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## The correlation between Yerba Mate and cancer - a review

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## Abstract

### Introduction and objective

Yerba Mate (YM) is a popular drink obtained from the dried and ground leaves of the *Ilex paraguariensis*. The beneficial effects of Yerba Mate on the cardiovascular system, lipid-lowering, anti-diabetic, hepatoprotective and stimulating properties are known, however, there are also reports supporting its toxicity, that the consumption of Yerba Mate may predispose to the development of cancer. The purpose of this article is to present and organize information on the correlation between drinking Yerba Mate and cancer.

### Review methods

A review of the available literature was performed by searching the PubMed and Google Scholar databases using the following keywords: Yerba Mate and cancer, Yerba Mate.

### Abbreviated description of the state of knowledge

Substances contained in Yerba Mate have a positive impact on the human body. They exert health-promoting effects, e.g. increasing HDL levels and enhancing the antioxidant effect. A particularly desirable effect of Yerba Mate is its modulating effect on the course of the carcinogenesis process. Current knowledge on this subject is not complete. There are no evidences that substances in Yerba Mate without other risk factors increase the risk of oesophageal cancer. It is worth emphasizing that the properties of the Yerba Mate components are related to the reduction of the development of metastases of other cancers.

### Conclusions

Despite the carcinogenic PAHs contained in the YM extract, there is no clear evidence that drinking it alone, without taking into account the temperature of the drink, could predispose to the development of esophageal cancer. Many substances found in YM have a beneficial effect on the human body.

Key words: yerba mate, cancer, risk factors

## Introduction

Yerba Mate (YM) is a popular drink obtained from the dried and ground leaves of the *Ilex paraguariensis*, occurring in America South and Asia, where it was used by indigenous people, among others, for medicinal purposes [1,2]. The traditional method of brewing it consists in pouring water with a temperature of 65 degrees Celsius to 80 degrees Celsius and leaving it for a few minutes. The highest consumption of Yerba Mate (YM) per capita is in Uruguay, Argentina and Brazil, where it is over 5 kg per year[1], however, this drink is also becoming more and more popular in Europe. In addition to the nutrients contained, Yerba Mate is a source of purine alkaloids (such as caffeine, theobromine or theophylline), terpenes, polyphenols as well as minerals and vitamins [2,3](Table 1)[1,2]. The preparation of Yerba Mate involves roasting and drying the leaves directly over a flame or in the smoke of burning wood, during which polycyclic aromatic hydrocarbons (PAHs) are formed, which are considered extremely harmful[1]. The beneficial effects of Yerba Mate on the cardiovascular system, lipid-lowering, anti-diabetic, hepatoprotective and stimulating properties are known[1, 2]. However, there are also reports supporting its toxicity, that the consumption of Yerba Mate may predispose to the development of cancer. The purpose of this article is to present and organize information on the correlation between drinking Yerba Mate and cancer.

Table 1. Substances contained in Yerba Mate and their properties

A group of chemical compounds	Examples of substances found in Yerba Mate	Key features
<b>Polyphenols</b>	Caffeic Acid, Caffeine, Chlorogenic Acid, Caffeoylshikimic acid, Feruloylquinic acid, Rutin, Quercetin	Antioxidant properties, inhibition of free radicals
<b>Purine Alkaloids</b>	Theophylline, Theobromine, Caffeine	Anticancer, antioxidant, diuretic (caffeine), cAMP-phosphodiesterase inhibitor, stimulant (theobramine)
<b>Caffeoyl derivatives</b>	3, 4-dicaffeoylquinic acid, 3, 5-dicaffeoylquinic acid, and 4, 5-dicaffeoylquinic acid	Antioxidant properties
<b>Saponins</b>	Ursolic acid	Antioxidant, hypercholesterolemic properties
<b>Minerals</b>	aluminum, chromium, copper, iron, manganese, nickel, potassium and zinc, phosphorus	Mineral-specific properties

## Materials and method

A review of the available literature was performed by searching the PubMed and Google Scholar databases using the following keywords: Yerba Mate and cancer, Yerba Mate, in the period from 2015 to the 18th of February 2023.

## Leaf preparation and chemical compounds

Yerba leaves, known botanically as *Ilex paraguariensis*, are a rich source of polyphenols, especially caffeoyl derivatives, which are responsible for antioxidant and anti-cancer properties, which include, among others, inhibition of cell growth, induction of apoptosis and reduction of angiogenesis. The characteristic taste of the infusion comes from saponins, which have anti-inflammatory properties. Xanthines are also an inseparable component of the leaves [4]. Processing Yerba Mate involves drying the leaves at very high temperatures (400-750 degrees Celsius) or exposing them to fire. This process is to prevent degradation and reduce the humidity of the leaves, so in the next step they are exposed to lower temperatures (90-350 degrees Celsius) in charcoal ovens, which increases the content of polycyclic aromatic hydrocarbons, which consequently reach high levels. In the absence of exposure to smoke, the PAH content would be lower [5].

## **Health-promoting properties**

It has become a fact that long-term consumption of Yerba Mate brings health-promoting and therapeutic effects. Researchers indicate the possibility of using its bioactive ingredients in the treatment of as many as 350 diseases, including breast cancer, asthma and Alzheimer's disease. They determined that the target of the pharmacological action of yerba mate is mainly amyloid-beta precursor protein and vascular endothelial growth factor A [6]. Among the many biological properties of YM, the protective effect on the cardiovascular system and the prevention of obesity are also noteworthy [7,8].

Paraoxonase (PON-1) is a marker of inflammation. It is associated with high-density lipoprotein (HDL) or leptin, which affects the feeling of satiety. Leptin levels are increased in overweight and obese people, and it also has antioxidant functions [9,10,11]. PON-1 is carried by HDL (high-density lipoprotein) and prevents the formation of atherosclerotic plaques by inhibiting LDL (low-density protein) oxidation [1]. It is noteworthy that the conducted research showed an increase in PON-1 activity in the plasma of people who consumed YM. In addition, they compared the effects of YM and other drinks, which are also rich in antioxidant polyphenols, on PON-1 and leptin levels in overweight and obese people. The results showed that YM had the highest polyphenol concentration and free radical scavenging capacity compared to other beverages [14]. Polyphenols contained in YM leaves, especially chlorogenic acid, protect PON-1 from inactivation [1]. The increase in PON-1 associated with the influence of YM contributes to the increase in HDL levels, thanks to interrelationships. Therefore, yerba mate extract indirectly protects against atherosclerotic disease [12].

An important pro-health effect of YM is also the one that reduces the level of LDL in the blood, thanks to which it reduces the risk of cardiovascular diseases. This is probably due to the blockade of cholesterol absorption in the small intestine or the inhibition of cholesterol synthesis in the liver, which can be attributed to such YM ingredients as: saponins, polyphenolic compounds and caffeine[1].

Yerba Mate is recommended for athletes and people who want to lose weight. YM consumption before exercise increases the oxidation of fatty acids, for which the methylxanthines contained in it are responsible [1,13].

Consumers particularly appreciate YM for its stimulating properties. Yerba Mate contains caffeine, so it can be an alternative to coffee while maintaining its central nervous system stimulating properties [1,14,15].

The use of YM extract in microfibrillation as a wound healing bandage turned out to be an unconventional approach. The leaf extract increases the resistance of the film and has antibacterial properties [16].

Chlorogenic acid and caffeic acid contained in Yerba Mate extract have photoprotective properties. In one study, the extract showed no cytotoxicity in fibroblasts and reduced the activity of myeloperoxidase and metalloproteinase-2 after exposure to UVB, preventing photoaging and biological effects associated with the development of skin cancers. UVB radiation significantly increases the activity of MMP (matrix metalloproteinase) and MPO (myeloperoxidase) [17]responsible for the destruction of collagen fibres [18] and generation of oxygen free radicals (ROS)[17].

## **Yerba Mate and esophageal cancer**

Consuming hot (>65 degrees Celsius) beverages probably increases the risk of developing esophageal cancer. However, it is worth determining the relationship between the degree of risk of cancer development and the temperature of consumption, and the content of PAHs in the leaves from which the infusion is prepared. In some South American countries

where YM is consumed in large quantities, the incidence of esophageal squamous cell carcinoma is high and more significant than in other Latin American countries. Studies also conducted on coffee and tea, which are consumed at similar temperatures as Yerba Mate, have also provided reports of a positive effect on the risk of developing esophageal cancer. Hence, it was concluded that the high temperature of consumption is responsible for this effect. However, in addition to the influence of temperature, it is worth considering the participation of PAHs. Consumption of food containing PAHs is associated with the occurrence of malignant tumors of various locations, e.g. in the esophagus [8, 19, 20]. As previously emphasized, PAHs present in YM are mainly the result of the seed drying process. Roasted coffee also contains PAHs unlike green coffee which is not roasted. However, there is no clear evidence that PAHs contained in Yerba Mate independently predispose to the occurrence of esophageal cancer. This is supported by the fact that an increased incidence of esophageal cancer appears in countries where beverages such as tea are consumed at higher temperatures than in other countries. The British drink tea at a relatively lower temperature and the incidence of squamous cell carcinoma in their society is lower. Therefore, the specific effect of the drink was excluded as a positive correlation, confirming only the effect of temperature [19].

According to the International Agency for Research on Cancer (IARC), Yerba Mate has been classified as "possibly carcinogenic to humans" due to its high ingestion temperature. In addition to the positive effect on the incidence of esophageal cancer, an association was also found between drinking YM and cancers of the kidney, bladder, lung and prostate, in which the thermal factor does not play a role. The amount of Yerba Mate taken was significantly related to the concentration of PAH metabolites in the urine. The more infusion a person took, the higher the concentration of PAH metabolites in their urine, it increased to the same extent as in the case of smoking cigarettes [5].

### **Yerba Mate and breast cancer**

The main cause of death related to breast cancer is its metastasis. Therefore, the ability to modulate them by YM properties can be very helpful. Studies on the effect of YM on breast cancer metastasis were carried out in mice, and various *in vivo* and *in vitro* models of breast cancer were tested. The number of metastases in treated mice compared to those not receiving YM extracts was reduced by 26% in the orthotropic model and 17% in the heterotropic model. It follows that YM affects some stages of the metastasis cascade. In addition, it was found that the tumors in mice taking the infusion were smaller than those in the control group, which was probably influenced by polyphenols that reduce angiogenesis. As a result, the vascular system of the tumors was poorly developed, thanks to which the spread of tumor cells to distant metastases was limited. Mice survival was increased as a result of the anti-metastatic effect. According to researchers, about 90% of cancer-related deaths do not result directly from the impact of the primary tumor, but from its metastases. The researchers emphasize the need for further studies to confirm the hypothesis that YM inhibits the spread of metastasis [4].

Ronco AL et al. investigated the association between breast cancer risk and YM consumption. Their work confirmed the inverse relationship of these factors. Moreover, the strongest opposite associations were found for reproductive factors related to estrogen levels, such as: earlier age at menstruation, lack of breastfeeding. Similar protective results were found to be better for high-calorie women. The fact is that most cases of breast cancer occur in postmenopausal women and are associated with increased exposure to estrogens. Incorrect, excessive body weight is also a factor in the development of hormone-dependent breast

cancer after menopause. It follows that the stronger the influence of Yerba Mate, the greater the exposure to estrogens during life, is the more valuable [21].

### **Yerba Mate and other cancers**

Yerba Mate leaves contain chlorogenic acid, which affects the expression of genes related to apoptosis and genes encoding stem cell markers in the case of lung cancer. Thus, it exhibits anti-cancer activity [22].

The *in vivo* anti-angiogenic and anti-cancer activity was also confirmed by the study of the activity of Yerba Mate extract in colon cancer models, indicating a link with the induction of apoptosis. The studies were carried out on mice in which the positive anticancer effect had no effect on the biological parameters and body weight of the animals. For this reason, YM has been recognized as a healthy dietary component and a natural source of potential anti-cancer agents [23].

Lodise et al. in their research showed that 4,5-dicaffeoylquinic acid (4,5-diCQA) is active against prostate cancer cells. The effect of the substance was due to the arrest of the cell cycle in the S phase, which was important in the tests, which confirmed the lack of toxicity in relation to non-cancerous cells. Therefore, the above-mentioned substance may be used in the treatment of prostate cancer [20].

### **Summary**

As mentioned above, despite the carcinogenic PAHs contained in the YM extract, there is no clear evidence that drinking it alone, without taking into account the temperature of the drink, could predispose to the development of esophageal cancer. Many substances found in YM have a beneficial effect on the human body. What's more, due to their antioxidant and anticancer properties, there are indications that they may be used in cancer therapy in the future.

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