaves, stems and roots. Flavonoids are often

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found in their glycosylated form and include flavanones, isoflavones, flavones, flavonols and flavanols, and anthocyanins. The phenolic acids of Myrtaceae plants are derived from hydroxycinnamic acid (C_6-C_3) and are rich in *p*-coumaric, caffeic, hydroxybenzoic, vanillic, gallic, and ellagic acids (Ahmad and Fareeda 2017; Celaj et al. 2021). The reported terpenoids are dominated by 1,8-cineole, *β*-pinene, linalool, terpinen-4-ol, *β*-caryophyllene, spathulenol, caryophyllene oxide, *β*-caryophyllene, germacrene D, germacrene B, (2E,6E)-farnesoic acid, germacrene D, germacrene B, 1-*epi*-cubenol, *α*-muurolol, *α*-muurolol, caryophyllene oxide, spathulenol, globulol, *α*-pinene, limonene, γ-eudesmol, (E)-*β*-farnesene, and *β*-bisabolol (Cascaes et al. 2015; Fábio et al. 2019).

Carotenoids also exist in myrtaceae plant matrices and are responsible for the plants' colors. They are divided into two groups including xanthophylls and carotenes. Several carotenoids were identified from this family such as *β*-cryptoxanthin, canthaxanthin, violaxanthin, *β*-citraurine, lycopene, monocyclic, and *β*-carotene (Donado-Pestana et al. 2018; Khoo et al. 2011). The richness of this family with diverse groups of phytochemical compounds suggested their potential wide range of biological activities. Many studies showed that Myrtaceae species exhibited several activities such as antibacterial, anticoagulant, antidiarrheal antifungal, antioxidant, cytotoxic, anti-inflammatory, anti-parasitic, and antidiabetic effects (Macedo et al. 2021; Sganzerla and da Silva 2022). The bioactivities of Myrtaceae species were attributed to their major bioactive phenolics, triterpenes and/or essential oil constituents (A. P. G. da Silva et al. 2022; de Oliveira Raphaelli et al. 2021; Qamar et al. 2022).

The mechanisms of action of the reported biological effects were variable depending on the major chemical compounds (ligands) and the used biological assay (cellular and molecular targets involved). The extracts, essential oils of Myrtaceae medicinal plants and their derivatives demonstrated anti-inflammatory, antidiabetic, neuroprotective, and antitumor effects *via* their interactions at the sub-cellular, cellular, and molecular levels. For instance, the antimicrobial effects are mediated through the interactions of the active compounds with bacterial cell wall, penetration, integration, interference with microbial replication, and cellular mechanisms (da Silva et al. 2022; Famuyide et al. 2019; Haro-González et al. 2021).

The diverse biological activities of Myrtaceae species promoted their application in several foods, cosmetic and pharmaceutical industries. The large scale applications of Myrtaceae plants' extracts and relevant compounds led to the development of ingenuous protocols for the extraction and purification of their bioactive compounds and volatile oils (Benvenutti, Zielinski, and Ferreira 2021). In this context, the aim of this review is to shed light on certain Myrtaceae plants widely used in food and pharmaceutical industries. We summarized the phytochemical content, developed formulations, registered patents, and industrial applications of certain Myrtaceae plants famous for their economic and therapeutic values.

Phytochemicals

Essential oils

The composition of essential oils from the Myrtaceae family varies with the species and the extraction protocol (Table 1). Recent experiments reported the variability in the composition of essential oils from *Eucalyptus* species. In the essential oil of *Eucalyptus citriodora* leaves, the main components were citronellal, geraniol, *β*-citronellol, and *δ*-cadinene (Aragão et al. 2015; Costa et al. 2015). In the leaves of *Eucalyptus globulus*, certain reports suggested the presence of 1,8-cineole as the major component (Boukhatem et al. 2014; Harkat-Madouri et al. 2015). On the other hand, a recent study reported that *p*-cymene, methyl eugenol, 4-terpinenol, and *s*-methyl 3-methylbutanethioate were the major constituents of the essential oils obtained from *Eucalyptus globulus* leaves (Hafsa et al. 2016). The presence of 1,8-cineole as well as *trans*-sabinene hydrate acetate, globulol, and longicyclene as major components was reported in another study on the essential oil composition of *Eucalyptus gunnii* (Caputo et al. 2020).

Another important species from this family is *Eugenia uniflora* (also popularly known as Pitanga), which was found to contain selina-1,3,7(11)-trien-8-one, germacrene D, *trans*-caryophyllene, and germacrene B as the main components of its leaves essential oils (Garmus et al. 2014). The essential oil extracted by hydrodistillation from the leaves of *Eugenia ulcate* contained sesquiterpenes as the largest fraction (75.6%), while *β*-caryophyllene (18.65%), *δ*-cadinene (10%) and *α*-pinene (6.75%) were also found in significant amounts (Magalhães et al. 2022). The tea tree leaves (*Melaleuca alternifolia*) essential oil was also investigated and revealed the presence of terpinen-4-ol, *γ*-terpinene, *α*-terpinene, 1,8-cineole, and *α*-terpineol as the major compounds across different studies (Liao et al. 2017; C. de S. Silva et al. 2019; Zhang et al. 2018). In case of guava (*Psidium guajava*), caryophyllene and its derivatives were identified by many researchers as the main components in the leaves of this plant. Other relevant components in the essential oil in guava leaves were limonene, 1, 8-cineole, *α*-humulene and *α*-selinene (El-Ahmady, Ashour, and Wink 2013; Hassan et al. 2020; Soliman et al. 2016; Souza et al. 2017; Weli et al. 2019). It is important to mention that plant part (leaves *vs.* fruit without seeds) was suggested as a factor affecting the composition of essential oil in *Psidium guajava* (El-Ahmady, Ashour, and Wink 2013).

For *Pimenta dioica*, the composition of essential oil obtained from the leaves varied among different studies (Chaudhari et al. 2020; Dima et al. 2014; Jiang et al. 2013). Based on the results of these studies, it seems reasonable to infer that the variability in the essential oil composition can be attributed to the natural variation in the plant (Jiang et al. 2013). Eugenol and different forms of caryophyllene were indicated as the major components in the essential oil obtained from clove (*Syzygium aromaticum*) (Fayemiwo et al. 2014; Sharma et al. 2017).

Table 1. Essential oil components found in species of Family Myrtaceae.

Species	Plant section/Source	Extraction method	Main components	Ref.
Eucalyptus citriodora	Leaves	Steam distillation	Citronellal, geraniol, β-citronellol, and δ-cadinene	(Aragão et al. 2015; Costa et al. 2015)
Eucalyptus globulus	Leaves	Steam distillation	*p*-Cymene, methyl eugenol, 4-terpinenol, *s*-methyl 3-methylbutanethioate, and γ-terpinene	(Hafsa et al. 2016)
Eucalyptus globulus	Leaves	Steam distillation	1,8-Cineole, α-pinene, and β-myrcene	(Boukhatem et al. 2014)
Eucalyptus globulus	Leaves	Steam distillation and Supercritical CO_2	1,8-Cineole, β-pinene, aromadendrene, and globulol	(Harkat-Madouri et al. 2015)
Eucalyptus grandis	Leaves	Steam distillation	α-Pinene, γ-terpinene, and *p*-cymene	(Aragão et al. 2015)
Eucalyptus gunnii	Leaves and herbaceous branches	Steam distillation	1,8 Cineole, *trans*-sabinene hydrate acetate, globulol, and longicyclene	(Caputo et al. 2020)
Eugenia uniflora	Leaves	Supercritical CO_2	Selina-1,3,7(11)-trien-8-one, germacrene D, *trans*-caryophyllene, and germacrene B	(Garmus et al. 2014)
Eugenia sulcata	Leaves	Hydrodistillation	Sesquiterpenes, β-Caryophyllene, δ-cadinene and α-pinene	(Magalhães et al. 2022)
Melaleuca alternifolia	Commercial product	n.i.	Terpinen-4-ol, γ-terpinene, α-terpinene, 1,8-cineole, and α-terpineol	(Liao et al. 2017; C. de S. Silva et al. 2019; Zhang et al. 2018)
Psidium guajava	Leaves	Steam distillation	β-Caryophyllene, limonene, β-caryophyllene oxide, α-selinene, and β-selinene	(El-Ahmady, Ashour, and Wink 2013)
Psidium guajava	Leaves	Steam distillation	Caryophyllene, $_D$-limonene, globulol, and *trans*-nerolidol	(Hassan et al. 2020)
Psidium guajava	Leaves	Steam distillation	*trans*-Caryophyllene, α-humulene, and β-bisabolol	(Souza et al. 2017)
Psidium guajava	Leaves	Steam distillation	*iso*-Caryphyllene, veridiflorene, farnesene, and limonene	(Weli et al. 2019)
Psidium guajava	Fruits without seeds	Steam distillation	β-Caryophyllene, 4α-selin-7(11)-enol, β-caryophyllene oxide, and α-selinene	(El-Ahmady, Ashour, and Wink 2013)
Pimenta dioica	Fruit	Steam distillation	α-Terpineol, β-linalool, γ-terpinene, and eucalyptol	(Chaudhari et al. 2020)
Pimenta dioica	Fruit	Steam distillation	Methyleugenol, eugenol, caryophyllene, and α-pinene	(Jiang et al. 2013)
Pimenta dioica	Fruit	Supercritical CO_2	Eugenol, methyleugenol, and α-phellandrene	(Dima et al. 2014)
Pimenta dioica	Fruit	Microwave heating	Methyleugenol, eugenol, caryophyllene, and α-pinene	(Jiang et al. 2013)
Syzygium aromaticum	Buds	Steam distillation	Eugenol, eugenyl acetate, β-caryophyllene	(Fayemiwo et al. 2014)
Syzygium aromaticum	Commercial product	n.i.	Eugenol, E-caryophyllene, and α-humulene	(Sharma et al. 2017)
Myrtus communis	n.i.	n.i.	α--pinene, 1,8-cineole, linalool, linalool acetate, and geranyl acetate	(Roozitalab et al. 2022)
Myrtus communis	Aerial parts	Hydrodistillation	Myrtenyl acetate, linalool and 1,8-cineole	(Ouedrhiri et al. 2022)

n.i.: not indicated.

Phenolic compounds

Phenolic compounds are highly valuable constituents of Myrtaceae family. Studies indicated the wide variability of polyphenols in this family and investigated the factors associated with this variability (Table 2). *Eucalyptus globulus* leaves were found to be rich in sideroxylonal A or B, cypellogin A or B, cypellocarpin C, and ellagic acid derivatives (Gullón et al. 2019). The residues of eucalyptus processing were rich in gallic and protocatechuic acids as the predominant polyphenols, demonstrating the variation in polyphenol content based on the used plant part (Celeiro et al. 2019).

The main phenolic compounds in *Eugenia uniflora* were quercetin, gallic acid, and isoquercetin (Siebert et al. 2020). The evaluation of the phenolic profile of *Myrciaria dubia* whole fruits (pulp and peel) revealed that gallic acid and rutin were the major phenolic compounds (Rodrigues et al. 2020). However, when only the pulp was considered, several phenolic compounds were reported as the main components including casuarictin, myricetin, potentillin, and syringic acid (Fujita et al. 2015). In *Myrciaria jaboticaba*, ellagic acid and gallic acid were found in the peels, seeds and juice (Inada et al. 2018, 2020; Siebert et al. 2020). Some polyphenols were highly abundant in the peels such as cyanidin-3-*O*-glucoside, which provides the characteristic purple color of this fruit (Inada et al. 2020).

Another relevant source of phenolic compounds is *Psidium guajava*. Recent experiments characterized the phenolic profile in different parts of this plant. In the leaves, the predominance of flavonoids was highlighted by the presence of guajaverin, catechin, avicularin, and quercitrin (Díaz-de-Cerio et al. 2016; Saber et al. 2018). Pink guava peels and flesh were found to contain a combination of flavonoids and phenolic acid derivatives (Rojas-Garbanzo, Zimmermann, et al. 2017). Cinnamoyl-*O*-hexoside, dimethoxycinnamoyl-*O*-hexoside, and quercetin-*O*-hexoside were found in both the peel and flesh. Proanthocyanidin B-Type (E)GC-(E)GC and galloyl-*O*-pentoside were only reported in the peel. The investigation of the metabolic profile of *Pimenta dioica* suggested its richness in flavonoids (Silva, Yerena, and Necha 2021).

Formylated phloroglucinols adducts

The formylated phloroglucinols is another class of interesting natural compounds found in the Myrtaceae family, especially

Table 2. Polyphenols found in Myrtaceae family.

Species	Plant section/Source	Extraction method	Main components	Ref.
Eucalyptus globulus	Leaves	Conventional solvent extraction, microwave heating, ultrasound, and deep eutectic solvent	Sideroxylonal A or B, cypellogin A or B, cypellocarpin C, and glucoside of dimethylellagic acid	(Gullón et al. 2019)
Eucalyptus globulus	By-products	Conventional solvent extraction	Gallic acid and protocatechuic acid	(Celeiro et al. 2019)
Eugenia uniflora	Juice	No extraction	Quercetin, gallic acid, and isoquercetin	(Siebert et al. 2020)
Myrciaria dubia	Whole fruit	Ultrasound	Gallic acid and rutin	(L. M. Rodrigues et al. 2020)
Myrciaria dubia	Pulp	n.i.	Castalagin, casuarictin, ellagic acid, myricetin, myricitin glycosides, potentillin, quercetin glycosides, syringic acid, and vescalagin	(Fujita et al. 2015)
Myrciaria jaboticaba	Peel and seed	Conventional solvent extraction	Cyanidin-3-*O*-glucoside, ellagic acid, gallic acid and quercetin-3-*O*-rutinoside	(Inada et al. 2020)
Myrciaria jaboticaba	Juice	No extraction	Gallic acid, quercetin-3-*O*-rutinoside, ellagic acid, and *trans*-cinnamic acid	(Inada et al. 2018)
Plinia cauliflora	Juice	No extraction	Gallic acid and ellagic acid	(Siebert et al. 2020)
Plinia Jaboticaba	Fruit	Hydromethanolic extract	Cyanidin, delphinidin-3-*O*-glucoside, pedunculagin, casuarinin, tellimagrandin I, strictinin, casuariin and free ellagic acid	(L. Rodrigues et al. 2021)
Psidium guajava	Leaves	Conventional solvent extraction	Guajaverin, catechin, avicularin, and quercitrin	(Díaz-de-Cerio et al. 2016)
Psidium guajava L. cv. 'Criolla'	Peel	Conventional solvent extraction	Cinnamoyl-*O*-hexoside, guavin B isomer, abscisic acid, quercetin-*O*-hexoside, quercetin-*O*-pentoside, and dimethoxycinnamoyl-O-hexoside	(Rojas-Garbanzo, Zimmermann, et al. 2017)
Psidium guajava L. cv. 'Criolla'	Flesh	Conventional solvent extraction	Catechin gallate, cinnamoyl-*O*-hexoside, dimethoxycinnamoyl-*O*-hexoside, phloretin-*C*-glucoside, and quercetin glucuronide	(Rojas-Garbanzo, Zimmermann, et al. 2017)
Pimenta dioica	Leaves	Conventional solvent extraction	Epicatechin, isoquercitrin, and quercetin-7-*O*-rhamnoside	(A. V. Silva, Yerena, and Necha 2021)

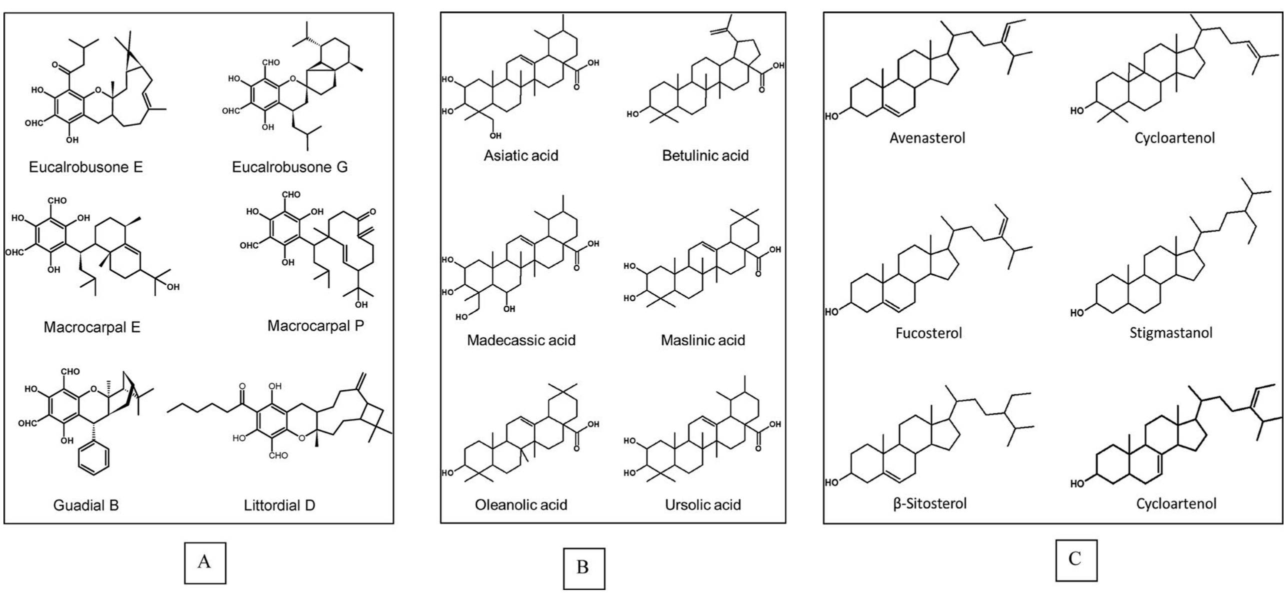

Figure 1. Representative examples of A: Formylated phloroglucinols, B: Selected triterpenoids found in Myrtaceae family, C: Phytosterols identified in Myrtaceae family.

in *Eucalyptus* species (Figure 1A). The leaves were suggested as the common source of these compound in different *Eucalyptus* species (*Eucalyptus camphora* ssp. *humeana*, *Eucalyptus camaldulensis*, *Eucalyptus cladocalyx*, *Eucalyptus leucoxylon*, *Eucalyptus sideroxylon*, *Eucalyptus viminalis*, and *Eucalyptus yarraensis*) (dos Santos et al. 2019). Macrocarpal A, J, L, and N and sideroxylonal A were identified in these *Eucalyptus* species.

It is important to notice that the formylated phloroglucinol profile varied in different plant parts. In *Eucalyptus globulus*, the presence of diformylphloroglucinol and macrocarpal E, P and Q were reported in the leaves (Chenavas et al. 2015). The fruits of this species contained eucalypglobulusals A-J, eucalyptin B, euglobal-III, euglobal-V, macrocarpal C, and macrocarpal E and Q (Pham et al. 2018; Qin, Jin, et al. 2018). The characterization of *Eucalyptus* *robusta* leaves indicated the presence of several eucalrobusones (Shang et al. 2019; Shang, Yang, Jian, et al. 2016; Shang, Yang, Liu, et al. 2016). Moreover, eucalyprobusals A-F, and eucalyprobusone B-F were identified in the fruits of *Eucalyptus robusta* (Liu et al. 2020). In *Eucalyptus tereticornis*, eucalteretials A-E were isolated from the twigs and leaves (Liu, Feng, et al. 2018). More recently, some studies indicated the presence of formylated phloroglucinols in other species of Myrtaceae family. The leaves of guava contain guadial A, psiguadial C and D, guapsidial A, guadials B and C and anduajadials C-F (Gao et al. 2013; Jian et al. 2015; Shao et al. 2012). Littordials A–E were isolated and characterized from the leaves of Araçá-rosa (*Psidium littorale*) (Xu et al. 2019). Cattleianal and cattleianone were identified from *Psidium cattleianum* leaves (Mahrous et al. 2021).

Triterpenes

Triterpenoids are present in abundance in the leaves of the Myrtaceae family (Figure 1B). In *Eucalyptus tereticornis* leaves, the identified triterpenoids were ursolic acid, oleanolic acid, and ursolic acid lactone (Acín et al. 2021; Ceballos et al. 2018). *Eucalyptus grandis* wood was found to be rich in triterpenes including betulinic, betulonic, and ursolic acids (Santos et al. 2017). The main triterpenes in *Eucalyptus globulus* stem were β-amyrin, asiatic acid, arjunolic acid, and squalene (Gominho et al. 2020). In another study by the same research group investigating the bark of this *Eucalyptus* species, a different triterpene profile was obtained including arjunolic acid, asiatic acid, betulinic acid, 3-acetyloleanolic acid, ursolic acid, and 3-acetylursolic acid. These results also supported previous findings that the composition of secondary metabolites including triterpenes differs in different plant parts.

Among species of the *Eugenia* genus (*Eugenia brasiliensis*, *Eugenia florida*, and *Eugenia uniflora*), the presence of betulinic acid, oleanolic acid, and ursolic acid was indicated in the leaves of these species (Lima et al. 2015). Another triterpene identified in *Eugenia uniflora* leaves was friedelin (Canabarro et al. 2020). In *Pimenta dioica*, the following triterpenoids were identified including corosolic, maslinic, oleanolic, and ursolic acids (Ladurner et al. 2017).

Psidium guajava is another species from the Myrtaceae family that contains many triterpenoids. In the leaves, compounds such as asiatic acid, betulinic acid, corosolic acid, guavenoic acid, lupeol, madecassic acid, maslinic acid, oleanolic acid, pedunculoside, pinfaensin, and ursolic acid were identified (Chao et al. 2020; Flores et al. 2015; Li et al. 2021; Lima et al. 2015). In the flesh, different studies indicated the presence of butelin, guavaenoic acid, lupeol, madecassic acid, oleanolic acid, quadranoside III, uvaol, and 2α,3β-dihydroxyursane (Liu, Feng, et al. 2018; Zhou et al. 2023). Another species in this genus that contains triterpenoids (betulinic acid, oleanolic acid, and ursolic acid) is *Psidium cattleianum* (Lima et al. 2015).

In *Syzygium aromaticum*, maslinic and oleanolic acids were commonly reported in different studies (Khathi et al. 2013; Ladurner et al. 2017; Ryu et al. 2016). Another triterpenoid found in this species is coumaroylmaslinic acid (Ladurner et al. 2017). In Araçá-rosa (*Syzygium cumini*), some identified triterpenoids were betulinic, oleanolic, and ursolic acids (Lima et al. 2015). These studies indicated the diversity of triterpenoids across species of the Myrtaceae family and their role as bioactive agents or raw material for the synthesis of other interesting compounds.

Phytosterols

Myrtaceae plants also contain phytosterols (Figure 1C). Several recent reports characterized this class of natural compounds among *Eucalyptus* species (*Eucalyptus botryoides*, *Eucalyptus camaldulensis*, *Eucalyptus globulus*, *Eucalyptus grandis*, *Eucalyptus maculata*, *Eucalyptus pellita*, *Eucalyptus rudis*, *Eucalyptus sideroxylon*, and *Eucalyptus viminalis*) (Arisandi et al. 2020; Ferreira, Miranda, and Pereira 2018; Gominho et al. 2020; Rodrigues et al. 2018; Santos et al. 2017). These studies indicated β-sitosterol as the most prevalent compound, regardless of the investigated plant part. The presence of other phytosterols was also reported in different plant parts and across different species. *Eucalyptus globulus* wood was found to contain campesterol, cycloartenol, fucosterol, β-sitostanol, stigmasterol, and stigmastanol (Gominho et al. 2020; Rodrigues et al. 2018). Another study indicated the presence of avenasterol in *Eucalyptus globulus* leaves (Correia et al. 2018).

The phytosterols profile of *Eucalyptus grandis* wood also indicated the presence of campesterol, citrostadienol, and β-sitostanol (Santos et al. 2017). Another relevant phytosterol is stigmastanol that was found in the bark, heartwood and sapwood of *Eucalyptus pellita* and the bark of *Eucalyptus sideroxylon* (Arisandi et al. 2020; Ferreira, Miranda, and Pereira 2018). A recent study indicated that *Eugenia uniflora* leaves contained γ-sitosterol (Canabarro et al. 2020). β-Sitosterol was identified in the seeds of this species (Lazzarotto-Figueiró et al. 2021). In *Psidium guava*, the characterization of phytosterol composition of the seeds indicated that campesterol, β-sitosterol, and stigmasterol were the main phytosterol compounds (Narváez-Cuenca et al. 2020; Prommaban et al. 2020).

Carotenoids

Carotenoids are another relevant lipophilic group of phytocomponents in Myrtaceae family, which vary among species. *Eucalyptus parramattensis* leaves contain neoxanthin, violaxanthin, antheraxanthin, lutein, zexanthin, and β-carotene (Dhami et al. 2020). In the pulp and peel of *Eugenia uniflora*, all-*trans*-β-cryptoxanthin, all-*trans*-α-carotene, all-*trans*-β-carotene, 9-*cis*-β-carotene, all-*trans*-rubixanthin, 9-*cis*-rubixanthin, and all-*trans*-lycopene were identified (de Assis et al. 2020).

A recent experiment characterized carotenoids in different parts of *Psidium guajava* L. cv. 'Criolla'fruit and indicated the presence of 15-*cis*-lycopene, and all-*trans*-lycopene in the pulp and pericarp (Rojas-Garbanzo, Gleichenhagen, et al.

2017). However, all-*trans*- β-carotene was only detected in pulp. In *Myrciaria dubia* fruits, β-carotene was mainly present in the skin (Azevedo et al. 2019). This study also showed that the ripened fruits had higher content of β-carotene than the unripe ones. Finally, the characterization of carotenoid profile in *Pimenta dioica* revealed the presence of β-carotene, lutein, and lycopene (Loizzo et al. 2016).

Optimization of extraction yield/targeted selection of bioactive compounds

Optimizing the extraction of bioactive compounds is dependent of the extraction technology and the experimental conditions (Table 3). Both extraction yield and activity of extracts can be improved when appropriate extraction conditions are applied. The following sections discuss some of the key aspects to obtain extracts rich in bioactive compounds with high biological activity.

Essential oils

Regarding the role of extraction technology, the use of steam distillation is the most common process to obtain the essential oils across different studies from Myrtaceae family (Table 1). Alternative extraction technologies were also proposed such as supercritical CO_2 and microwave heating. For instance, a study on *Eucalyptus globulus* leaves indicated that steam distillation and supercritical CO_2 extraction methods produced essential oils with similar major components especially 1,8-cineole, β-pinene, aromadendrene, and globulol (Harkat-Madouri et al. 2015). A similar outcome was reported for *Pimenta dioica* essential oil for the extraction with hydrodistillation and microwave-assisted methods (Jiang et al. 2013). Moreover, the use of supercritical CO_2 extraction method was also applied to obtain the essential oil from the leaves of *Eugenia uniflora* (Garmus et al. 2014) and the fruit of *Pimenta dioica* (Dima et al. 2014). These studies indicated that the yield of essential oils obtained from Myrtaceae family varied in terms of the technology applied during extraction and the conditions applied, particularly the relative proportion among components. Thus, the selection of extraction technology should be considered when targeting oils enriched with specific constituents.

Phenolic compounds

Myrtle berries are widely consumed in the Mediterranean areas because of its distinctive flavor and health-benefiting antioxidants (Giampieri, Cianciosi, and Forbes-Hernández 2020). The anthocyanin and phenolic content of *Myrtus communis* berries could be enhanced using ultrasound-assisted extraction. The most influencing variables were determined by Box-Behnken design (González de Peredo et al. 2019). The highest contents of total phenolics and anthocyanins (45 mg EAG/g and 30 mg/g, respectively) were obtained using high percentage of methanol (92.8% and 74.1% for total phenolic and anthocyanins, respectively), neutral pH 5 and short extraction time (2 minutes). Bouaoudia-Madi et al. (2019) reported that the optimized ultrasound assisted extraction of myrtle pericarps exhibited 2-fold increase in the total phenolic content as compared with microwave-assisted and conventional methods (241.66 *vs.* 119.59 and 76.40 mg GAE/g, respectively). In another study, the pressurized liquid extraction (PLE) was performed to optimize the phenolics recovery from myrtle leaves using Box-Behnken design (Díaz-De-Cerio et al. 2018). This optimized technique resulted in enriched gallic and ellagic acid derivatives in addition to higher total phenolic content compared with ultrasound assisted extraction (30 versus 22.4 mg/g leaf dried weight).

Some studies reported the optimization of extraction of the anthocyanin from Jambolan fruits (*Syzygium cumini*). For instance, a study recovered anthocyanins from the fruit skins by applying Plakett–Burman design (Chaudhary and Mukhopadhyay 2013). The results indicated that the highest anthocyanin yield (763.80 mg) was obtained using 20% ethanol and 1% acetic acid. Another study compared the anthocyanins extraction using PLE technology and ultrasound methods using a non-factorial design (Sabino et al. 2021). The ultrasound extraction method provided the most effective method by yielding 60.5 mg cyaniding-*O*-glucoside.g^{-1} DF under the optimum conditions whereas other extaction methods yielded 47.0 and 54.2 mg cyaniding-*O*-glucoside.g^{-1} DF. The mechanism that explains the increased efficiency of ultrasound is related to the cavitation phenomenon, which promotes the disruption of vegetables cell releasing enclosed components by increasing pores in cellular wall, fragmentation of cellular structure particles, turbulence within solvent, and swelling of the vegetable matrix (Kumar, Srivastav, and Sharanagat 2021).

In a related experiment, the effect of solvent (pure solvents and mixtures of water, acetone and ethanol) was investigated in the extraction potential of polyphenolics with antioxidant activity from Jambolan fruits (de Morais Sousa et al., 2022). The authors found that a binary mixture of water and acetone (0.5:0.5, v/v) was the most efficient solvent composition, resulting in > 90% of the maximum multi-response values.

Response surface methodology was also utilized to enhance the antioxidant potentials of *S. aromaticum* flower buds extract. The solid to liquid ratio and ethanol concentration proved as significant parameters affecting the phenolic and flavonoid contents and consequently the antioxidant properties (Köprü et al. 2020). Recently, Sirichan and colleagues employed Box-Behnken design with RSM to optimize ultrasound assisted extraction of antioxidant compounds (total flavonoid and phenolic contents) with potential antioxidant properties from makiang seed (*Cleistocalyx nervosum*) (Sirichan et al. 2022). The effect of temperature, time, and amplitude were evaluated on the extraction yield. The optimized conditions for the maximum extraction yield were: temperature (51.82 °C), amplitude (40.51%) and time (31.87 min). Gallic acid was found as the major phenolic component of makiang seed extract. In another study, different solvents (methanol, water, and ethanol) along

Table 3. List of optimized extraction methodologies for myrtaceous plants and/or phytoconstituents.

Plant Name	Method of extraction	Factors	Optimized conditions	Design	Bioactivity/economical outcome	References
Eugenia punicifolia D.C.	Maceration	Solvent extraction system their binary and ternary combinations	Ethanol based extracts	Simplex centroid design and surface response methodology	Ethanol based extracts showed highest antioxidant and antiproliferative activities	(C. Dos Santos et al. 2020)
Eugenia uniflora L.	Ultrasound-Assisted Extraction	Ethanol concentration, extraction time, and temperature	Ellagic acid yield = 26.0 µg/mL 44% ethanol (w/w), 22 min, and 59 ° C.	Box Behnken design	–	(Assunção et al. 2017)
Myrtus communis (fruits)	Ultrasound-assisted extraction	pH, solvent composition, solvent-sample ratio, number of cycles, temperature and ultrasound's amplitude	For phenolics: 92.8% methanol in water, 60, 65.48% ultrasound amplitude, 0.2 s cycles, pH 6.8, and 10 solvent: 0.5 g sample For anthocyanins: 74.1% methanol in water, 10 ℃, 30% ultrasound amplitude, 0.3 s cycles, pH 7, and 18 mL solvent:0.5 g sample	Box Behnken design	Suggested to be applied industrially on raw materials	(González de Peredo et al. 2019)
Myrtus communis (pericarp)	Ultrasound-assisted extraction	Ethanol %, irradiation time and amplitude	Solvent:70% ethanol (*v/v*), 7.5 min and 30% amplitude	Box–Behnken Design	Higher phenolic content	(Bouaoudia-Madi et al. 2019)
Myrtus communis (leaves)	Pressurized liquid extraction	Solvent ratio, temperature and time	Solvent ration: 71% ethanol/water, 137 °C and 19 min	Box Behnken design	Improved phenolic content to be used as nutraceutical	(Díaz-De-Cerio et al. 2018)
Syzygium aromaticum (flower buds)	Maceration	Ethanol concentration and liquid/solid ratio	4.03 mL/g (solvent to solid matter) and 53.2% ethanol	Central Composite Rotatable design	Improved antioxidant and antiradical properties	(Köprü et al. 2020)
Syzygium cuminii (pulp and peel)	Pressurized liquid extraction	Temperature, ethanol % and extraction cycles	90 °C, 80% ethanol, and one extraction cycle	Non-factorial design	Increased anthocyanins content	(Sabino et al. 2021)
Syzygium cuminii (pulp and peel)	Bath ultrasound extraction	Temperature, time, and ethanol %	32.5 °C, 40 min of extraction, and 80% ethanol	Non-factorial design	Increased anthocyanins content	(Sabino et al. 2021)
Syzygium cuminii (pulp and peel)	Probe ultrasound extraction	Ultrasound power, ethanol %, and time	5000 W/L ultrasound power density, 79.6% of ethanol, and7.5 min	Non-factorial design	Increased anthocyanins content	(Sabino et al. 2021)
Syzygium cuminii (fruit Skin)	Soaking for 4 h on orbital shaker (100 rpm, 48 °C)	Solvent %, acid type and acid %	20% ethanol +1% acetic acid.	Plakett–Burman design	Increased anthocyanins content and enhanced colorant for food industries	(Chaudhary and Mukhopadhyay 2013)
Syzygium cuminii (fruits)	Ultrasound (80 kHz/20 W, 20 min)	Solvent composition: (separately, binary or ternary mixtures)	Solvent: binary mixture of (0.5:0.5, v/v) water and acetone	Simplex-centroid design	Optimized antioxidant activity	(de Morais Sousa et al., 2022)

with their binary and ternary combinations were tested to extract *E. punicifolia* leaves through simplex-centroid mixture design and surface response methodology (Dos Santos et al. 2020). The ethanol extract exhibited the highest phenol content (412.6 mg GAE/g). A related experiment with *Eugenia uniflora* L. indicated that ultrasound could be applied in the extraction of ellagic acid (Assunção et al. 2017). The optimum condition yielded an extract with 26.0 µg ellagic acid/mL. Applying emerging technologies and optimizing the extraction are effective strategies to improve the recovery of polyphenols. Particularly, ultrasound can be indicated as one of the most relevant strategies.

Phloroglucinol adducts and meroterpenoids

The extraction of phloroglucinol adducts and meroterpenoids from Myrtaceae involves the use organic solvents and take several hours to be accomplished. One example is the study carried out with *Eucalyptus loxophleba* leaves to isolate loxophlebals, sideroxylonal and other related compounds (Sidana et al. 2010, 2011). The proposed extracts in these studies involve the extraction of the dried plant material in Soxhlet apparatus using a mixture of methylene chloride:methanol (8:2). The obtained sideroxylonal (phloroglucinol) enriched extract was further applied on VLC column to be fractioned with gradient system of hexane:ethyl acetate (100:0 to 0:100) followed by chloroform:methanol (100:0 to 80:20) to obtain the major sub-fractions.

Phrologlucinol-based compounds were also extracted from the fruits of *Melaleuca Leucadendron* by percolation with CH_2Cl_2 (Wu et al. 2020). The fruits extract was passed through column using petroleum ether and ethyl acetate. The selected fraction was applied on ODS column through methanol:water. This led to the isolation of twelve novel 5-methoxy-4-methyl-benzyl phloroglucinol-terpenoid hybrids. This method was further adopted for the same purpose using other myrtaceous plants including *Psidium cattleianum*, *Eucalyptus cinerea,* and *Callistemon citrinus* (Mahrous et al. 2021; El Gaafary et al. 2022; Saber et al. 2018; Shehabeldine et al. 2020; Soliman et al. 2014).

In a related experiment, the air-dried aerial parts of *Eucalyptus tereticornis* were extracted by percolation with ethyl acetate. The obtained extract was passed through silica gel column and gradients of petroleum ether and acetone were used as the solvent system. The obtained sub-fractions passed through Sephadex column using chloroform and methanol to obtain the bioactive formyl phloroglucinol meroterpenoids (Liu, Feng, et al. 2018). Other authors performed another procedure involving the alcohol extraction of *Syzygium samarangense*, *Syzygium austroyunnanense, Baeckea frutescens, Melaleuca leucadendron, Leptospermum brachyandrum* and *Psidium littorale.* This step was then followed by fractionation and utilization of the hexane and chloroform fractions for the separation of phloroglucinols aglycones and the ethyl acetate for their glycosides (Qin, Zhi, et al. 2018; Xie et al. 2019; Yang et al. 2018; Zou et al. 2018). Both methods (percolation and Soxhlet apparatus) seems adequate to obtain phloroglucinol adducts and meroterpenoids due to extensive period to maximize the recovery of these compounds, but this characteristic is also an important limitation that has to be overcome. In this sense, exploring the use of emerging extraction technologies (such as ultrasound, microwave heating and supercritical CO_2, for instance) can be seen as a relevant advance for future studies.

Triterpenes, phytosterols and carotenoids

The isolation from triterpenes involves the use of different technologies and strategies: soxhlet extraction, conventional solid-liquid, ultrasound and supercritical CO_2. The use of organic solvents (such as dichloromethane or methylene chloride with methanol) is a common choice to extract triterpenes, especially for Soxhlet extraction (Arisandi et al. 2020; Gominho et al. 2020, 2021; Okba, El Gedaily, and Ashour 2017; S. A. O. Santos et al. 2017). In the case of conventional liquid-solvent extraction, different solvents have been used and include methanol or ethanol in aqueous or ternary solutions with hexane, NaOH, and formic acid (Acín et al. 2021; Ceballos et al. 2018; Flores et al. 2015; Lima et al. 2015).

The use of alternative methods, beyond the conventional solid-liquid and Soxhlet methods, has been reported in some studies. Ultrasound seems an interesting option with a reduced extraction time (around 15 min) (Ladurner et al. 2017). This characteristic can be seen as an important advantage in comparision with other methods that can last for several hours, especially with Soxhlet equipment (Arisandi et al. 2020; Gominho et al. 2020). In the same line of thought, the use of supercritical CO_2 is another relevant technology. In this case, limited information exists at this moment, to the best of our knowledge (Canabarro et al. 2020). Current evidence suggest that advances in the development of technologies and optimization of extraction conditions are necessary to obtain extracts rich in triterpenoids due to the scarcity of studies that comprehensive evaluate the extraction of triterpenes from Myrtaceae.

In case of phytosterols, the use of soxhlet extraction is the most common method reported in literature for different species of the Myratceae family (Arisandi et al. 2020; Ferreira, Miranda, and Pereira 2018; Gominho et al. 2020; Prommaban et al. 2020; P. F. Rodrigues et al. 2018; S. A. O. Santos et al. 2017). Conversely, conventional solid-liquid extraction method is less reported (Correia et al. 2018; Lazzarotto-Figueiró et al. 2021). Supercritical CO_2 extraction recieved attention from researchers as potential alternative method to obtain phytosterols from Myratceae family (Canabarro et al. 2020; Narváez-Cuenca et al. 2020). Particularly for *Eugenia uniflora* leaves, the increase in the temperature (from 40 to 80 °C) and pressure (from 15 to 25 MPa) seems to the reduce efficiency capacity of this technology and mild conditions seems to be the recommended strategy (Canabarro et al. 2020).

In the case of carotenoids, the use of conventional solid-liquid extraction methods applying mainly acetone but minimal information exist in terms of alternative extraction methods (Azevedo et al. 2019; de Assis et al. 2020; Dhami et al. 2020; Loizzo et al. 2016; Rojas-Garbanzo, Gleichenhagen, et al. 2017). In this sense, seems reasonable to suggest that further experiment can be carried out to obtain riterpenes, phytosterols and carotenoids using innovative emerging technologies, especially supercritical CO_2 and ultrasound, which have been accumulating scientific evidence for their use in the last decade.

Encapsulation and protective techniques for delivery of myrtaceae bioactive phytochemicals

The inclusion of plant nutraceuticals and/or bioactive compounds in innovative delivery systems offers many advantages. These advantages include enhanced bioavailability, increased pharmacological activity, sustained delivery, decreased toxicity, targeting diseased organ, increased palatability, and improved appearance (Fang et al. 2006; Khogta et al. 2020; Saber et al. 2018; Saraf and Ajazuddin 2010). Numerous research studies explored the use of plant extracts/essential oils of Myrtaceae plants to prepare different pharmaceutical formulae, such as nanoliposomes, nanoemuslions, nanodispersion, and multilamellar liposomes. Examples of different formulations of Myrtaceous plants together with their impacts regarding the industrial or biological importance are depicted in Table 4 and Figure 2.

One of the possible strategies to deliver the bioactive compounds found in Myrtaceae family consist in the production of nanoemulsions by mixing an emulsifying agent with the essential oil and applying agitation, heating, ultrasound or microwave (Aziz et al. 2019; Magalhães et al. 2022; Roozitalab et al. 2022; Wei et al. 2021). The formation of a stable system is a great advantage to protect the bioactive compounds but the optimization of the process is dependent on some key factors. One of the key factors is the proportion of essential oil in the nanoemulsion as indicated by recent studies (Aziz et al. 2019; Magalhães et al. 2022). This variable can affect the droplet size, polydispersity index, and viscosity.

The use of surfactant (compounds capable of reducing surface tension between two liquids) seems to have a key role in the formation of stable nanoemulsions. One class of compounds studied is Tween that can be classified in terms of fatty acid composing the molecule. Due to this aspects some studies explored the use of different Tween and indicated contrasting results about the optimum compound for proper formation of nanoemulsion, in terms of particle size and thermodynamic stability (Aziz et al. 2019; Roozitalab et al. 2022). This outcome suggested that the composition of essential oil may play an important effect in producing stable nanoemulsions.

The use of emerging technologies has also been explored in the formation of nanoemulsions (Table 4). For instance, current evidence indicates that microwave heating can improve the complexation of *Syzygium aromaticum* essential oil into β-cyclodextrin (Hernández-Sánchez et al. 2017). Moreover, this study also indicated that post-encapsulation treatment might be relevant to improve the stability of the nanoemulsion, especially with freeze-drying. Another emerging technology with potential application in the production of stable nanoemulsions is ultrasound. In this case, the application of ultrasound during the emulsification process led to a stabilization for 60 days regardless of the temperature (-20, 4 and 25 °C) (Wei et al. 2021).

The production of liposomes seems to be another interesting strategy to deliver bioactive compounds from Myrtaceae. Recent studies indicated that it is possible to obtain stable solid liposomes but the concentration of bioactive compounds in the liposome and the proportion of components of the encapsulating material are key factors that must be evaluated. Regarding the effect of bioactive compounds concentration, a study carried out with *Eucalyptus citriodora* essential oil indicated 4 mg/mL as the optimum level due to the reduced particle size, particle size distribution and low zeta potential. In another experiment, the effect of encapsulating material composiotn revealed that reducing the proportion of cholesterol in the binary mixture with phosphatidyl choline should be be achieved to obtain small liposomes (Saber et al. 2018).

The production of nanoparticles can be considered to deliver bioactive compounds from Myrtaceae family. In this case, a new composite is formed by heating and stirring $AgNO_3$ and $Zn(CH_3CO_2)_2$ with extracts rich in bioactive compounds. Some examples were listed in previous reports (Arumugam et al. 2021; Madakka, Jayaraju, and Rajesh 2021). The main outcome from these studies was the formation of particles that retain or improve the biological effect related to the original extract.

The preservation of biological activity and health-related aspects is a key aspect that has been considered in the aforementioned studies and favors the use of encapsulation technologies and delivery systems to obtain new and stable high-added value ingredients for the development of healthier and functional foods. For instance, the encapsulated extracts and essential oils obtained from Myrtaceae family can also exert antioxidant, antimicrobial, anticancer, and anti-inflammatory in vitro (Arumugam et al. 2021; Madakka, Jayaraju, and Rajesh 2021; Roozitalab et al. 2022; Wei et al. 2021). Studies in vivo also supported the use of encapsulation technologies to deliver activity compounds. Recent experiments supported the anti-inflammatory, analgesic, and hepatoprotective effects (Aziz et al. 2019; Magalhães et al. 2022; Saber et al. 2018). Moreover, the encapsulation (particularly nanoemulsification) can also reduce the oral toxicity of essential oils. This effect was observed in vivo for *Melaleuca alternifolia* essential oil (Wei et al. 2021). The collective evidence from recent studies supports the use of encapsulating technologies and delivery systems to preserve the biological effect of the original extract or essential oil, but the optimization of process (especially for the concentration of bioactive compounds and the encapsulating material composition) is still necessary. The assessment of encapsulating stability and the preservation of biological activity, especially during long storage periods, is a necessary aspect that must be considered in future studies to strengthen the progression to larger production scales and the development of commercial solutions.

The developments of commercial applications with Myrtaceae bioactive compounds has also attracted the interest for patenting products to foster their insertion and commercialization in the pharmaceutical and food market. Patents containing Myrtaceae plants are listed in Table 5. Nayak and Aithal (2019)

Table 4. Synthesized formulations of myrtaceous plants and/or their phytoconstituents.

Source	Formulation type	Method of preparation	Formula characterization	Bioactivity/Industrial application	References
Melaleuca alternifolia essential oil	Nanoemulsion	Ultrasonic emulsification	Droplet size, polydispersity index, zeta potential, TEM; Emulsion stability (dynamic light scattering and resistance to centrifugation), and acute and sub-chronic toxicity tests in vivo	Antimicrobial activity against *Escherichia coli* and *Salmonella* sp.; stable emulsion during storage, and decreased oral toxicity of tea tree oil	(Wei et al. 2021)
Eugenia sulcata essential oil	Nanoemulsion	Phase inversion method (heating)	Droplet size, polydispersity index, dynamic lightning scattering technique; and anti-inflammatory assay in vitro and in vivo	Droplet size and polydispersity index were affected by the level of essential oil, surfactants and water; Increased the inhibition effect of *Eugenia sulcate* essential oil on purinergic receptor in vitro and the inflammatory response in mice	(Magalhães et al. 2022)
Eucalyptus globulus essential oil	Nanoemulsion	Spontaneous emulsification	Morphology, thermodynamic stability, viscosity, particle size, polydispersity index, pH; and transdermal analgesic test in vivo	Micellar diameter and viscosity were affected by essential oil level; Thermodynamic stability and optical properties, viscosity were affected by surfactant level and composition; Particle size, polydispersity index, and pH were affected by surfactant and essential oil levels and surfactant composition; Transdermal analgesic effect	(Aziz et al. 2019)
Myrtus communis L. essential oil	Nanoemulsion based gel	Spontaneous emulsification	Particle size distribution and rheological properties; and anti-cancer, antioxidant and antimicrobial test in vitro	Droplet size and particle size distribution were affected by surfactant level and composition; Increased anticancer activity against A-375 melanoma cells. Promising antimicrobial and antioxidant activities	(Roozitalab et al. 2022)
Syzygium aromaticum essential oil	β-Cyclodextrin complex	Microwave-assisted complexation	Field emission scanning electron microscopy and quantification by GC-MS	Optimized complexation of clove oil (microwave irradiation followed by freeze drying)	(Hernández-Sánchez et al. 2017)
Eucalyptus citriodora essential oil	Solid liposomes	Thin-film hydration technique	SEM and DSC; Release rate and particle size	Enhanced structural stability of the solid-liposomes	(Lin et al. 2019)
Psidium guajava and *Psidium cattleianum* extracts	Nanoliposomes of cholesterol and phosphatidyl choline	Thin-film hydration technique	Entrapment efficiency, particle size, polydispersity index, zeta potential, photomicroscopy and TEM; Hepatoprotective test in vivo	Particle properties were affected by the proportion of components composing the encapsulating material composition; In vivo hepatoprotection	(Saber et al. 2018)
Syzygium cumini extract	ZnO nanoparticles	Heating with continuous stirring	Field emission scanning electron microscope coupled with energy dispersive X-ray (EDX), X-ray diffraction, FT-IR analysis; Anti-cancer activity	Antioxidant and anti-cancer activity in vitro	(Arumugam et al. 2021)
Syzygium jambolanum extract	Ag nanoparticles	Heating with continuous stirring	UV-VIS, SEM, EDX and FTIR, Antioxidant and antimicrobial activity	Antioxidant and antimicrobial properties	(Madakka, Jayaraju, and Rajesh 2021)

DSC: Differential scanning calorimetry, EDX: energy dispersive X-ray spectrometer, FTIR: Fourier transform infrared spectroscopy, GC-MS: Gas Chromatography coupled with Mass Spectrometry, SEM: scanning electron microscope, and TEM: transmission electron microscopy.

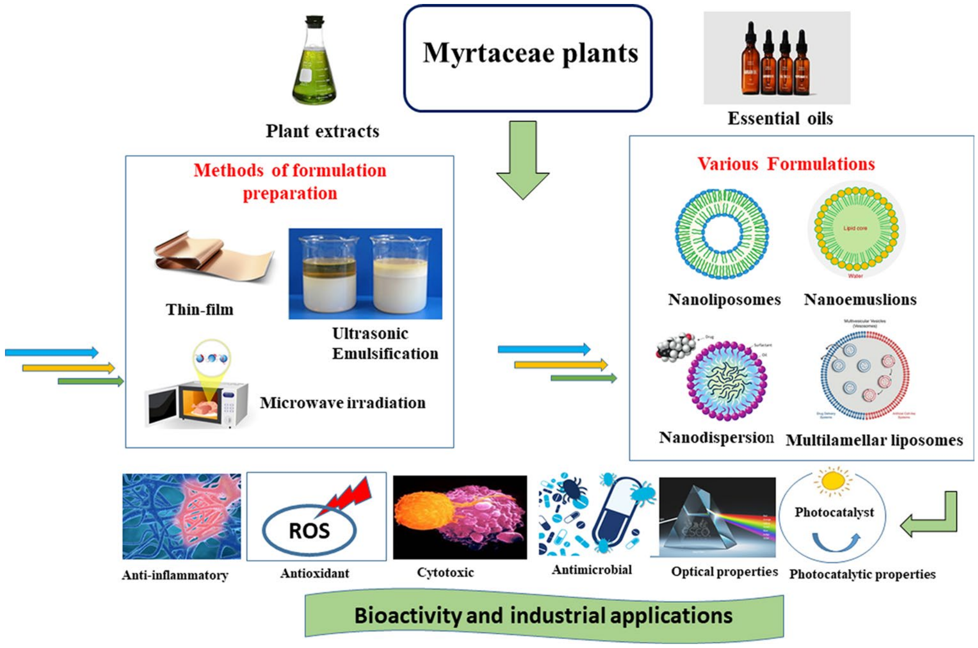

Figure 2. Formulations of Myrtaceae plants-based dosage forms together with their impacts regarding the industrial or biological applications.

Table 5. Important registered patents, which explain the different formulations of Myrtaceae plants for pharmaceutical purposes. Q5

Patent no	Patent Title	years	Country	Formulation	Usage	Ref
US 2019 / 0201474A1	Herbal oil formulation for topical use and medicinal applications thereof	4-07-2021	USA	A topical herbal oil formulation, comprising a blend of essential oils extracted from bark of *Heterophragma roxburghii,* and other natural sources such as *Syzygium aromaticum*	For the treatment of diabetic foot, gangrene, athlete ' s foot, burn wounds, bed sore, chronic open wounds, and snake bite	(Nayak and Aithal 2019)
US 2016/0367617 A1	Herbal product for its administration to diabetic people and the process to obtain it	22-12-2016	USA	Dry composition comprising dry pulverized *Syzygium cumini* seeds and dry pulverized *Bauhinia forficate* leaves	Given to diabetic patients to reduce the level of glucose	(Navajas, Pinto, and Maluendas 2016)
US 8.496,914 B2	Antibacterial oral rinse formulation for preventing coronary artery disease	30-07-2013	USA	Composition of active ingredients such as green tree extract, tea tree oil and mint oil	Antibacterial oral rinse formulation	(Bonfiglio 2013)
CN102204962B	Preparation method of itching-relieving mosquito repellent aerogel patch	20-03-2013	China	Heating of polyisobutylene medical hot melt glue followed by mixing with Melaleuca oil with the addition of tourmaline powder and sodium carboxymethyl cellulose	Itching-relieving mosquito repellent	(Peihong, Xiaodan, and Jinan 2013)
US20150352165A1	Clindamycin phosphate, salicylic acid and tea tree oil combinations	10-12-2015	USA	Combination of clindamycin phosphate, tea tree oil and salicylic acid	Topical applications for the treatment of skin infections and acne vulgaris	(Pisak et al. 2015)

registered patent US 2019/0201474A1 of herbal oil formulation for the treatment of diabetic gangrene, cellulite based gangrene, snake bites, bed sores and other wounds. In this dosage formulation, a blend of plants containing herbal oils including *Syzygium aromaticum* were added to the aqueous extract of *Heterophragma roxburghii* bark. In another patent US 2016/0367617 A1, Navajas and colleagues described the usage of a mixture of *Syzygium cumini* seeds and *Bauhinia forficata* leaves to control the blood glucose level in diabetic patients. For the formulation dosage forms, the seeds of *Syzygium cumini* and the leaves of *Bauhinia forficate* were pulverized to 60 mesh size and were further grinded, dried and both parts homogenized. The obtained product was capsulized and packed (Navajas, Pinto, and Maluendas 2016). A combination of tea tree oil, green tea extract and mint oil was developed in a proper dosage under the patent (US 8.496,914 B2) as antibacterial oral rinse formulation for hygiene activities to guard against myocardial infarction and other coronary diseases, which may result as a complication of bacteremia (Bonfiglio 2013). Peihong and colleagues registered the patent

CN102204962B, which reported the formation of itch relieving mosquito repellent. It was prepared by heating the polyisobutylene medical hot melt glue to form the component A. *Melaleuca* oil was extracted through steam distillation to form component B. In the next step, tourmaline powder and sodium carboxymethyl cellulose were added slowly to the component A followed by the addition of component B. Then antipruritic glue was obtained which was released on paper or cloth to develop the patch (Peihong, Xiaodan, and Jinan 2013). A registered patent US20150352165A1 reported the inclusion of clindamycin phosphate, tea tree oil and salicylic acid for the treatment of skin infections and acne vulgaris. For the preparation of mixture I, distilled water was added to carbomer to obtain a homogeneous dispersion then further triethanolamine was added for neutralization. Then dimethicone was added to inhibit foaming (mixture I). Mixture II was formed by the addition of ethanol and water to form a carrier phase for the gel formulation. Certain amounts of tea tree oil, clindamycin phosphate and salicylic acid were added to mixture II. Then poloxamer and glycerin were added. Mixture II and I were mixed to obtain gel formulation with constant stirring. Perfume was added to the final mixture (Pisak et al. 2015).

Applications in food production and preservation

The phytochemicals found in Myrtaceae family were used to produce functional foods and showed an outstanding technological role in food production, safety, and preservation. The essential oils and polyphenol-rich extracts were tested in many foods such as meat, fish, meat products, vegetables, and baked foods (Table 6 and Figure 3). The importance of using Myrtaceae phytochemicals is mainly related to their antimicrobial and antioxidant activity, which delay the growth of pathogenic microorganisms and slow the progression of oxidative reactions in lipids and natural pigments in foods.

One of the main fields of applications of these compounds is the production and preservation of meat, fish, and meat products. *Pimenta dioica* essential oil was used as a pretreatment to reduce the attachment of *Salmonella heidelberg* in turkey skin (Nair and Johny 2017). The immersion of muscle pieces in an emulsion solution led to a significant reduction in *Salmonella heidelberg* counts. Another study explored the incorporation of *Melaleuca alternifolia* essential oil into minced beef and indicated an inhibition of the growth of *Listeria monocytogenes* (Silva et al. 2019).

The production of active films is an interesting strategy to explore the technological value of Myrtaceae phytochemicals. In terms of microbial inhibition, the use of liposomes loaded with *Melaleuca alternifolia* essential oil in chitosan nanofiber inhibited the growth of *Salmonella typhimurium* and *Salmonella enteritidis* in chicken meat (Cui et al. 2018). Another experiment with chicken meat indicated a similar antimicrobial effect of *Syzygium aromaticum* essential oil in linear low-density polyethylene film against *Salmonella typhimurium* and *Listeria monocytogenes* growth (Mulla et al. 2017). The microbial spoilage and accumulation of total volatile basic nitrogen containing compounds in carp fillets was delayed by using a chitosan film with *Eucalyptus globulus* essential oil (Kootenaie et al. 2017).

Table 6. Application of Myrtaceae plant extract in food production and processing.

Food products	Source	Effect in food	Ref.
Turkey skin	*Pimenta dioica* essential oil in nanoemulsion	Slowed the growth of *Salmonella* Heidelberg	(Nair and Johny 2017)
Ground beef	*Melaleuca alternifolia* essential oil	Inhibited *Listeria monocytogenes* growth	(C. de S. Silva et al. 2019)
Chicken meat	*Melaleuca alternifolia* essential oil liposomes in chitosan nanofiber	Slowed the growth of *Salmonella typhimurium* and *Salmonella enteritidis*	(Cui et al. 2018)
Chicken meat	*Syzygium aromaticum* essential oil in linear low-density polyethylene film	Slowed *Salmonella typhimurium* and *Listeria monocytogenes* growth	(Mulla et al. 2017)
Carp fillets	*Eucalyptus globulus* essential oil in chitosan film	Slow microbial growth and total volatile basic nitrogen accumulation	(Kootenaie et al. 2017)
Lamb sausage	*Eugenia uniflora* leaf extract	Reduced loss of redness and lipid and protein oxidation	(de Carvalho et al. 2019)
Beef burgers	*Myrciaria cauliflora* peel extract	Reduced lipid oxidation	(Heck et al. 2020)
Sliced maize cob	*Pimenta dioica* essential oil	Inhibited the aflatoxin B1 production by *Aspergillus flavus*	(Chaudhari et al. 2020)
Maize	*Pimenta dioica* essential oil encapsulation in chitosan	Inhibited the aflatoxin B1 production by *Aspergillus flavus* and lipid peroxidation	(Chaudhari, Singh, Das, Deepika, and Dubey, 2022)
Fumigated Maize samples	*Melaleuca cajuputi* essential oil	Inhibited the aflatoxin B1 production by *Aspergillus flavus* and lipid peroxidation	(Chaudhari, Singh, Das, Kujur, et al., 2022)
Maize	*Pimenta dioica* and *Syzygium aromaticum* essential oil	Inhibited the maize fungus (*Fusarium verticillioides)*	(Achimón et al. 2021)
Barley, cabbage, and watermelon juice	*Syzygium aromaticum* essential oil with cinnamaldeyde	Inhibited the growth of *Bacillus cereus*, *Yersinia enterocolitica*, *Staphylococcus aureus*, and *Escherichia coli*	(Siddiqua et al. 2015)
Lemon slices	*Syzygium aromaticum* essential oil in chitosan film	Inhibited peroxidase and polyphenol oxidase activities, and preservation of aroma active compounds	(H. Li et al. 2020)
Herbal drink	*Melaleuca citrolens* leaves infusion	Rich in phenolics and improved antioxidant potential with high aroma	(Nirmal et al. 2022)
Cookies	*Myrciaria dubia* processing by-products extract	Improved total phenolic content and antioxidant activity	(das Chagas et al. 2021)
Cookies	*Psidium guajava* seed essential oil	Similar texture and color to control cookies	(Raihana et al. 2017)

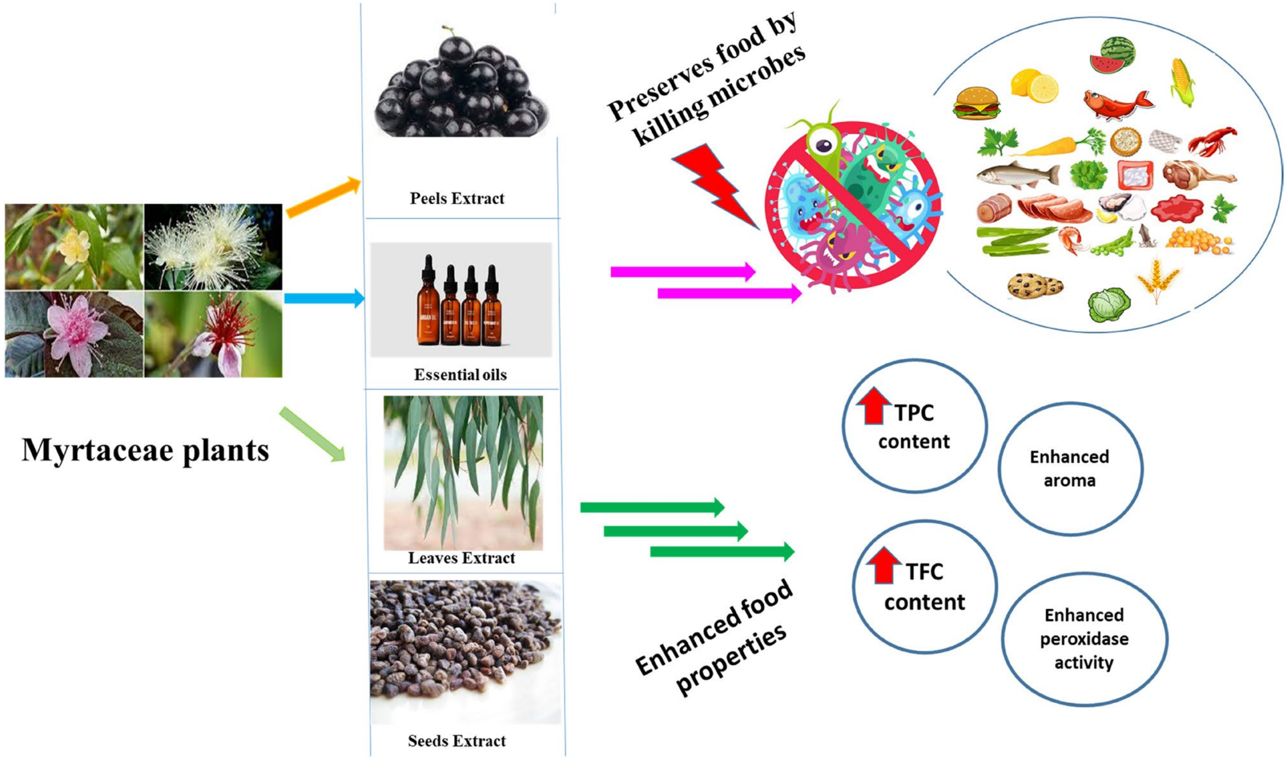

Figure 3. Applications of essential oils and different extracts of myrtaceae plants in food preservation and enhancement of food properties.

In meat products, the protective effect of extracts obtained from Myrtaceae species against spoilage was observed in different studies. A relevant example is the incorporation of *Eugenia uniflora* leaves extract in lamb sausages that delayed the oxidation of myoglobin, lipids, and protein oxidation (de Carvalho et al. 2019). Another interesting natural extract from *Myrciaria cauliflora* peel was used to improve the preservation of meat products. It reduced the progression of lipid oxidation in beef burgers (Heck et al. 2020).

The phytochemicals found in *Myrtaceae* family were found to favor the preservation and safety of food of vegetable origin. An example of this protective effect was obtained from the use of *Pimenta dioica* essential oil against the growth of *Aspergillus flavus* and the production of aflatoxin B1 in slices of maize cobs (Chaudhari et al. 2020). The direct addition of essential oils to real foods poses serious problems, thereof, Chaudhari and colleagues prepared the nanoemulsion of *Pimenta dioica* essential oil. The essential oil was encapsulated in chitosan nanoemulsion through ionic gelation technique. The results showed that the nanoemulsion was more effective at low doses against *Aspergillus flavus*, aflatoxins B1 and lipid peroxidation in preserved maize samples. So nanoemulsions of *Pimenta dioica* essential oil could be used as a promising agent to extend the shelf life of food products (Chaudhari, Singh, Das, Deepika, and Dubey, 2022).

The growth of several pathogenic microorganisms were reduced in barley, cabbage, and watermelon juice by combining *Syzygium aromaticum* essential oil with cinnamaldehyde (Siddiqua et al. 2015). The use of a chitosan film containing *Syzygium aromaticum* essential oil also improved the preservation of lemon slices (Li et al. 2020). The inhibition of endogenous enzymatic activity and loss of aroma were attenuated using this active essential oil coating.

Cookies are another interesting food to explore the development of functional foods with phytochemicals obtained from Myrtaceae species. In case of *Myrciaria dubia* extract (rich in polyphenols), the antioxidant potential of cookies was improved (das Chagas et al. 2021). In a related experiment, the incorporation of *Psidium guajava* seeds essential oil did not affect the sensory properties of cookies (Raihana et al. 2017). These studies supported the use of *Myrtaceae* active compounds in the development of food products due to their technological effect. Further research is still necessary to explore the food preserving effects of Myrtaceae products in terms of extending the shelf life of other food products such as dairy products and processed vegetable foods.

Conclusions and perspectives

In this work, we focused on certain important plants of family Myrtaceae including *Eucalyptus* sp., *Eugenia uniflora*, *Syzygium aromaticum, Psidium guajava*, *Pimenta dioica, Myrtus communis*, *Myrciaria* sp., and *Melaleuca alternifolia.* Recent studies highlighted the importance of Myrtaceae plants as being rich in both phytochemicals and nutritional compounds and therefore they are widely implicated in industrial and pharmaceutical fields. The encompassed bioactive compounds in different Myrtaceae matrices constitute a remarkable source of lead compounds with potential applications against infectious diseases, diabetes, cancer, and inflammatory chronic diseases.

However, there are some major limitations for the pharmaceutical use of these species and their phytochemicals. Firstly, pharmacokinetic studies should be fully investigated and validated to reveal the absorption, distribution, metabolism, and release rates of these bioactive compounds. The major problem of using new bioactive compounds in pharmaceutical applications is the pharmacogenomic response related to human body capacity to metabolize the administrated natural drugs. Secondly, the safety of main compounds from Myrtaceae should also be extensively assessed using chronic toxicity profiling with different doses to comply with nutraceuticals' risk assessment criteria. The pharmacodynamic profile of these main compounds should be investigated particularly for the treatment of intrinsic diseases such as diabetes and cancer to get precise therapeutic index.

To enhance the pharmacological selectivity, some studies suggested the use of formulations of Myrtaceae plants and their bioactive compounds with promising health beneficial or industrial outcomes. However, further efforts should be made to evaluate these formulations for the mass production to meet large industrial scale. Certain formulations were investigated for some Myrtaceae medicinal plants like *M. communis* essential oils and these investigations should be further extended to other important species. The screening of bioactive compounds from other Myrtaceae species could allow the identification of novel bioactive substances with cosmetic, industrial, and pharmaceutical relevance.

Finally, some species of this phytochemically enriched botanical family such as certain *Lophomyrtus* sp., *Syzygium* sp. and *Metrosideros* sp. seem to be endangered due to uncontrolled exploitation or ecological threats. In this sense, biotechnological investigations aimed at regenerating these species using different biotechnological tools such as tissue culture, cryopreservation and photoautotrophic micropropagation should be considered as an important measure to protect the endangered plants of the Myrtaceae family (Nadarajan et al. 2021).

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