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Yerba mate – properties and potential applications in medicine

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Abstract

Yerba mate (*Ilex paraguariensis* A. St.-Hil.) is rich in approximately 200 chemical compounds responsible for its biological activity, including beneficial effects on lipid metabolism, oxidative balance, and anti-inflammatory properties. The polyphenols present in the infusion exhibit in vitro anticancer properties by inhibiting cancer cell proliferation, angiogenesis, and inducing apoptosis. Yerba mate infusion supports weight reduction by activating metabolic pathways such as the AMP-activated protein kinase (AMPK) pathway, leading to increased lipolysis, thermogenesis, and browning of white adipose tissue. Yerba mate may counteract osteoporosis by reducing bone tissue degradation and increasing bone mineralization in perimenopausal women. Studies conducted on wild-type C57BL/6/J mice (WT) have demonstrated the beneficial effects of yerba mate extract on gut microbiota composition. A significant reduction in pro-inflammatory bacteria, such as *Eubacterium rectale* and *Enterobacteriaceae*, was observed, along with an increase in beneficial bacterial populations, including *Lactobacillus* and *Lactococcus*. The gut microbiota composition was analyzed by isolating microbial DNA and assessing bacterial abundance using fecal samples collected on days 0, 7, and 14 after yerba mate extract administration. This review highlights recent advances in understanding the health benefits of yerba mate, focusing on its impact on gut microbiota and molecular mechanisms regulating lipid metabolism. Scientific research highlights the potential health benefits of yerba mate infusion in preventing and managing diabetes, obesity, cardiovascular diseases, osteoporosis, and certain cancers. However, further studies are required to establish the safety of yerba mate consumption. *(Farm Współ 2025; 18: 88-95) doi: 10.53139/FW.20251814*

Keywords: yerba mate, infusion, microbiome, obesity, neoplastic diseases

Introduction

Yerba mate is a tea derived from the leaves, twigs, shoots, and stems of the yerba mate tree (*Ilex paraguariensis*), an evergreen species that grows naturally in South America. According to the Guarani Indians, believed to be the creators of this brew, yerba mate should be prepared with hot water (85–95°C) rather than boiling water, as boiling diminishes its flavor and the properties for which it has been valued for centuries [1,2]. Currently, the yerba mate infusion consumption reaches over one million people worldwide [3,4], particularly in Argentina, Brazil, Uruguay, and Paraguay [3-5], where it is an essential part of cultural traditions [3,4]. Numerous scientific studies highlight the health benefits and therapeutic effects of long-term yerba mate infusion consumption in conditions such as breast cancer, asthma, Alzheimer's disease, diabetes, atherosclerosis, and obesity [6]. On the other hand, there are reports suggesting a correlation between yerba mate use and an increased risk of cancer [4,7]. Issues related to cancer prevention, diagnosis, treatment, the efficacy of potential drugs, and the role of dietary components in cancer prevention and progression are widely studied. This narrative review aims to summarize scientific data regarding the possible health benefits of yerba mate consumption. Although several review articles have addressed the general health-promoting properties of yerba mate, few have comprehensively analyzed

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the molecular mechanisms underlying its effects on obesity, cardiovascular diseases, and cancer, while also considering its impact on gut microbiota composition. This review aims to fill this gap by integrating the latest findings on these aspects and providing an up-to-date perspective on the potential medical applications of yerba mate.

Methodology

The methodology for this study followed that of a scoping review [8] with updates [9]. The main phases were: (1) The research question, "What is known about yerba mate and its impact on human health?", was designed to be broad in scope to capture various aspects of the topic. (2) Identifying relevant studies - We searched on PubMed and Google Scholar using key terms such as yerba mate AND (health OR disease prevention). In addition, we reviewed references from relevant literature and reviews discussing the overall health impacts of yerba mate. Studies in English were included without restrictions on publication date but were limited to those available until November 30, 2024.

Chemical composition of yerba mate

Approximately 200 chemical compounds have been isolated from the infusion of yerba mate, including alkaloids (xanthines: caffeine, theobromine, theophylline), polyphenols (flavonoids, anthocyanins, proanthocyanidins, phenolic acids) and saponins [1,2,10]. The biological activity of yerba mate is mainly attributed to polyphenols [5,6,11-14] (chlorogenic acid, ellagic acid, flavonoids), methylxanthine alkaloids [5,6,11] (caffeine, theobromine), and terpenoids [6,11]. The total phenolic content in the extract ranges from 675 to 733 mg/mL yerba mate [14]. Methylxanthines, saponins, and polyphenols positively influence lipid metabolism and oxidative balance [10]. Yerba mate extract which was generated by aqueous extraction (20% leaves of *Ilex paraguariensis*), exhibits free radical scavenging activity, with approximately 60% inhibition of DPPH (2,2-diphenyl-1-picrylhydrazyl) activity on average [14]. Additionally, yerba mate infusion is rich in components such as magnesium, calcium, iron, zinc, manganese, and others [1,2]. Łukomska et al have shown that the number of extractions influences the mineral content, including fluoride, in yerba mate infusion. In this study, 10-gram samples were brewed with 50 mL of water at 85°C, with hot infusions repeated twice. The results showed that hot water significantly increased fluoride release ($p = 0.03$), while subsequent extractions released progressively less fluoride, with a significant reduction observed in the third infusion ($p = 0.003$). [15]. Each additional brewing of yerba mate decreases the infusion's polyphenol content and antioxidant properties [2]. Treviso et al. investigated the impact of a 7-day fermentation at 25°C or 30°C on the characteristics of yerba mate kombucha. They demonstrated that the total phenolic content remained unchanged after fermentation, in contrast to acetic acid, ethanol, and chlorophyll levels. After a 7-day fermentation process, the infusion becomes acidic and develops a bitter, vinegar-like taste, which makes the unfermented infusion more likely to be chosen by consumers [16]. The individual properties of chemical compounds isolated from yerba mate infusion are presented in table I.

Neoplastic diseases

Carcinoma of the breast is the second most common malignant tumor in women [17]. Estimated projections for cancer incidence and mortality in 2040 in the United States predict changes: breast cancer is

Table I. The properties of chemical compounds isolated from yerba mate infusion

Chemical compounds	Properties
Polyphenols [including flavonoids, 4,5-di-caffeoylquinic acid (4,5-diCQA), chlorogenic acid]	antioxidant [2] and lipolytic [10] properties, slow down the absorption of carbohydrates in the intestine [34], inhibits the cell cycle of prostate cancer cells in the S phase [8], anti-inflammatory properties [24], and affects the intestinal microbiota [13,41,42]
Terpenoids [including carotenoids, saponins]	increase triglyceride levels [29], hemolytic, antibacterial, antiviral, antifungal, hypocholesterolemic [2], antioxidant [10,19] and lipolytic [10] properties, give the infusion a bitter taste [2]

expected to be the most common cancer, followed by melanoma [18].

Some studies suggest that high yerba mate infusion consumption, combined with elevated dietary levels of certain antioxidants (mainly carotenoids and glutathione), reduces the risk of breast cancer in women (OR = 0.63 and OR = 0.65). The yerba mate drinking habit duration correlates with the health benefits associated with long-term infusion consumption (OR = 0.62) [19]. A study conducted in Brazil on 78 women, with an average age of 55 and diagnosed with breast cancer, revealed that 78.5% consumed yerba mate chimarrão infusions in amounts ranging from approximately 0.5 to 4 L per day. Decreases in reduced glutathione ($p < 0.0001$) and metallothionein levels ($p = 0.001$), as well as an increase in catalase activity ($p = 0.0225$), were observed in yerba mate chimarrão consumers compared to non-consumers. The median serum caffeine concentration among these patients was 0.431 μg/mL, with the highest levels found in obese women [17].

Cell lines from mouse mammary tumors (a sarcomatoid mammary carcinoma cell line F3II, a highly invasive and metastatic variant) and human mammary adenomas were tested for sensitivity to yerba mate extract prepared from leaves through aqueous extraction in concentrations from 0.03 to 2.5 mg/mL for 24 and 72 hours. A statistically significant decrease in the growth of both mouse and human cells in vitro was observed between the control and yerba mate-treated groups. These preclinical findings suggest a potential role for yerba mate as an adjuvant in clinical breast cancer treatment, as it may affect cancer cell metabolism during metastasis [20].

Barg et al. demonstrated that oral and topical applications of yerba mate and green tea prevented lipid peroxidation and DNA damage in Wistar rats exposed to ultraviolet radiation [21]. Polyphenols in yerba mate leaves showed photochemoprotective effects and reduced UV-induced damage. Cuelho et al. found that yerba mate components possess antioxidant activity, are non-cytotoxic to fibroblasts, and reduce myeloperoxidase and metalloproteinase-2 activity following acute UVB exposure [22].

Colorectal cancer (CRC) is the third most common cancer among men and women, prompting the search for effective treatments. In vitro and in vivo experiments using CRC models showed that yerba mate extract at doses of 0.15 to 15 mg/mL inhibits the proliferation of CT26 and COLO 205 cells (with IC50 values of 0.25 and 0.46 mg/mL, respectively) via apoptosis induction, as evidenced by TUNEL assays ($p < 0.05$). Western blot analysis revealed reduced anti-apoptotic protein Bcl-2 in cells treated with yerba mate extract. In a mouse tumor model, oral administration of yerba mate at 1.6 g/kg/day inhibited angiogenesis and tumor growth without affecting body weight or vital parameters. The cytotoxic effects of yerba mate in vitro on mouse and human CRC cells suggest its antiproliferative potential [14]. Wnuk et al. found that yerba mate extract increases levels of apoptotic and necrotic cells, reduces the nuclear division index (NDI), and suggests aneugenic effects [7]. Puangpraphant et al. utilized chlorogenic acid derivatives (CQA), including 3,4-, 3,5-, and 4,5-dicaffeoylquinic acid (4,5-diCQA), isolated from yerba mate leaves at concentrations of 80 to 200 μM, on CRC cells. A 50% reduction in pro-inflammatory parameters was observed, with greater inhibition of the PGE2/COX2 pathway than the NO/iNOS pathway. These findings suggest that CQA derivatives inhibit human CRC cell proliferation via apoptosis induction, highlighting the potential application of yerba mate as an anticancer agent, based on in vitro study using four cell cultures: mouse macrophage, normal human colon fibroblast and two types of human colon cancer cells [23]. Additionaly, yerba mate may serve as a dietary component for oncology patients [14], but further research is required.

The primary cause of bladder cancer is smoking. Bates et al. suggested an association between yerba mate consumption using a bombilla and smoking, with an increased risk of bladder cancer. However, they did not establish a clear dose-response relationship, and the small sample size may have affected the statistical accuracy. The data suggest no correlation between bladder cancer and yerba mate consumption in non-smokers. Consequently, yerba mate does not appear to be a carcinogenic factor for the bladder, though long-term, large-scale epidemiological studies are needed [4].

Lopes et al. identified carcinogenic polycyclic aromatic hydrocarbons in commercial yerba mate infusions, suggesting a link between yerba mate consumption and an increased risk of esophageal squamous cell carcinoma [24]. Conversely, Amigo-Benavent et al. demonstrated reduced cancer cell viability at all tested concentrations. Dietary-attainable concentrations of yerba mate extract (0.1, 1, and 10 μg/mL) showed

no cytotoxic effects. Yerba mate was utilized without additional milling or leaf selection, and the extract was obtained through a three-step organic solvent extraction process. The sample was initially treated with 2N HCl in aqueous methanol, followed by acetone extraction [25].

Prostate cancer is the most common adenocarcinoma in men over 50, with a long latency period. Santiano et al. reported that yerba mate consumption in rats slightly reduced body weight, delayed tumor onset ($p < 0.01$), and decreased tumor volume ($p < 0.05$). In vitro studies showed reduced viability, proliferation, and adhesion of cancer cells ($p < 0.001$) and delayed migration of LNCaP ($p < 0.05$) and DU-145 ($p < 0.005$) prostate cancer cells. Yerba mate intake demonstrated greater efficacy against androgen-sensitive cell lines (LNCaP) [26]. Lodise et al. examined the effects of dicaffeoylquinic acids, components of *Ilex paraguariensis*, on DU-145, LNCaP, and PC-3 prostate cancer cells. The most active compound, 4,5-dicaffeoylquinic acid (4,5-diCQA), at a 50% inhibitory concentration (5 μM), suppressed cancer cell growth under normoxic and hypoxic conditions by arresting the cell cycle in the S phase. This study opens therapeutic possibilities for 4,5-diCQA in clinical prostate cancer treatment [8].

Cittadini et al. demonstrated the neuroprotective effects of orally administered tea extract *Ilex paraguariensis* (which was prepared from 1 g of pulverized airdried sample, and 10 mL of 83°C water, filtered and lyophilized) at 50 mg/kg/day for three weeks on the brains of mice with lung adenocarcinoma, emphasizing the importance of diet in neurological prevention in cancer conditions [12].

Obesity

Yerba mate polyphenols, such as flavonoids, phenolic acids, caffeine, and saponins [1,2,6,10,11], may contribute to weight loss [9]. A significant link to obesity is observed in AMP-activated protein kinase (AMPK), which regulates lipid metabolism pathways in various tissues and adipocytes [27]. Activation of this pathway inhibits lipogenesis (lipid synthesis) and increases lipolysis (lipid breakdown) [28]. A study by Pachura et al. demonstrated increased lipolysis in rats after yerba mate administration [29]. Further research showed that yerba mate extract activates AMPK in adipocytes, reducing the expression of proteins such as SREBP1c and FAS, which are involved in fatty acid synthesis and accumulation. AMPK activation by yerba mate also increases hormon-sensitive lipase (HSL) levels, which are responsible for lipid breakdown. Additionally, through inhibition of mTOR and S6K, AMPK limits adipogenesis, the formation of new fat cells. AMPK activation by *Ilex paraguariensis* extract also mediates increased expression of uncoupling protein 1 (UCP1), which supports thermogenesis, promoting fatty acid burning and weight reduction [28].

Kim et al. found that a 12-week supplementation of yerba mate aqueous extract derived from dried leaves at a dose of 3 g/day, divided into portions, led to weight reduction and a decreased waist-to-hip ratio [3]. Chlorogenic acid, rutin, and quercetin in yerba mate infusion play a critical role in managing obesity by affecting inflammatory markers in the hypothalamus and adipocytes and through anti-inflammatory effects [24]. Yerba mate extract significantly increases levels of GLP-1 (glucagon-like peptide-1), a peptide signal regulating appetite, and leptin, a hormone that controls fat tissue mass by reducing appetite and food intake. Hussein et al. observed a significant reduction in body weight, body mass index (BMI), and food consumption in mice treated with yerba mate extract at 50 and 100 mg/kg doses over three weeks. These results suggest potential anorectic effects of yerba mate [30].

Further studies analyzing white adipose tissue (WAT) morphology showed a reduction in adipocyte size and induced browning of WAT—a process that increases mitochondria quantity and UCP1 protein expression. This results in enhanced thermogenesis, increased energy expenditure, and prevention of excessive fat accumulation [31]. It has been demonstrated that yerba mate, prepared daily by dissolving 7.49 g of yerba mate powder in 296 mL of water and administered to six-month-old mice, increases oxygen utilization by mitochondria in adipose tissue, but not in other examined tissues. It also raises ATP levels in skeletal muscle while decreasing them in adipose tissue, which explains weight loss induced by yerba mate consumption [32]. Pedro et al. investigated the effect of yerba mate extract, prepared by drying and milling the leaves and branches of *Ilex paraguariensis* mixed in a 70:30 ratio, on lipid metabolism in Wistar rats fed a high-fat diet. The findings revealed a reduction in visceral fat gain and plasma LDL levels. The researchers concluded that yerba mate preparations could completely reverse high-fat diet-induced hepatic lipogenesis [33], though further research is required.

Metabolic and cardiovascular diseases and obesity

Wistar rats with diabetes were subjected to a 30-day yerba mate treatment. The results showed improved glycemia levels in diabetic rats, although they remained elevated, while insulin levels did not change after 30 days of treatment with yerba mate [10].

Nutrigenomic studies suggest that yerba mate supports obesity reduction and may indirectly lower the risk of cardiovascular diseases. Consumption of yerba mate infusion extract significantly alters gene expression in immune cells, impacting metabolic and immune pathways. Polyphenols in yerba mate reduce inflammatory marker expression while modulating metabolic pathways related to lipid and glucose regulation ($p < 0.05$). A study by Pachura et al. demonstrated that standardized fractions of saponins and terpenoids from *Ilex aquifolium* (the European taxon of holly) reduced liver steatosis and increased triglyceride levels in a rat model [29].

Research published in the *British Journal of Nutrition* highlights the impact of yerba mate on the expression of genes responsible for metabolism and cardiometabolic health. Yerba mate infusion consumption altered the expression of 2,635 genes, including 2,385 protein-coding genes, 6 miRNAs, and 244 long non-coding RNAs (lncRNAs). Yerba mate influences key signaling pathways, such as PI3K-Akt, MAPK, and cAMP, which are crucial for glucose metabolism, lipid metabolism, and inflammatory responses. Specifically, changes included the FOXO3 gene, associated with oxidative stress response and protection against cardiometabolic diseases, as well as TNFSF11 and VWF genes, which play roles in atherosclerosis development and inflammatory processes. Reduced expression of these genes suggests protective effects on the cardiovascular system ($p < 0.05$). Yerba mate infusion also protects against oxidative stress [32].

Another study conducted on Wistar rats demonstrated the antidiabetic potential of yerba mate. Active components of the plant, particularly chlorogenic acid and various flavonoids, inhibit alpha-glucosidase activity, slowing carbohydrate absorption in the intestine [34]. Yerba mate also appears to enhance glycogen synthesis in the liver, providing an additional mechanism for glucose regulation. Advanced glycation end products (AGEs), which are linked to diabetic complications, were significantly reduced under in vitro conditions following yerba mate infusion, suggesting a protective effect against cell damage caused by hyperglycemia [35].

Studies confirm the beneficial effects of yerba mate on carbohydrate metabolism; however, its efficacy in managing type 2 diabetes and insulin resistance requires further clinical research [35].

Gut microbiota

The human intestine is colonized by a diverse array of microorganisms, including bacteria belonging to *Firmicutes*, *Bacteroidetes*, and *Actinobacteria*. Over half of the *Firmicutes* phylum consists of members of the *Clostridia* class, the predominant class within this group. This is followed by *Bacteroidia*, *Bifidobacteriales*, *Enterobacterales*, and *Lactobacillales*, each contributing significantly to the microbiota composition [36]. Moreover microbiota performs essential metabolic and immunological functions in the host organism, including the capacity to ferment undigested dietary polysaccharides, leading to the production of short-chain fatty acids (SCFAs). Dysregulation of the microbiota-gut-brain axis can amplify a range of central nervous system (CNS) disorders through the altered production of metabolites, such as SCFAs. Furthermore, through its interaction with the central nervous system via the gut-brain axis, the microbiome alleviates disorders within the gastrointestinal tract and other organs, cognitive impairments, and depressive-like behaviors. It influences the host's neuropsychological and behavioral functioning [37].

Hydrophobic extracts macerated with hexane or extracted using supercritical CO_2 at 300 bars and 50°C are rich in antimicrobial compounds. These have demonstrated antibacterial potential against bacteria such as *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Staphylococcus aureus*, and *Bacillus cereus*, which contribute to gut dysbiosis [38]. Another study confirmed strong antibacterial activity against *Staphylococcus aureus*, *Listeria monocytogenes*, and *Salmonella enteritidis*, but not against *Escherichia coli* [39].

An in vivo study conducted on 61 C57BL/6/J wild-type (WT) mice (both males and females) aged 8–12 weeks, which were administered an extract via gavage at a dose of 0.025 g for 7 days—prepared by dissolving 1 g of the dry leaf extract in 8 mL of water at 60°C, followed by cooling and filtration—significantly affects gut microbiota composition by reducing bacteria from the *Eubacterium rectale/Clostridium coccoides* group

and the *Enterobacteriaceae* family while increasing *Lactobacillus* and *Lactococcus* populations. To assess gut microbiota, fecal samples were collected on days 0, 7, and 14 after extract administration. From each mouse, 100 mg of these samples were used for microbial DNA isolation, and the abundance of specific gut bacterial groups was quantified using the qPCR method.

These microbiota modifications may promote the polarization of intestinal macrophages toward the M2 type, aiding in the reduction of intestinal inflammation. Regulating gut dysbiosis and promoting beneficial bacterial growth can alleviate symptoms of gastrointestinal inflammation. However, findings suggest that yerba mate does not directly affect M2 macrophage polarization but instead influences the gut environment to induce such changes [13]. Yerba mate consumption helps manage gut dysbiosis by reducing *Eubacterium rectale/Clostridium coccoides* and *Enterobacteriaceae* while increasing *Lactobacillus/Lactococcus*, thereby mitigating intestinal inflammation symptoms ($p < 0.05$) [13,40].

Chemical studies on yerba mate indicate that chlorogenic acid, a dominant bioactive compound in the extract, exhibits anti-inflammatory properties by reducing the production of pro-inflammatory cytokines like IL-6 and TNFα [13]. Chlorogenic acid also influences gut microbiota, further supporting its anti-inflammatory effects at the intestinal level [13,41,42]. Figure 1 shows the main properties of yerba mate.

Other health aspects of yerba mate consumption

Research by Pereira et al. on female Wistar rats showed that yerba mate, partly through reducing oxidative stress, minimizes bone tissue degradation during the perimenopausal period, thereby reducing the risk of osteoporosis [43]. A study by Conforti et al. involving 146 women who consumed at least 1 liter of yerba mate infusion daily for a minimum of 4 years found that these women had 9.7% higher lumbar spine bone mineral density and 6.2% higher femoral neck bone mineral density compared to non-yerba mate consumers at the same menopausal stage [44].

In a rat model simulating postmenopausal conditions (ovariectomy), regular yerba mate consumption significantly limited weight gain within weeks. Triglyceride, total cholesterol, and LDL levels also decreased, approaching those observed in control groups. These findings suggest that yerba mate may aid in the prevention and treatment of metabolic disorders associated with menopause [31].

An intriguing effect of yerba mate consumption is its potential influence on lifespan. While current studies cannot conclusively determine whether yerba mate infusions impact human longevity, research on *Drosophila melanogaster* showed a significant lifespan extension following supplementation with *Ilex paraguariensis* at a dose of 10 mg/mL [45].

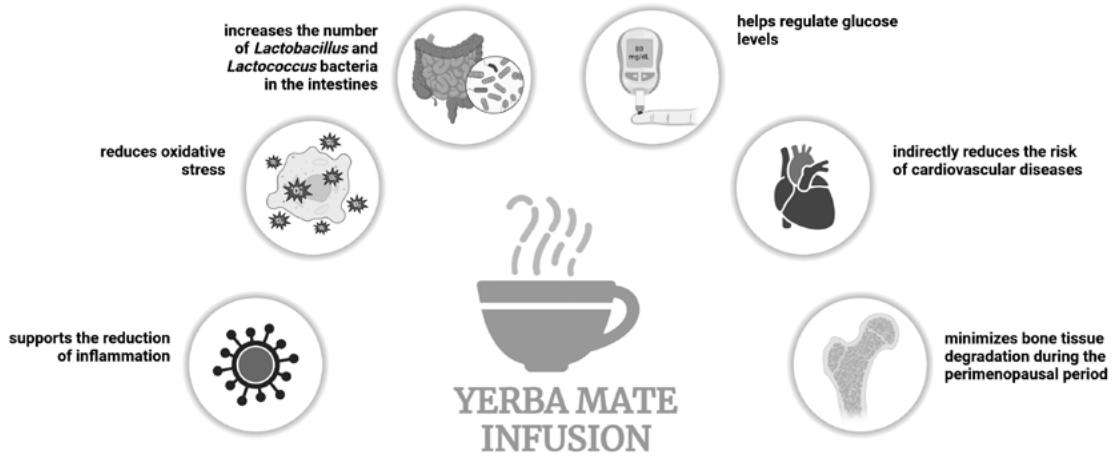

Figure 1. Properties of yerba mate

Conclusion

The presented studies highlight the positive health effects of yerba mate infusion consumption, including its impact on gut microbiota. Potential medical applications of yerba mate include cancer prevention, prophylaxis and treatment of diabetes, obesity, cardiovascular diseases, and osteoporosis. However, further human studies are necessary to better establish the physiological relevance and safety of yerba mate consumption.

Conflict of interest
None

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