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Yerba Mate and Coffee as sources of bioactive compounds supporting oral health and cancer prevention – A review of protective mechanisms

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Abstract

Introduction: Yerba mate (Ilex paraguariensis) and coffee (Coffea spp.) are beverages rich in bioactive compounds such as polyphenols, caffeine, and chlorogenic acid, which exhibit antioxidant, anti-inflammatory, and anticancer properties. Their regular consumption may positively influence oral health by modulating the oral microbiome, reducing oxidative stress, and supporting tissue regeneration. Studies indicate that yerba mate may inhibit the proliferation of cancer cells, while coffee, due to its antioxidant content, enhances protective mechanisms against oral cancers. This paper analyzes the beneficial effects of these beverages on oral health and their potential role in cancer prevention.

Material and Methods: To examine the protective effects of yerba mate and coffee on oral health and cancer prevention, studies on the bioactive compounds present in these beverages, their impact on the oral microbiome and inflammatory processes, as well as their role in modulating oxidative stress and supporting tissue regeneration, were considered.

Description of the state of knowledge: Yerba mate and coffee are rich sources of bioactive compounds that may positively influence oral health and reduce the risk of cancer. The

polyphenols, alkaloids, and phenolic acids contained in these beverages exhibit antioxidant, anti-inflammatory, and antiproliferative properties, which may be relevant in the prevention of neoplastic diseases. Phenolic compounds present in yerba mate and coffee can modulate the oral microbiota by limiting the growth of pathogenic bacteria such as *Porphyromonas gingivalis* and *Streptococcus mutans*, which are associated with periodontal disease and dental caries. Moreover, their anti-inflammatory and antioxidant effects may support mucosal regeneration and accelerate wound healing in the oral cavity.Studies suggest that yerba mate may inhibit cancer cell proliferation by modulating signaling pathways such as PI3K/Akt and NF-κB, which are involved in tumor development. Coffee, due to its high content of chlorogenic acid and other polyphenols, may reduce oxidative stress and exert a protective effect on the epithelial cells of the oral mucosa. While both beverages demonstrate protective effects, their combined consumption may enhance health-promoting outcomes, for example, by strengthening antioxidant mechanisms and regulating immune responses. However, further research is needed to determine the optimal dosage and frequency of consumption in the context of oral health and cancer prevention.

Conclusions: Yerba mate and coffee may support oral health and cancer prevention due to the presence of bioactive compounds with antioxidant, anti-inflammatory, and antiproliferative properties. Polyphenols, caffeine, and theobromine influence cellular metabolism, promote mucosal regeneration, and inhibit the growth of cariogenic bacteria. Additionally, the modulation of signaling pathways may limit cancer cell proliferation and support apoptosis. Both beverages also contribute to enamel protection by reducing demineralization. Despite their potential benefits, further research is needed to determine the optimal mode of consumption and the long-term effects of regular intake.

Key words: Yerba mate,Coffee,Oral health,Antioxidants,Polyphenols,Cancer prevention,Microbiome modulation,Anti-inflammatory effects,Oxidative stress,Bioactive compounds

Introduction

Yerba mate (Ilex paraguariensis) and coffee (Coffea spp.) are among the most widely consumed beverages globally, valued not only for their sensory properties but also for their potential health-promoting effects. They contain numerous bioactive compounds such as polyphenols, caffeine, phenolic acids, and flavonoids, which exhibit antioxidant, anti-inflammatory, and anticancer properties [1–3]. In recent years, there has been growing interest in their impact on oral health, including effects on the microbiome, mucosal inflammation, and cancer prevention [4,5]. Yerba mate is rich in various bioactive substances, including chlorogenic acid, theobromine, rutin, and quercetin, which exert protective effects on the human body [1,6]. Similarly, coffee contains potent antioxidants, such as chlorogenic acid and caffeine, which may protect cells from oxidative stress and support regenerative processes [4,7]. Regular consumption of these beverages has been associated with beneficial effects on metabolism, the cardiovascular system, and immune defense mechanisms, which may also be relevant in the context of oral health [1,8].Compounds found in yerba mate and coffee may influence the oral microbiota by inhibiting the growth of pathogenic bacteria such as *Streptococcus mutans* and *Porphyromonas gingivalis*, which are key contributors to dental caries and periodontal disease [1,4]. Furthermore, the anti-inflammatory and antioxidant properties of these beverages may support mucosal healing and limit degenerative processes in oral tissues [9].Coffee and yerba mate may also affect the acid-base balance in the oral cavity. Some studies have shown that polyphenols present in these beverages may support enamel remineralization, counteracting demineralization and reducing the risk of dental erosion [3,7]. Additionally, the presence of caffeine may modulate immune responses and reduce gingival inflammation, which is particularly important in the prevention of periodontal diseases [10,11]. One of the key research areas is the potential role of yerba mate and coffee in oral cancer prevention. Oxidative stress and chronic inflammation play significant roles in carcinogenesis, and the bioactive compounds in these beverages may reduce these risk factors [9,12]. Polyphenols such as chlorogenic acid and quercetin have demonstrated the ability to inhibit cancer cell proliferation and induce apoptosis by modulating signaling pathways such as PI3K/Akt and NF-κB [4,6,13]. Epidemiological studies suggest that moderate coffee consumption may lower the risk of developing certain oral cancers due to its anti-inflammatory and antioxidant properties [12]. Similar effects may be observed with yerba

mate; however, some studies emphasize that consuming this beverage at high temperatures may increase the risk of mucosal damage, which could be a contributing factor in cancer development [14].The aim of this review is to analyze the beneficial effects of yerba mate and coffee on oral health and their role in cancer prevention. In particular, the impact of these beverages on the oral microbiome, inflammatory and carious processes, enamel protection, and molecular anticancer mechanisms will be discussed. A review of current research will allow for an assessment of the extent to which yerba mate and coffee may support oral health and whether their consumption could be considered a component of cancer prevention strategies.

Material and methods

A literature review was conducted based on scientific articles from the PubMed and ResearchGate databases, published between 2014 and 2025. The analysis included clinical studies and systematic reviews on the role of Yerba mate (*Ilex paraguariensis*) and coffee(*Coffea spp.*) in Oral Health and Cancer Prevention. The literature search was performed using specific keywords, such as *Yerba mate,Coffee,Oral health,Antioxidants,Polyphenols,Cancer prevention,Microbiome modulation,Anti-inflammatory effects,Oxidative stress,Bioactive compounds*

Description of the state of knowledge

Yerba mate (*Ilex paraguariensis*) and coffee (*Coffea* spp.) are rich sources of bioactive compounds that exhibit a wide range of health-promoting properties. Their effects include antioxidant, anti-inflammatory, antiproliferative, and protective actions on the oral epithelial cells [1]. Pharmacological analyses indicate that yerba mate contains at least 16 key bioactive constituents that interact with 229 biological targets, and its potential applications cover more than 300 different diseases, including cancers, diabetes, atherosclerosis, and neurodegenerative disorders [4]. Coffee, rich in chlorogenic acid, caffeine, and other polyphenols, demonstrates similar effects by supporting cellular protection against oxidative stress and modulating inflammatory responses [3,7]. Both beverages influence critical metabolic pathways, such as PI3K/Akt, NF-κB, and MAPK, which are implicated in the development of cancer and inflammatory diseases [4]. Their synergistic action may further enhance the body's

defense mechanisms, particularly in the context of oral health and cancer prevention [7].

Bioactive Compounds in Yerba Mate and Coffee

Yerba mate (*Ilex paraguariensis*) and coffee (*Coffea* spp.) are rich sources of bioactive compounds that exhibit numerous health-promoting properties, including antioxidant, anti-inflammatory, antibacterial, and potentially anticancer effects. The most important groups of bioactive compounds found in these beverages include polyphenols, alkaloids, terpenoids, and other constituents with documented effects on cellular metabolism and oral health [3,4,15]. Polyphenols such as chlorogenic acid, quercetin, rutin, and catechins play a key role in neutralizing free radicals and inhibiting inflammatory processes, thereby contributing to the protection of periodontal tissues and the oral mucosa from oxidative damage and degradation caused by chronic inflammation [1,16]. Chlorogenic acid, which is abundant in both coffee and yerba mate, exhibits strong antioxidant activity, reducing oxidative stress in cells and protecting DNA, proteins, and lipids from damage [4,17] . Furthermore, chlorogenic acid has been shown to inhibit the growth of cariogenic bacteria such as *Streptococcus mutans* and periodontal pathogens like *Porphyromonas gingivalis*, suggesting its potential role in the prevention of oral diseases [1]. Quercetin, one of the main flavonoids present in yerba mate, has the ability to inhibit the activity of pro-inflammatory cytokines, including interleukin-6 and tumor necrosis factor alpha (TNF-α), which may help reduce inflammation in the oral cavity and support the regeneration of damaged tissues [4,18]. Rutin, also found in yerba mate, strengthens blood vessels and improves microcirculation, which may aid in wound healing and the regeneration of the oral mucosa following dental procedures [1,19]. Catechins, particularly abundant in yerba mate, exhibit strong antibacterial activity and may inhibit the growth of bacteria responsible for periodontal disease, as well as limit degradation processes that weaken the tooth-supporting structures [4,20]. In addition to polyphenols, alkaloids such as caffeine and theobromine play a significant role in the biological effects of yerba mate and coffee. Caffeine is a potent metabolic stimulant, but its effects extend beyond stimulation of the nervous system, as it also exhibits anti-inflammatory and antibacterial properties [21]. Studies suggest that caffeine may reduce the activity of proteolytic enzymes responsible for the degradation of periodontal tissues, which could be important in the prevention of gum diseases [22]. Moreover, caffeine has been shown to influence the expression of inflammatory markers in oral epithelial cells by reducing the production of pro-inflammatory mediators and

modulating the immune response [23].Theobromine, another key alkaloid, in addition to its stimulant properties, has the ability to strengthen enamel by increasing the bioavailability of calcium and phosphate [24]. Clinical studies suggest that theobromine may effectively reduce the risk of enamel demineralization and support its remineralization, making it a potential alternative to fluoride in the prevention of dental caries [24,25]. Another important group of bioactive compounds includes terpenoids, such as ursolic acid and oleanolic acid, which are present in yerba mate and demonstrate potent anti-inflammatory and cytoprotective properties [26]. Ursolic acid has the capacity to inhibit the proliferation of cancer cells and induce apoptosis, which may be relevant for oral cancer prevention [26,27]. Oleanolic acid supports tissue regeneration and reduces mucosal damage caused by chronic inflammation, indicating its potential use in the treatment of periodontal disease and precancerous conditions [26]. In addition to these key compounds, both yerba mate and coffee provide essential micronutrients such as calcium, magnesium, zinc, and vitamin C, all of which play a role in maintaining the health of teeth and oral mucosa [28]. Calcium and phosphorus are necessary for proper enamel and bone mineralization, while zinc possesses antibacterial properties and may enhance the mucosal barrier's resistance to infection [29].

Antioxidant and Anti-Inflammatory Activity, and Support for Periodontal Health and Wound Healing

Oxidative stress and chronic inflammation play a key role in the pathogenesis of various oral diseases, including periodontal disease and oral cancers. The bioactive compounds found in yerba mate and coffee exhibit the ability to neutralize free radicals and inhibit the activity of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) [5]. The polyphenols present in these beverages may also inhibit the activity of enzymes involved in extracellular matrix degradation, thereby contributing to the protection of periodontal tissues and the oral mucosa [5]. Regular consumption of these drinks may enhance the immune system, which is particularly relevant in the context of protecting the oral cavity against bacterial and viral infections [30]. Moreover, certain constituents of yerba mate and coffee have been shown to modulate immune responses, potentially limiting chronic inflammation and supporting tissue healing processes [30,31].In the context of oral health, the antioxidant and anti-inflammatory effects of these beverages may contribute to gum protection, reduction of periodontal disease risk, and support for mucosal regeneration following injuries or dental procedures [31]. Periodontal health and effective oral wound

healing depend on the balance between inflammatory processes, fibroblast activity, and the delivery of nutrients to regenerating tissues [5,30,32]. Within these processes, the bioactive components of infusions may play an important role by supporting both reparative and protective mechanisms. Studies suggest that caffeine and flavonoids can stimulate fibroblast proliferation and enhance collagen production, which are crucial for tissue healing in the oral cavity following trauma or surgical interventions [33]. Additionally, these compounds may improve microcirculation, facilitating the transport of oxygen and nutrients to sites undergoing regeneration [8,30]. For maintaining periodontal health, the impact of yerba mate and coffee on extracellular matrix metabolism is also significant. Certain compounds in these beverages have been shown to regulate the activity of matrix metalloproteinases (MMPs), which are involved in tissue remodeling and may contribute to the progression of periodontal diseases when excessively active [34]. Inhibiting destructive enzymes may help preserve periodontal integrity and limit bone tissue degradation [30]. Furthermore, some compounds found in yerba mate may exhibit pro-angiogenic properties, promoting the formation of new blood vessels in damaged areas, thereby supporting efficient wound healing [32].

Potential Role in the Inhibition of Cancerous Processes

Contemporary research suggests that the health-promoting properties of *yerba mate* and coffee stem from their ability to modulate numerous biological processes at the molecular level. Network pharmacology analyses have demonstrated that the bioactive compounds in these beverages interact with multiple biological targets, including both regulators of oxidative stress and key signaling proteins involved in carcinogenesis [1]. Oxidative stress is a major contributor to the malignant transformation of oral epithelial cells, and polyphenols such as chlorogenic acid, quercetin, and catechins effectively neutralize reactive oxygen species (ROS), protecting cellular structures from oxidative damage [35]. Moreover, flavonoids present in *Ilex paraguariensis* infusions, including rutin and kaempferol, may enhance the activity of antioxidant enzymes such as superoxide dismutase and catalase, thereby strengthening cellular defense against oxidative stress [19,36]. *Yerba mate* also modulates the activity of signaling proteins related to tumorigenesis, such as AKT1, STAT3, and MAPK1, which are crucial regulators of cell survival and inflammatory responses [4,37]. Furthermore, its compounds exhibit affinity for TP53 and TNF, indicating a potential impact on apoptotic mechanisms and immunomodulation [4,38]. Coffee, due to its content of chlorogenic acid and other polyphenols, may enhance protection against oxidative damage by

regulating transcription factors such as NF-κB and AP-1 [4]. Abnormal proliferation of cancer cells represents another critical process in tumor development, and chlorogenic acid may inhibit the activity of the NF-κB transcription factor, which promotes cancer cell growth and shields them from apoptosis [30]. Quercetin and kaempferol inhibit the PI3K/Akt signaling pathway, which controls cell cycle progression and cancer cell proliferation, while theobromine present in *yerba mate* has demonstrated the ability to reduce the proliferation rate of cancer cells, potentially slowing the progression of oral cancer [24,25,39].Apoptosis, or programmed cell death, is a key defensive mechanism against cancer, and polyphenols found in both beverages may restore cancer cell sensitivity to apoptosis by activating pro-apoptotic proteins such as Bax and inhibiting anti-apoptotic proteins like Bcl-2 [39]. Ursolic and oleanolic acids may activate caspases—key enzymes in the apoptotic process of cancer cells —while catechins modulate the p53 pathway, which is frequently deactivated in oral cancers [26,27]. Inhibition of angiogenesis and metastasis represents another crucial aspect of the anticancer activity. Chlorogenic acid, present in both coffee and *yerba mate*, may suppress the expression of vascular endothelial growth factor (VEGF), thereby limiting neovascularization and oxygen supply to tumors [38]. Kaempferol and quercetin have been shown to inhibit matrix metalloproteinase (MMP) activity, enzymes responsible for extracellular matrix degradation that facilitate cancer cell invasion into adjacent tissues [4,40]. Flavonoids in *Ilex paraguariensis* may also reduce the expression of integrins—proteins responsible for cancer cell adhesion to new tissues—which is a critical step in the metastatic process [4]. Dysbiosis of the oral microbiome can contribute to cancer development by promoting chronic inflammation and producing toxins that facilitate malignant transformation. Catechins and caffeine exhibit antibacterial properties, reducing populations of pathogens such as *Porphyromonas gingivalis* and *Fusobacterium nucleatum*, which are associated with an increased risk of oral cancer [4,41,42]. Polyphenols in *yerba mate* may also inhibit the growth of bacteria that produce DNA-damaging toxins in oral epithelial cells, thus lowering the risk of cancer-related mutations.The protective effects of these beverages may therefore derive from their impact on cancer cell metabolism, as well as their ability to regulate inflammation and the oral microbiome [17,43,44]. Their bioactive components may support oral cancer prevention by reducing oxidative stress, inhibiting cancer cell proliferation, inducing apoptosis, and modulating angiogenesis and metastasis [4,5,35,45]. In addition, their capacity to modulate the oral microbiota, combined with anti-inflammatory properties, further enhances their chemopreventive potential [42].

Protection Against Caries and Erosive Lesions

Yerba mate and coffee may contribute to the reduction of carious and erosive processes through mechanisms involving their bioactive compounds, which modulate the oral microbiota and support remineralization processes [41,44]. Phenolic compounds present in these beverages have demonstrated the ability to inhibit bacterial enzyme activity that promotes enamel demineralization, thereby potentially contributing to enamel protection [17,43,44]. Additionally, alkaloids such as caffeine and theobromine may influence the metabolism of cariogenic bacteria by reducing their adhesion to tooth surfaces, thus limiting the formation of bacterial biofilm [4,24,25,46]. The anti-inflammatory and antioxidant properties of these beverages are also of significance, as they may support the regenerative processes of periodontal tissues and neutralize free radicals involved in enamel damage [7]. However, it is important to note that their impact on oral health depends on various factors, including the mode of consumption, frequency, and the temperature of the beverage [5]. Some studies suggest that these beverages may support enamel remineralization under specific conditions; however, their acidic pH—particularly in the case of coffee—may, in some instances, contribute to erosion [2,15]. Therefore, understanding the balance between the beneficial effects of bioactive compounds and the potential side effects associated with long-term consumption of these beverages is crucial [41].

Synergistic Effects of Yerba Mate and Coffee

Although yerba mate and coffee differ in their chemical composition and origin, they share numerous health-promoting properties that may complement each other, enhancing their overall beneficial impact on the body. Their bioactive components—such as polyphenols (chlorogenic acid, rutin, quercetin), alkaloids (caffeine, theobromine), terpenoids (ursolic acid, oleanolic acid), and other antioxidant and anti-inflammatory compounds—may act synergistically to support oral health and exert anticancer effects [4,24,25]. One of the main mechanisms underlying this synergy is the reduction of oxidative stress. Both beverages are rich in polyphenols, which are potent antioxidants capable of neutralizing free radicals and inhibiting lipid peroxidation [47]. Studies have shown that chlorogenic acid, found in both drinks, protects oral epithelial cells from oxidative damage, which is crucial in cancer prevention [1]. Additionally, alkaloids such as caffeine and theobromine demonstrate the

ability to modulate inflammatory responses by reducing levels of pro-inflammatory cytokines, including interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) [48]. Their combined action may effectively suppress chronic inflammation of the oral mucosa, which plays a significant role in the prevention of periodontal diseases and oral cancers [4].The oral microbiome plays a key role in maintaining the health of the mucosa and periodontium. Bioactive compounds from both infusions may influence the composition of the bacterial microflora by limiting the growth of pathogens responsible for oral diseases. The polyphenols present in these beverages exhibit bacteriostatic effects against *Streptococcus mutans* and *Porphyromonas gingivalis*, the main etiological agents of dental caries and periodontal diseases [15]. Moreover, caffeine may modulate immune responses and reduce bacterial adhesion to tooth and gum surfaces, further limiting inflammation [41]. An important aspect of this synergy is their potential role in oral cancer prevention. Epidemiological studies suggest that regular coffee consumption may be associated with a reduced risk of certain oral cancers, a benefit attributed to its strong antioxidant and anti-inflammatory properties [49]. *Ilex paraguariensis*, in turn, contains compounds capable of inhibiting cancer cell proliferation through the regulation of signaling pathways such as PI3K/Akt and NF-κB, which are key in carcinogenesis [30]. The synergistic action of polyphenols and alkaloids from both beverages may more effectively inhibit angiogenesis and promote apoptosis in cancer cells, suggesting their potential role in oral cancer prevention [2,4]. Furthermore, both beverages may support the regeneration of the oral mucosa and wound healing processes. Certain phenolic compounds found in these infusions stimulate the proliferation of fibroblasts and keratinocytes, facilitating epithelial repair and accelerating tissue healing following injury [43,50]. Chlorogenic acid and flavonoids also improve microcirculation, enhancing the delivery of oxygen and nutrients to damaged tissues, thereby promoting regeneration [17,51,52]. The presence of caffeine may further enhance these effects by improving endothelial function and increasing blood flow in the oral mucosa [53]. The combined action of these mechanisms suggests that yerba mate and coffee may offer natural support for tissue regeneration and protection against complications arising from mucosal damage. The synergy between *Ilex paraguariensis* and *Coffea* spp. indicates potential benefits from their moderate and regular consumption. However, further studies are necessary to determine the optimal proportions and underlying mechanisms of their effects on human health.

Conclusions

Yerba mate and coffee play a significant role in oral health protection and potential cancer prevention. The bioactive compounds they contain, such as polyphenols, alkaloids, and phenolic acids, exhibit antioxidant, anti-inflammatory, and antiproliferative properties, which may support the body's defense mechanisms. The presence of caffeine and theobromine influences cellular metabolism by modulating immune responses and reducing oxidative stress. Polyphenols, including chlorogenic acid and quercetin, promote the regeneration of the oral mucosa and inhibit the growth of bacteria responsible for dental caries and periodontal diseases. Moreover, the bioactive constituents of these beverages may regulate key signaling pathways, such as PI3K/Akt and NF-κB, thereby limiting cancer cell proliferation and promoting apoptosis. Their effects also include enamel protection by reducing demineralization and supporting remineralization processes. The synergistic effects of yerba mate and coffee may enhance their beneficial impact on oral health; however, further research is needed to determine the optimal consumption patterns and the long-term effects of their regular use.

Disclosure:

Author's Contribution Statement:

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