Plant Foods for Human Nutrition (2022) 77:495–503
https://doi.org/10.1007/s1130-022-01008-8

Phenolic Compounds Present in Yerba Mate Potentially Increase Human Health: A Critical Review

Andreia Candal de Vasconcellos1 · Jeverson Frazzon1 · Caciano Pelayo Zapata Noreña1

Accepted: 22 August 2022 / Published online: 28 September 2022
© The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2022

Abstract

Yerba Mate (YM) is a food product derived from Ilex paraguariensis whose constituents obtained from its extract, mainly the phenolic fraction, have been linked to numerous health benefits, such as cardiovascular protection, weight reduction, glucose control, and gene modulation. However, evidences linking phenolic compounds (PC) intake and human health are still limited and often contentious. Several researches have shown that key PC elements are poorly absorbed in humans and exist predominantly as conjugates, which may not be bioactive but may play a crucial role when interacting with the gut microbiota (GM). As the intestine is the largest microorganism-populated organ in the human body, GM has been regarded as a “microbial organ”, acting as a second genome for modulating the host’s health phenotype. For this reason, the study of intestinal microbiota has received considerable attention in recent years. Its impact on the development of nutrition-related diseases must motivate broader researches on the interaction between YM’s PC and GM regarding the production of metabolites that may influence human health. This review aimed to gather and assess the available information about how PC from YM may impact host metabolism and the immune system and GM.

Keywords Tea · Polyphenol · Antioxidant · Intestine · Stimulant

Introduction

The aging of the world’s population is placing emphasis on the development of health-care policies and research methodologies to enhance nutrition and human health relationships. Bioactive compounds (BAC) of natural origin, which are secondary metabolites derived from seeds, food, and fermentation-based metabolic products, are currently on researchers focus [1]. Several factors, including food matrix, molecule size, environmental factors, and association with gastrointestinal material, can inhibit BAC bioavailability and absorption in host cell systems and target sites. As a result, the isolation of such natural BAC can result in promising multifunctional extracts that can be used in food applications to aid in health-promoting effects in host cell systems [2].

For instance, the most common plant-based BAC from food are phenolic compounds (PC). Numerous health benefits associated to them have made the interest and demand for phenolic-rich foods, identified as preventive diets, increase. In addition, because of their antioxidant properties and mechanisms such as enzymatic activity modulation, cellular signaling, and gene expression, foods high in phenolic compounds have been linked to the prevention of several chronic diseases [3].

Nevertheless, the same emerging interest has been observed regarding yerba mate (YM) as a food product derived from Ilex paraguariensis A. St. Hil. (mate) whose constituents obtained from its extract, mainly its phenolic fraction, have been linked to numerous health benefits. In Brazil, Paraguay, Uruguay, and Argentina, it is usually consumed as a tea-like beverage [4].

It is estimated that among the countries with the largest consumption of YM, Uruguay has the greatest per capita (8–10 kg/hab/year); Argentina’s consumption is around 6.5 kg/hab/year and in southern Brazil it is ingested 3–5 kg/hab/year [5]. Nowadays, YM products are also consumed in different countries, including Germany, Syria, and the United States for the production of energy drinks and teas.

1 Institute of Food Science and Technology, Federal University of Rio Grande do Sul, Av. Bento Gonçalves, 9500, CEP 91501-970 Porto Alegre, RS, Brazil

✉ Jeverson Frazzon
jeverson.frazzon@ufrgs.br
More recently, the consumption of YM products has been amplified to other countries such as Italy, France, Spain, Japan, Australia, Russia, and Korea since its taste and stimulant properties are very attractive [6]. In addition, the use of mate has already surpassed the tradition of infusion, starting to be used in the manufacture of cosmetics and in the pharmaceutical industry [7].

This plant is a rich source of several bioactive chemicals that apparently have their health effects influenced in a synergistic or complementary manner. Beyond that, it seems clear that the several benefits may not be exclusively related to a specific nutrient, but rather to the interaction between them, the human body and the GM [8]. The interaction between GM and PC has been extensively addressed by a plethora of studies using animal models or in-vitro colonic models. Although the findings reveal that dietary PC increases the number of beneficial bacteria and antimicrobial activity against pathogenic bacteria on GM, the main elements of PC are poorly absorbed by animals, and are mostly present as non-active conjugates when in the bloodstream [9].

Therefore, in order to take advantage of the nutritional effects of BAC, improvements in the absorption rate of these components should be studied, at the same time as potential food sources rich in PC must be known in better details so that we can safely introduce them into our diet. GM modulation through dietary changes has proven to be a key to improvements on PC absorption by animals. Several aspects present in GM modulation, such as eating habits seem to be particularly important in defining its characteristics. Long-term diet may not only have a crucial effect on the human GM but also, slight diet changes may affect the species composition [10]. For instance, diets rich in PC are reported to change the nature of GM, which in turn, may metabolize phenolics into bioactive compounds, improving their regulatory bioavailability [11].

Despite several researches displaying interaction between GM and PC have already been published there are almost no studies on the effect of YM and its PC on the human GM. This is certainly a relevant topic that should be better investigated once YM is a potential source of PC even when compared with most beverages and food products already studied [12].

For this reason, to know better the impact of PC from YM on gut microbiota (GM) and human health, this review has gathered and assessed relevant papers selected from Science Direct, Scopus, Web of Sciences, PubMed, Scielo, and Google Scholar databases resulting in a total of 74 publications were selected, considering the novelty and the impact in the area of this review.

An Overview on Yerba Mate’s Health Benefits

Over the last two decades, clinical trials have explored the use of YM in the prevention and treatment of a variety of health conditions [13]. Figure S1, of the supplementary material, shows the processing flow for YM products and details of the production processes in different countries.

Several authors have linked YM to a wide range of health benefits, including antioxidant capabilities [8, 14], vasodilator functions [15], gene modulation and DNA damage defense [16], hypoglycemic effects [17], anti-obesity and weight loss properties [13, 18], cardioprotective effects [19], cholesterol improvement [20] and thermogenic effects [21].

Heck and Mejia [4] described that YM extracts are especially rich in CGAs (ester formed by quinic acid, QA, and caffeic acid, CA). The hydrolytic products, QA and CA are significant as chemicals of high interest and present great commercial values. For instance, CA has demonstrated antioxidant capacity, with several mechanisms concerning metal ion chelation, inhibitory effects to some specific enzymes involved in free-radical generation and free-radical scavenging [22].

Studies in vitro and in vivo have presented a wide variety of biological activities of mono and di-caffeoylquinic acids, also found on YM extracts. Caffeoylquinic acids derivatives exhibited antioxidant capacity and anti-inflammatory activity [23], apoptosis-mediated cytotoxicity and α-glucosidase inhibitory effects [24], hypoglycaemic properties [25], anti-obesity effects, and lipid metabolism improvement [26]. Table S1, of the supplementary material, presents a compilation of studies suggesting some of YM beneficial health effects.

Different chemical components responsible for YM’s health benefits have already been identified, such as organic acids, minerals, enzymes, vitamins, amino acids, xanthines, saponins, lignin, lutein, cellulose, and especially PC [27]. For instance, methylxanthines, the main stimulant compounds present in YM, have presented several biological properties, including peripheral vasoconstriction, central nervous system and myocardial stimulation, smooth muscle relaxation, neuroprotective, hypoglycemic, anti-inflammatory, diuretic, and cardioprotective effects, among other benefits [28].

Some studies have also linked the effects of YM health benefits regarding its antioxidant capacity and more recent global health outbreak. In general, the antioxidant capacity of food products is already known to be related to free radical neutralization by PC even though, their potential within the human body is still arguable [29]. However, the main antioxidant effect in YM seems to be primarily due to the PC in the extract, delocalizing electrons and forming intra-molecular hydrogen bonds [4, 19].
De Lima et al. [8] investigated the ability of YM to protect rat brain from chemically induced reactive oxygen species (ROS), glutathione balance disturbance, mitochondrial dysfunction, and lipid peroxidation. Glutathione depletion and mitochondrial dysfunction were both prevented by YM, and both benefits were associated to its ability to decrease ROS formation. Their results have also suggested that the preventive properties of YM may be due to a coordinated action amongst the numerous components in the extract, rather than just the phenolic fraction.

Augusti et al. [30] have very recently published a review on the utilization of dietary bioactive substances, such as PC, as a potential supplement to decrease COVID-19 symptoms. The synthesis of PC-derived postbiotics has been hypothesized to boost host’s antioxidant and immune response against SARS-CoV-2 infection, along with GM remodeling.

**Phenolic Compounds in Yerba Mate**

In YM leaves, the PC fraction represents 7–10% of the dry weight. Its main PC fraction is composed by hydroxycinnamates, a family of esters formed mostly by QA and a plethora of distinct hydroxycinnamic acids, such as ferulic acid, p-coumaric acid, and CA accounting for up to 95% of the phenolic content. The remaining 5% of the PC fraction is composed by flavonols [31]. Among flavonoids found in Yerba Mate are rutin, quercetin 3-rhamnoside and 3-glucoside, kaempferol 3-rhamnoside and 3-glucoside, and luteolin diglycoside [5].

CA is considered an important biosynthetic precursor representing the main hydroxycinnamic moiety, forming mono- and dicaffeoylquinic acid isomers and counting over 90% of the total PC, with 5-caffeoylquinic acid being the main hydroxycinnamate in YM [15, 31].

In detailed research, Mateos et al. [32] found 58 PC in YM, such as four isomers of caffeoyl-2,7-anhydro-3-deoxy-2-octulopyranosonic acid, two isomers of tri methoxy cinnamoyl shikimic acid, di- and tri-methoxy cinnamoyl quinic acids and 4-sinapoyl quinic acid. In addition, 2-methylxanthines and 46 PC were also found. Alike the aforementioned ratio, in their study, hydroxycinnamic acid derivatives and flavonols represented 90 and 10% of YM’s PC, respectively. Along with rutin (7.1–7.8%), 5-caffeoylquinic (21.1–22.4%), 4-caffeoylquinic (12.6–14.2%), 3-caffeoylquinic (26.8–28.8%), and 3,5-dicaffeoylquinic acids (9.5–11.3%) were the most abundant phenols, and caffeine was the major methylxanthine (90%) [33].

These phenolic compounds can also be obtained from numerous vegetable sources, although in different compositions and amounts when compared to those found in YM. In particular, Meinhart et al. [12] analyzed the existence of CGAs in 89 plants infusions. They found these compounds in 93% of infusions, however, YM presented the greatest content of CGAs (52.6 mg in 100 mL), being an important source of this nutrient compared to other beverages and food products.

Likewise, according to Duarte and Farah [34], 100 mL of chimarrão has double the quantity of 3,4-dicaffeoylquinic acid, 15 times more 3,5-dicaffeoylquinic acid, and six times more 4,5-dicaffeoylquinic acid than the same volume of coffee. The values of 5-caffeoylquinic acid in 100 mL of chimarrão are on average 100, 60, and 20 times higher than in the same amount of white, green, and black tea, respectively [35]. Similar results were obtained for tererê extract, which presented amounts 300, 100, and 50 times greater than white, green, and black tea infusions, respectively [35].

In addition, YM-based drinks produced 120 times more 5-caffeyolquinic acid than mountain tea and 15 times more than chamomile tea when aqueous extracts of YM and Mediterranean herbs were compared [36]. Infusions commonly consumed in South America, such as those prepared from macela (Achyrocline satureioides) and carqueja (Baccharis trimera) leaves, showed concentrations of dicaffeyolquinic acids isomers 100 times lower than those in chimarrão and tererê extracts [35]. Therefore, chimarrão and tererê are great alternative sources of CGAs.

**Interaction Between PC and the GM**

The human body provides a nutrient-rich environment for intestinal bacteria, and the microbiota, in its turn, performs essential functions not exerted by humans, such as the production of valuable nutrients, modulation of bile acid metabolism, intestinal cell barrier, and immune system regulation. The balance of gut bacteria has been associated with immunological fortification, prevention of autoimmune disorders and immune inflammation, and preservation of the integrity of the intestinal epithelium (which avoids permeation of pathogens and immune-triggering compounds into the blood circulation) [37–39]. Polyphenols might indirectly regulate these functions by modulating the composition and activity of this microbiota [38]. In addition, some polyphenols are involved with the immune system, mainly with immunoglobulin A [40].

It also plays an important role in breaking down original complex PC into phenolic metabolites that are absorbed in the small intestine region [41].

In its turn, the bioavailability and bioactive impact of PC and their metabolites seem to influence GM composition. For instance, dietary PC is able to increase the number of beneficial bacteria and antimicrobial activity against pathogenic...
bacteria, although most researches have been performed in animal models or in-vitro colonic models [42]. In fact, there is also a strong relationship between PC activity modifying GM and, consequently, impacting Bacteroides/Firmicutes balance. Several studies have shown the importance of this ratio since decreased values indicate lower index of insulin resistance, adiposity, and obesity [39]. This ratio changes across the lifetime. It is lower in the first years of life (0.4), rises in adulthood (10.9), and diminished during elderliness (0.6) [43].

Phenolic compounds are poorly absorbed by the stomach and the small intestine, being that the small intestine absorbs from 5 to 10% of the total phenolic intake [38, 39, 44–46]. The low absorption is due to molecular structure complex and polymerization of polyphenols, while free aglycones can be absorbed efficiently [44, 46]. Next, unabsorbed polyphenols are carried to the large intestine, where are metabolized and biotransformed by the gut microbiota [38, 44, 45, 47]. Enzymes from gut microbiota degrade polyphenols into bioactive phenolic metabolites which might regulate the metabolic functions and composition of gut microbiota [38–40, 44]. Polyphenols are metabolized via dihydroxylation, glucosidase, esterase, demethylation, and decarboxylation, resulting in more simple phenolic structures by cleavage, hydrolysis, and reduction reactions [37, 46, 48]. Some of these metabolites produced have higher bioactivity and bioavailability than their precursors, such as simple phenolic acids and lactones [44–46, 49]. This way, the interaction between polyphenols and gut microbiota promotes the production of active phenolic metabolites, which in turn results in the modulation of gut microbiota composition [38, 50]. Phenolic metabolites prompt the swap of the gut microbiota population, usually favoring the growth of beneficial over pathogenic gut microbiota [39, 47]. For this reason, phenolic compounds act as prebiotics [38, 40, 44, 47]. For instance, caffeic and ferulic acids act selectively, reducing the rates of growth of pathogens without disturbing beneficial microorganisms [39, 44]. In addition, caffeic and chlorogenic acids might reduce the firmicutes-bacteroidetes ratio of the gut microbiota [51]. Polyphenols are also related to the prevention of gut dysbiosis, caused by the imbalance of gut microbiota [38, 46]. In addition, gut bacteria produce short-chain fatty acids by fermentation of dietary fibers and resistant starch, which have several health benefits, such as supplying energy to intestinal epithelial cells, reducing inflammation, absorbing minerals, and maintaining the gut immune homeostasis [45, 47].

According to Loo et al. [44], quercetin suppresses the development of Escherichia coli, Staphylococcus aureus, Salmonella typhimurium, and Lactobacillus rhamnosus at minimum inhibitory concentrations (MIC) ranging from 62.5 to 250 g mL$^{-1}$, however, it seems to suppress the growth of Bacteroides gallaecutronics, Enterococcus cacaee, Lactobacillus spp., Ruminococcus gauvreauii, Bifidobacterium cataenulatum, and E. coli at doses ranging from 4 to 50 g mL$^{-1}$.

Other studies have reported MIC of hydroxycinnamic acids (HCA) ranging from 125 to 1,000 µg mL$^{-1}$ to strains of S. aureus, E. coli, S. typhimurium, and L. rhamnosus [44]. HCA on GM has also been reported to increase the lactic acid bacteria growth in the human intestine as a consequence of a high dose of CGAs. At the same time, a positive effect on the adhesion of probiotic bacteria such as L. acidophilus has been proved to be caused by CA presence [39].

As it can be seen, numerous studies have shown that PC modulate the microbial intestinal community through prebiotic or antimicrobial action against pathogenic intestinal bacteria [52].

As a consequence, there has been an increase in the number of studies associating the antioxidant, anti-inflammatory, antiadipogenic, antidiabetic, cardioprotective, neuroprotective, and anticycnicogenic effects of phenolic-rich substances through interaction with GM, in recent years [53]. However, there are almost no published studies on the effect of YM and its PC on the human GM, and this is certainly a relevant topic that should be better investigated. On the other hand, different sources of PC have already been assessed regarding their beneficial impact on human GM.

For instance, Gil-Sánchez et al. [54] researched grape pomace, a wine product rich in fibers and PC, two elements of foods in which bioaccessibility involves the microbiota. In this study, the in vitro colonic digestion of grape pomace extracts was analyzed for the first time. From the release of the main bioaccessible phenolic metabolites of grape pomace extract, various benzoic, phenylacetic, and phenyl propionic acids have been identified. It was observed a significant increase in the amounts of acetic, propionic, and butyric acids posteriorly to enhanced feeding indicating microbial fermentative activity [54]. Moreover, most classes of bacteria increased during chronic feeding, with the highest increases for groups of Lactobacillus and Bacteroids.

Nash et al. [55] published an overview of recent studies in humans concerning the impact of PC from grape and red wine on GM. All studies confirmed the regulation of those ingested PC performed by the intestinal microbiota, through the increase in the number of phenolic metabolites found in blood, urine, ileal fluid, and fecal fluids. According to the authors, the consumption of grape and red wine-derived PC may modulate GM and lead to beneficial microbial ecology improving human health. In addition, GM has demonstrated to modulate grape and red wine PC, suggesting an important two-way relationship [55].
Ramirez-Pérez et al. [56] also demonstrated a two-way interaction where host metabolism may be affected by both microbial modifications of bile acids, either by altering bile acid receptors signals as well as the microbiota composition. It becomes increasingly clear that the GM of individuals may determine the health effects of PC and several other bioactive compounds.

Despite all these demonstrated benefits for the regulation of GM, the observed limitation in animal absorption of key PC elements requires researches aimed at improving the bioaccessibility of bioactive chemicals derived from plant sources [9].

**Approaches to Enhance the Bioavailability of Phenolic Compounds**

Researches in the digestion processes of YM and other plants revealed a modification in the number of bioactive compounds after it passes through the several compartments of the gastrointestinal tract (GIT) due to enzymatic actions, metabolic activity of the GM and pH alterations [57]. Temperature and length of digestion may also influence the final qualitative and quantitative outcome. For instance, only one-third of all CGAs amount is absorbed in the small intestine while two-thirds reach the colon where they may be metabolized by the microbiota [58].

In accordance with this finding, Gómez-Juarristi et al. [59] evaluated the bioavailability of YM's PC in healthy humans. They found that aside from unmetabolized caffeoyl-, feruloyl-, and p-coumaroilquinic acids, more than 34 metabolites with quick onset and clearance in plasma have been discovered, implying small intestine absorption. These chemicals accounted for 13.1% of the metabolites found in urine. In addition to feruloylglycine, delayed absorption of dihydrocaffeic, dihydroferulic, and dihydrocoumaric acids and their phase II metabolites, accounting for 81.0% of excreted metabolites, revealed bacterial origin and intestinal absorption, suggesting that YM's PC are highly metabolized, mainly by the microbiota.

Furthermore, GM not only appears to be responsible for most of the PC metabolism, but it can also be modified through specific interventions in order to favorably affect human metabolism. Notwithstanding, GM must be first maintained so as to exert its main function properly. In this regard, pre- and probiotics may play an important role.

Prebiotics such as inulin, fructooligosaccharides, and galactooligosaccharides have demonstrated to improve intestinal permeability, decrease inflammation, and improve insulin control in vivo [60].

Probiotics as *Lactobacillus* spp. and *Bifidobacterium* spp. are equally beneficial to human health even when used isolated. However, combinations of pre- and probiotics have suggested a better potential in the GM and host health than isolated consumption, since the combination of both components stimulate bacteria growth and survival in the gastrointestinal tract [61].

In addition, isolated nutrients are rarely consumed and for this reason, in recent years, science has been evaluating the ability of dietary and nutritional patterns to adjust GM in pathological conditions. It seems that a long-term adherence to a high-fiber, phenolic compounds-enriched and vegetable-protein-based diet may provide benefits to the GM composition, as well as improvement in obesity and metabolic syndrome symptoms [41].

Diet has been shown to be a primary predictor of GM composition. Different degrees of in vivo scientific evidence support nutrition as a crucial component in GM modulation since certain foods, bioactive chemicals, and dietary patterns may impact health outcomes via their effect on the GM. In this context, it is crucial to understand how specific nutrients, such as PC may act in the modulation of the GM in order to clarify their action and effect in the human body. The discovery that food may have a significant impact on host-microbe interactions suggests that future treatment techniques to change the GM and reduce dysbiosis caused by nutrition-related disorders should be pursued [41].

Nowadays, dietary polyphenols have been used as an emerging therapy in the prevention of several diseases. For instance, the association between gut microbiota and polyphenols was related to the improvement of the signs of depression, mitigation of cognitive dysfunction, improvement in blood flow and vasodilation in cerebrovascular circulation, and acting as a neuronal protector due to diminishing neuroinflammation [62, 63], with immunomodulatory effect [40]. In addition, dietary polyphenols can prevent inflammatory processes, cardiovascular diseases, obesity, cancer, and type 2 diabetes [37, 46]. These properties were also reported for yerba mate, being yerba mate tea is recommended as dietary therapy [5, 33].

It is salient to promote investigations focusing on metagenomic, transcriptomic, and proteomic that help to comprehend the interaction between dietary polyphenols and gut microbiota, for this way, to know the genes and microorganisms that participate in the metabolism of these polyphenols, and thus, elucidate how the dose and polyphenol compounds from yerba mate extract impact on the gut microbiome and the immune system [37].

Aside from the maintenance of GM, the extraction method used to obtain PC elements from plant sources has to be efficient and provide a high quantity of compounds in order to improve PC absorption by human GIT. It is already known that different extraction conditions such as time, temperature, type of solvent, and concentration...
may affect PC composition. Conventional methods for bioactive compounds extraction can be an alternative to increase their bioavailability and include solvent maceration, direct boiling, distillation, compression, etc. [64], although, such processes are time-consuming and can lead to the degradation of thermolabile compounds. Traditional methods such as Soxhlet and maceration present numerous disadvantages, including the employment of large amounts of organic solvents that may be toxic and also harmful to the environment, in addition to their high consumption of energy and time [65].

The stability of bioactive compounds derived from natural sources is a crucial factor for their effective integration into various food systems. In this context, methods such as microwave-assisted extraction emerged as an alternative to reduce the exposure times of bioactive compounds to high temperatures, energy costs, and environmental degradation [65]. Ultrasound-assisted extraction represents another option for the acquisition of bioactive compounds, using acoustic energy to improve the release and diffusion of target compounds from several matrices [66].

Subsequently, as natural antioxidants are significantly sensitive to the environment, in order to have its efficacy improved, they may also be protected from the surrounding medium through several methods. Recent techniques such as encapsulation may be valuable options for this purpose. The encapsulation process packs particles with the assistance of an encapsulating material in order to protect internal compounds and their functionalities. Protective delivery vehicles may also permit targeted release in tissues such as the small intestine, in addition to encasing, protecting, and conveying the desired bioactive molecules into the circulatory system [67].

In particular, in the pharmaceutical and nutritional domains, the use of encapsulated micro and nanoparticles for efficient oral administration of biomolecules has been a growing trend. Modern bioactive carriers, which mainly apply natural dietary macromolecules as functional materials, are meant to increase bioactive component absorption, physicochemical stability, and bioavailability through several routes while not presenting safety or health risks [68]. Successful application of these bioengineered vehicles of food compounds can bring benefits beyond basic nutrition to human health.

Encapsulation may also represent an alternative to transform some of the product’s characteristics, enhancing its appearance or avoiding unpleasant interactions with the carrier food matrix [67]. Phenolics having greater water solubility may be more readily liberated from the food matrix, dissolved in digestive juice, and absorbed by the small intestine mucosa during digestion. Hydrophobic molecules, on the other hand, are more likely to interact with other food components like fibers and lipids, delaying or reducing absorption [69]. Several wall materials can be used for food encapsulation, such as fibers, proteins, and gums. However, depending on the structure and features of each encapsulating agent, the employment of multiple agents may result in varied physical attributes [70].

Several biocompatible and biodegradable polysaccharides have been designed into micro or nanoparticles in an attempt to address the absorption issues of PC. Cyclodextrins, cyclic oligosaccharides presenting a hydrophilic outer surface and a lipophilic inner chamber, are a viable choice. Likewise, chitosan is another type of polysaccharide positively charged often employed for entrapping hydrophilic molecules. Because of interactions with the negatively charged mucus layer, the chitosan-based particles promote absorption by facilitating the passage through the tight junctions [71].

Furthermore, dietary proteins such β-lactoglobulin, β-casein, gelatin, and isolated soy protein are appealing as macronutrients and functional components, making them suitable materials for carriers to efficiently transport nutraceuticals. As can be seen, by the use of electrostatic interactions, proteins and polysaccharides may be designed to produce self-assembled particles [68].

In fact, encapsulated PC compounds have already demonstrated higher bioavailability and stability [72]. According to Berté et al. [73], spray-dried YM extract presented greater amounts of phenolic acids compared to the leaves. Becker et al. [74] assessed the antioxidant capacity and clinical effects of spray-dried YM extract capsules in healthy individuals. The ingestion of the capsules increased the antioxidant biomarkers while decreasing lipid peroxidation both in the short and long term.

**Concluding Remarks**

*Ilex paraguariensis* has been shown to have several health advantages. Although many of these benefits are not yet fully established, multiple studies have shown that the plant has the potential to be a promising functional food product, mostly due to its phenolic component. Because the relationship with the GM is essential for PC metabolism, the final fraction of YM compounds ingested as well as their mode of action in the human body should be better understood.

In this context, authors should exercise caution in light of the abundance of repetitive and misleading information, since multiple poor research can dilute solid works. Inter-individual variation, on the other hand, emerges within rigorous research, such as varied responses to PC utilization depending on the individual. Before precise findings can be drawn, it is necessary to determine the probable interplaying
elements surrounding the PC and GM interaction in human health. Also, because PC bioavailability and effects are frequently contested, it is critical to qualify the various YM products in terms of PC, as well as understand how different extractions and modes of consumption impact the degree of phenolic migration to water as well as absorption by the human body.

Subsequently, as natural antioxidants are significantly sensible, in order to have its efficacy improved, they may also be protected from the surrounding medium through several methods. Recent techniques such as encapsulation could be valuable options for this purpose. Protective or encapsulated delivery vehicles may also permit targeted release in tissues such as the small intestine, in addition to encasing, protecting, and conveying the desired bioactive molecules into the circulatory system [67].

**Abbreviations**

- BAC: Bioactive compounds
- CGAs: ester formed by quinic acid (QA) and caffeic acid (CA)
- DNA: Deoxyribonucleic acid
- GIT: the gastrointestinal tract
- GM: the gut microbiota
- HCA: Hydroxycinnamic acids
- PC: phenolic compounds
- ROS: reactive oxygen species
- YM: Yerba Mate

**Supplementary Information** The online version contains supplementary material available at [https://doi.org/10.1007/s11130-022-01008-8](https://doi.org/10.1007/s11130-022-01008-8).

**Author Contribution** All authors contributed to the study conception and design. The first draft of the manuscript was written by Andreia Candal de Vasconcellos and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

**Funding** The authors would like to thank FAPERGS, CAPES, CNPq – Brazil for the financial support.

**Data Availability** Not applicable.

**Code Availability** Not applicable.

**Declarations**

**Conflict of Interest** The authors have no conflicts of interest to declare that are relevant to the content of this article.

**References**

1. Shetty K, Sarkar D (2019) Introduction: Metabolic-driven ecological rationale to advance biotechnological approaches for functional foods. In: Shetty K, Sarkar D (eds) Functional Foods and Biotechnology, 1st edn. CRC Press, Florida, pp 1–4. [https://doi.org/10.1201/9781003003830](https://doi.org/10.1201/9781003003830)
2. Banwo K, Olojede AO, Adesulu-Dahunse AT, Verma DK, Thakur M, Tripathy S, Singh S, Patel AH, Gupta AK, Aguilier CN, Utama GL (2021) Functional importance of bioactive compounds of foods with potential health benefits: A review on recent trends. Food Bioci 43:101320. [https://doi.org/10.1016/j.fbio.2021.101320](https://doi.org/10.1016/j.fbio.2021.101320)
3. Dragan M, Deval C, Dubray C, Mazur A, Morand C (2011) Hesperidin displays relevant role in the nutrigenomic effect of orange juice on blood leukocytes in human volunteers: a randomized controlled cross-over study. PLoS ONE e26669. [https://doi.org/10.1371/journal.pone.0026669](https://doi.org/10.1371/journal.pone.0026669)
4. Heck CI, Mejia EG (2007) Yerba mate tea (Ilex paraguariensis): A comprehensive review on chemistry, health implications, and technological considerations. J Food Sci 72:138–151. [https://doi.org/10.1111/j.1750-3841.2007.00535.x](https://doi.org/10.1111/j.1750-3841.2007.00535.x)
5. Gawron-Gzella A, Chana-J-Kaczmarek J, Cielecka-Piontek J (2021) Yerba Mate - A long but current history. Nutrients 13:3706. [https://doi.org/10.3390/nu13113706](https://doi.org/10.3390/nu13113706)
6. Meinhart AD, Bizzotto CS, Ballus CA, Rybka ACP, Sobrinho MR, Cerro-Quintana RS, Teixeira-Filho J, Godoy HT (2010) Methylxanthines and phenolics content extracted during the consumption of mate (Ilex paraguariensis St. Hili) beverages. J Agric Food Chem 58:2188–2193. [https://doi.org/10.1021/jf903781w](https://doi.org/10.1021/jf903781w)
7. Reichert CL, Friedrich JC, Cassol GH, Pessin CF, Mitsui ML, Donaduzzi CM, Cardozo-Junior EL (2013) Chemical stability and dissolution study of mate (Ilex paraguariensis St. Hili) extract and some formulations. Int J Pharm Sci Technol 8:33–49.
8. de Lima ME, Colpo AC, Maya-López M, Rosa H, Túnez I, Galván-Arzate S, Santamaría A, Felmer V (2017) Protective effect of Yerba Mate (Ilex paraguariensis St. Hili,) against oxidative damage in vitro in rat brain synaptosomal/mitochondrial P2 fractions. J Funct Foods 34:447–452. [https://doi.org/10.1016/j.jff.2017.05.026](https://doi.org/10.1016/j.jff.2017.05.026)
9. Clifford MN, Hoyt JJ, Crozier A (2013) Human studies on the absorption, distribution, metabolism, and excretion of tea polyphenols. Am J Clin Nutr 98:1619S–1630S. [https://doi.org/10.3945/ajcn.113.058958](https://doi.org/10.3945/ajcn.113.058958)
10. Wu GD, Chen J, Hoffmann C et al (2011) Linking long-term dietary patterns with gut microbial enterotypes. Science 334:105–108. [https://www.science.org/doi/10.1126/science.1208344](https://www.science.org/doi/10.1126/science.1208344)
11. Anhê FF, Choi BSY, Dyck JRB, Marette A (2019) Host-microbe interplay in the cardiometabolic benefits of dietary polyphenols. Trends Endocrinol Metab 30:384–395. [https://doi.org/10.1016/j.tem.2019.04.002](https://doi.org/10.1016/j.tem.2019.04.002)
12. Meinhart AD, Caldeirão L, Damin FM, Teixeira-Filho J, Godoy HT (2018) Analysis of chlorogenic acids isomers and caffeic acid in 89 herbal infusions (tea). J Food Compos Anal 73:76–82. [https://dx.doi.org/10.1016/j.jfca.2018.08.001](https://dx.doi.org/10.1016/j.jfca.2018.08.001)
13. Kim SY, Oh MR, Kim MG, Chae HJ, Chae SW (2015) Anti-obesity effects of Yerba Mate (Ilex Paraguariensis): a randomized, double-blind, placebo-controlled clinical trial. BMC Complement Altern Med 15:338. [https://doi.org/10.1186/s12906-015-0859-1](https://doi.org/10.1186/s12906-015-0859-1)
14. Colpo A, Rosa H, Lima ME, Pazzini CEF, de Camargo VB, Basante FE, Felmer V (2016) Yerba mate (Ilex paraguariensis St. Hili) based beverages: How successive extraction influences the extract composition and its capacity to chelate iron and scavenge free radicals. Food Chem 209:185–195. [https://doi.org/10.1016/j.foodchem.2016.04.059](https://doi.org/10.1016/j.foodchem.2016.04.059)
15. Yu SI, Yue SW, Liu Z, Zhang T, Xiang N, Fu H (2015) Yerba mate (Ilex paraguariensis) improves microcirculation of volunteers with high blood viscosity: a randomized, double-blind, placebo-controlled trial. Exp Gerontol 62:14–22. [https://doi.org/10.1016/j.exger.2014.12.016](https://doi.org/10.1016/j.exger.2014.12.016)
16. Fernandes ES, Machado MO, Becker AM, Andrade F, Maraschin M, Silva EL (2012) Yerba mate (Ilex paraguariensis) enhances the gene modulation and activity of paraoxonase-2: In vitro and in vivo studies. Nutr 28:1157–1164. https://doi.org/10.1016/j.nut.2012.04.011

17. Ribeiro MC, Santos Á, Riachi LG, Rodrigues ACB, Coelho GC, Marcellini PS, de Maria CAB (2017) The effects of roasted yerba mate (Ilex paraguariensis A. St. Hil.) consumption on glycemia and total serum creatine phosphokinase in patients with traumatic brain injury. J Funct Food 28:240–245. https://doi.org/10.1016/j.jff.2016.11.024

18. Arçari DP, Bartchewsky W, Dos Santos TW, Oliveira KA, Funck A, Pedrazzoli J, De Souza MF, Saad MJ, Bastos DH, Gambero A, Carvalho PO, Ribeiro ML (2009) Antiobesity effects of yerba mate extract (Ilex paraguariensis) in high-fat diet-induced obese mice. Obesity 12:2127–2133. https://doi.org/10.1038/oby.2009.158

19. Schinella G, Fantinelli JC, Mosca SM (2005) Cardioprotective effects of Ilex paraguariensis extract: evidence for a nitric oxide-dependent mechanism. Clin Nutr 24:360–366. https://doi.org/10.1016/j.clnu.2004.11.013

20. Arçari DP, Porto VB, Rodrigues ERV, Martins F, Lima RJ, Sawaya ACHF, Carvalho PO (2011) Effect of mate tea (Ilex paraguariensis) supplementation on oxidative stress biomarkers and LDL oxidisability in normo and hyperlipidaemic humans. J Funct Food 3:190–197. https://doi.org/10.1016/j.jff.2011.04.001

21. Martineti A, Hostettmann K, Schutz Y (1999) Thermogenic effects of commercially available plant preparations aimed at treating human obesity. Phytother 6:231–238. https://doi.org/10.1007/S0944-7113(99)80014-2

22. Chen JH, Ho CT (1997) Antioxidant activities of caffeic acid and its related hydroxycinnamic acid compounds. J Agric Food Chem 45:2374–2378. https://doi.org/10.1021jf970055t

23. Ooi KL, Muhammad TST, Tan ML, Sulaiman SF (2011) Cytotoxic, apoptotic and anti-α-glucosidase activities of 3,4-di-O-caffeoyl quinic acid, an antioxidant isolated from the polyphenolic-rich extract of Elephantopus mollis Kunth. J Ethnopharmacol 135:685–695. https://doi.org/10.1016/j.jep.2011.04.001

24. Ong KW, Hsu A, Song L, Huang D, Tan BKH (2011) Polyphe-

25. Chen JH, Ho CT (1997) Antioxidant activities of caffeic acid and its related hydroxycinnamic acid compounds. J Agric Food Chem 45:2374–2378. https://doi.org/10.1021jf970055t

26. Cho AS, Jeon SM, Kim MJ, Yeo J, Seo KI, Choi MS, Lee MK (2010) Chlorogenic acid exhibits anti-obesity property and improves lipid metabolism in high-fat diet-induced obese mice. Food Chem Toxicol 48:937–943. https://doi.org/10.1016/j.fct.2010.01.003

27. Filip R, Sebastian T, Ferraro G, Anesini C (2007) Effect of yerba mate extracts and isolated compounds on peroxidase secretion of rat submandibular glands. Food Chem Toxicol 45:649–655. https://doi.org/10.1016/j.fct.2006.10.014

28. Bastos DHM, Fornari AC, Queiroz YS, Torres EAFS (2006) Bioactive compounds content of Chimarrão infusions related to the moisture of yerba maté (Ilex paraguariensis). J Agric Food Chem 54:8394–8403. https://doi.org/10.1021/jf051748s

29. Pettit S, Scully C (2009) Polyphenols, oral health and disease: A review. J Dent 37:413–423. https://doi.org/10.1016/j.jdent.2009.02.003

30. Augusti PR, Conterato GMM, Denardin CC, Prazeres ID, Serra AT, Bronze MR, Emanuelli T (2021) Bioactivity, bioavailability, and gut microbiota transformations of dietary phenolic compounds: implications for covid-19. J Nutr Biochem 97:108778. https://doi.org/10.1016/j.jnutbio.2021.108778

31. Piovezan-Borges ACP, Valério-Júnior C, Gonçalves IL, Mielniczki-Pereira AA, Valduga AT (2016) Antioxidant potential of yerba mate (Ilex paraguariensis St. Hil.) extracts in Saccharomyces cerevisiae deficient in oxidant defense genes. Braz J Biol 76:539–544. https://doi.org/10.1590/1519-6984.01115

32. Mateos R, Baeza G, Sarriá B, Bravo L (2018) Improved LC-MSn characterization of hydroxycinnamic acid derivatives and flavonols in different commercial mate (Ilex paraguariensis) brands. Quantification of polyphenols, methylxanthines, and antioxidant activity. Food Chem 241:232–241. https://doi.org/10.1016/j.foodchem.2017.08.085

33. Rzasa-Duran E, Kryczyn-Poprawa A, Drabicki D, Podkowa A, Sułkowska-Ziaja K, Szewczyk A, Kala K, Opoka W, Zieba P, Fidurski M, Muszynska B (2022) Yerba Mate as a source of elements and bioactive compounds with antioxidant activity. Antioxidants 11:371. https://doi.org/10.3390/antiox11102371

34. Duarte GS, Farah A (2011) Effect of simultaneous consumption of milk and coffee on chlorogenic acids’ bioavailability in humans. J Agric Food Chem 59:7925–7931. https://doi.org/10.1021/jf201906p

35. Marques V, Farah A (2009) Chlorogenic acids and related compounds in medicinal plants and infusions. Food Chem 113:1370–1376. https://doi.org/10.1016/j.foodchem.2008.08.086

36. Kogiannou DAA, Kalogeropoulos N, Kefalas P, Polissiou MG, Kalior AC (2013) Herbal infusions, their phenolic profile, antioxidant and anti-inflammatory effects in HT29 and PC3 cells. Food Chem Toxicol 61:152–159. https://doi.org/10.1016/j.fct.2013.05.027

37. Catalayka G, Venema K, Lucini L, Rocchetti G, Delmas D, Daglia M, De Filippis A, Xiao H, Quiles JL, Xiao J, Capanoglu E (2020) Interaction of dietary polyphenols and gut microbiota: Microbial metabolism of polyphenols, influence on the gut microbiota, and implications on host health. Food Front 1:109–133. https://doi.org/10.1002/fl2.25

38. Kasprzak-Drozd K, Oniszczuk T, Stasiak M, Oniszczuk A (2021) Beneficial effects of phenolic compounds on gut microbiota and metabolic syndrome. Int J Mol Sci 22:3715. https://doi.org/10.3390/ijms22073715

39. Leonard W, Zhang P, Ying D, Fang Z (2021) Hydroxycinnamic acids on gut microbiota and health. Compr Rev Food Sci Food Saf 20:710–737. https://doi.org/10.1111/1541-4337.12663

40. Mas AL, Brigante FI, Salvadori E, Ribotta P, Martinez ML, Wunderlin DA, Baroni MV (2022) Novel cookie formulation with defatted sesame flour: evaluation of its technological and sensory properties. Changes in phenolic profile, antioxidant activity, and gut microbiota after simulated gastrointestinal digestion. Food Chem doi. https://doi.org/10.1016/j.foodchem.2022.133122

41. Sánchez-Tapia M, Tovar AR, Torres N (2019) Diet as regulator of gut microbiota and its role in health and disease. Arch Med Res 50:259–268. https://doi.org/10.1016/j.arcmed.2019.09.004

42. Jamar G, Estadella D, Pisani LP (2017) Contribution of anthocyanin-rich foods in obesity control through gut microbiota interactions. BioFactors 43:507–516. https://doi.org/10.1002/biof.1365

43. Duda-Chodak A, Tarko T, Satora P, Sroka P (2015) Interaction of dietary compounds, especially polyphenols, with the intestinal microbiota: A Review. Eur J Nutr 54:325–341. https://doi.org/10.1007/s00394-015-0852-y

44. Loo TY, Howell K, Chan M, Zhang P, Ng K (2020) Modulation of the human gut microbiota by phenolics and phenolic fiber-rich foods. Compr Rev Food Sci Food Saf 19:1268–1298. https://doi.org/10.1111/1541-4337.12563

45. Lee SY, Lee DY, Kang JH, Jeong WJ, Kim HW, Oh DH, Yoon SH, Hur SJ (2022) Relationship between gut microbiota and colorectal cancer: Probiotics as a potential strategy for...
60. Cani PD, Possemiers S, Van de Wiele T et al (2009) Changes in gut microbiota in obesity and type 2 diabetes. Nat Rev Gastroenterol Hepatol 6:117–125. https://doi.org/10.1038/nrgastro.2008.197
61. Gordon JI (2012) Honor thy gut symbionts redux. Science 336:1251–1253. https://doi.org/10.1126/science.1224686
62. Frolinger T, Sims S, Smith C, Wang J, Cheng H, Faith J, Ho L, Hao K, Pasinetti GM (2019) The gut microbiota composition affects dietary polyphenols mediated cognitive resilience in mice by modulating the bioavailability of phenolic acids. Sci Rep 9:3546. https://doi.org/10.1038/s41598-019-39994-6
63. Filosa S, Di Meo F, Crispi S (2018) Polyphenols-gut microbiota interplay and brain neuromodulation. Neural Regen Res 13:2055–2059. https://doi.org/10.4103/1673-5374.241429
64. Chemat F, Rombaut N, Sicaire AG, Meulemiestre A, Fabiano-Tixier AS, Abert-Vian M (2017) Ultrasound assisted extraction of food and natural products. Mechanisms, techniques, combinations, protocols and applications. Rev Ultrason Sonochem 34:540–560. https://doi.org/10.1016/j.ultrasonch.2016.06.035
65. Mandal V, Mohan Y, Hemalatha S (2007) Microwave assisted extraction - An innovative and promising extraction tool for medicinal plant research. Pharmacogn Rev 1:7–18
66. Laborde JL, Bouyer C, Caltagirone JP, Gérard A (1998) Acoustic cavitation field prediction at low and high frequency ultrasound. Ultrasoundics 36:581–587. https://doi.org/10.1016/S0041-624X(97)00176-6
67. Khan SS, Oliveira JC, Crean AM (2010) Microencapsulation as a tool for incorporating bioactive ingredients into food. Crit Rev Food Sci Technol 50:1913–1918. https://doi.org/10.1080/0012230703044222
68. Hu B, Liu X, Zhang C, Zeng X (2017) Food macromolecule based nanodelivery systems for enhancing the bioavailability of polyphenols. J Food Drug Anal 25:3–15. https://doi.org/10.1016/j.jfda.2016.11.004
69. Zhao D, Simon JE, Wu Q (2020) A critical review on grape polyphenols for neuroprotection: Strategies to enhance bioefficacy. Crit Rev Food Sci Nutr 60:597–625. https://doi.org/10.1080/0012230703044222
70. Chen KN, Chen MJ, Liu JR, Lin CW, Chiu HY (2005) Optimization of incorporated prebiotics as coating materials for probiotic microencapsulation. J Food Sci 70:M260–M266. https://doi.org/10.1111/j.1365-2621.2005.tb09981.x
71. Peptu CA, Ochiuz L, Alupea L, Peptu C, Popa M (2014) Carbohydrate based nanoparticles for drug delivery across biological barriers. J Biomed Nanotechnol 10:2107–2148. https://doi.org/10.1166/jbn.2014.1950
72. Fang Z, Bhandari B (2011) Effect of spray drying and storage on the stability of bayberry polyphenols. Food Chem 129:1139–1147. https://doi.org/10.1016/j.foodchem.2011.05.093
73. Berti KAS, Beux MR, Spada PK, Salvador M, Hoffmann-Ribiari R (2011) Chemical composition and antioxidant activity of yerba-mate (Ilex paraguariensis A.St.-Hil., Aquifoliaceae) extract as obtained by spray drying. J Agric Food Chem 59:5523–5527. https://doi.org/10.1021/jf2008343
74. Becker AL, Cunha HP, Lindenberg AC, de Andrade F, de Carvalho T, Boaventura BCB, da Silva EL (2019) Spray-Dried yerba mate extract capsules: Clinical evaluation and antioxidant activity. Food Res Int 156:111327. https://doi.org/10.1016/j.foodres.2019.111327
75. Cani PD, Possemiers S, Van de Wiele T et al (2009) Changes in gut microbiota control inflammation in obese mice through a mechanism involving GLP-2-driven improvement of gut permeability. Gut 58:1091–1103. https://doi.org/10.1136/gut.2008.165886