

Efficiency of daily kombucha consumption in reducing glycemic levels and hypercholesterolemia

Eficiência do consumo diário de kombucha na redução dos níveis glicêmicos e da hipercolesterolemia

Eficiencia del consumo diario de kombucha para reducir los niveles de glucemia y la hipercolesterolemia

DOI:10.34119/bjhrv7n2-323

Originals received: 03/08/2024

Acceptance for publication: 03/29/2024

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ABSTRACT

Diabetes is one of the most common comorbidities in the world. The scientific community is constantly looking for therapeutic alternatives, pharmacological or not, to treat this disease. In this concern, an integrative review of studies published on this topic in the last ten years was carried out. Experimental studies have shown glycemic and lipid rates reduction in diabetic

guinea pigs under daily kombucha consumption. Such studies showed blood sugar levels reduction of up to 56% of these specimens, as well as a significant reduction of free radicals, hepatoprotection and reduction of transaminases in these animals.

Keywords: kombucha, diabetes, cholesterol.

RESUMO

O diabetes é uma das comorbidades mais comuns no mundo. A comunidade científica está constantemente buscando alternativas terapêuticas, farmacológicas ou não, para tratar essa doença. Nesse sentido, foi realizada uma revisão integrativa de estudos publicados sobre esse tema nos últimos dez anos. Estudos experimentais têm mostrado redução nos níveis glicêmicos e lipídicos em cobaias diabéticas que consomem kombucha diariamente. Tais estudos demonstraram uma redução nos níveis de açúcar no sangue de até 56% nesses espécimes, além de uma redução significativa de radicais livres, hepatoproteção e redução de transaminases nesses animais.

Palavras-chave: kombucha, diabetes, colesterol.

RESUMEN

La diabetes es una de las comorbilidades más comunes en el mundo. La comunidad científica está constantemente buscando alternativas terapéuticas, farmacológicas o no, para tratar esta enfermedad. En este sentido, se realizó una revisión integrativa de estudios publicados sobre este tema en los últimos diez años. Estudios experimentales han demostrado una reducción en los niveles de glucosa y lípidos en cobayos diabéticos que consumen kombucha diariamente. Tales estudios mostraron una reducción en los niveles de azúcar en la sangre de hasta un 56% en estos especímenes, además de una reducción significativa de los radicales libres, protección hepática y reducción de transaminasas en estos animales.

Palabras clave: kombucha, diabetes, colesterol.

1 INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disorder leading to hyperglycemia, resulting from defects in pancreatic β cells (Type I DM) or decreased insulin receptor sensitivity (Type II DM). The American Diabetes Association (AMERICAN DIABETES ASSOCIATION - ADA, 2019) establish fasting blood glucose levels up to 100 mg/dL, but values above this may lead to hyperglycemic crises and silent progression due to pancreatic dysfunction. Early intervention in Type 2 diabetes control is crucial for positive clinical outcomes. (KLONOFF, 2008)

Factors influencing DM2 include lifestyle, high-fat and high-calorie diets, obesity, intestinal microbiota, and genetic predisposition. Dietary approaches, particularly focusing on functional foods, offer less aggressive alternatives for diabetes control. (BARBOZA *et al.*,

2020) Functional foods, with added health benefits, are associated with improved antioxidant enzymes, suppression of pro-inflammatory cytokines, insulin sensitivity, and hypocholesterolemia, essential for preventing and controlling DM2.(GARCIMART; BENED, 2021)

The connection between gut microbiota, short-chain fatty acids (e.g., butyrate, propionate), and metabolic disorders linked to insulin resistance in DM2 is noteworthy.(SANNA *et al.*, 2019) Modifying the gut microbiota can alter host metabolism, influencing energy uptake in DM2 individuals.(SHARMA; TRIPATHI, 2019; WU, G. D. *et al.*, 2011)

Complementary therapies involving probiotics (beneficial live commensal bacteria) have been established, alongside the consumption of resistant fibers as prebiotics.(IATCU; STEEN; COVASA, 2021) Functional foods, like fermented ones (yogurts, kefir, kimchi, sauerkraut, and kombucha), have gained attention. This review aims to characterize evidence and effects of kombucha supplementation as a non-pharmacological therapy based on existing literature.

1.1 HISTORICAL ORIGIN

The first historical record of kombucha dates back to around 220 B.C. and gained popularity for its purported health-promoting properties.(LAUREYS; BRITTON; CLIPPELEER, 2020) When it became popular in Japan, it was called "kombucha," a combination of the words "kombu" and "cha," which mean seaweed and tea, respectively. The story goes that the drink was introduced to the Japanese people by a Korean doctor named Kombu, with the purpose of addressing digestive issues.(ABACI; SENOL DENIZ; ORHAN, 2022) Additionally, the earliest medical reports related to this fermented beverage come from the Russian Army in the First World War (1914-1918). The secret Russian home remedy was known to alleviate headaches, gastric pains, and regulate intestinal activities. As trade routes expanded, kombucha spread, especially after the Second World War when the beverage was introduced to Germany and subsequently popularized throughout Europe.(ABACI; SENOL DENIZ; ORHAN, 2022)

The beverage is produced through the aerobic fermentation of green tea (*Camellia sinensis*) and sugar, with a symbiotic culture of bacteria and yeast (SCOBY), typically taking 7 to 10.(COTON, M. *et al.*, 2017; LAUREYS; BRITTON; CLIPPELEER, 2020) Although the typical production involves green tea, various presentations of *Camellia sinensis*, such as black,

white, or oolong tea, can be used, emphasizing that the variations come from the same plant. For production, 10g of tea leaves per liter of water can be used, with the addition of 50g of sugar serving as a substrate for fermenting bacteria and yeast. It is important to note that before adding the SCOBY, the mixture should be at room temperature, around 25°C, to avoid sterilizing the beverage. Despite the desired liquid not being sterile, it is crucial for utensils and equipment to be sterilized and handled in clean areas during kombucha production to control the growth of invasive microorganisms and prevent unwanted contamination.

1.2 CHEMICAL COMPOSITION OF KOMBUCHA

SCOBY is a biofilm of microorganisms consisting of various acid-producing bacteria (e.g., *Acetobacter xylinum*, *Acetobacter aceti*, *Acetobacter pasteurianus*, and *Gluconobacter oxydans*) and yeasts (such as *Saccharomyces sp.*, *Zygosaccharomyces kombuchaensis*, *Torulopsis sp.*, *Pichia spp.*, *Brettanomyces sp.*, and *Zygosaccharomyces bailii*). (GAGGIÀ *et al.*, 2018; KAPP; SUMNER, 2019; VINA *et al.*, 2014) Fermentation transforms kombucha into a cocktail of chemical components, including polyphenols, organic acids, fiber, ethanol, amino acids (such as lysine), essential elements like copper (Cu), iron (Fe), manganese (Mn), nickel (Ni), and zinc (Zn), water-soluble vitamins like vitamin C and various B vitamins, carbon dioxide, antibiotics, and hydrolytic enzymes. (JAYABALAN, Rasu *et al.*, 2014; KAPP; SUMNER, 2019) Other acids identified in the beverage include glucuronic acid, the main therapeutic agent, along with tartaric, malic, and citric acids, which contribute to the slightly sour taste of kombucha.

The compounds obtained at the end of the fermentation process, directly related to observed biological effects, depend on the metabolic pathway followed, such as lactic, alcoholic, and/or acetic. (MARTÍNEZ LEAL *et al.*, 2018; WATAWANA *et al.*, 2015) pH levels during kombucha fermentation should be controlled, and preferably fermentation should be stopped or delayed when reaching pH values around 4.2, as overproduction of acetic acid can be counterproductive. (KUMAR, V.; JOSHI, 2016) Fermentation delay can be achieved by bottling and refrigerating the beverage. (KOVACEVIC *et al.*, 2014)

1.3 MECHANISM OF ACTION OF KOMBUCHA

The most abundant bacteria in kombucha belong to the *Acetobacter* and *Gluconobacter* genera. (JAYABALAN, Rasu *et al.*, 2014; MARTÍNEZ LEAL *et al.*, 2018) These genera,

belonging to the Acetobacteraceae family, are Gram-negative aerobic bacilli capable of converting ethanol into acetic acid, which undergoes further oxidation to CO₂ and H₂O depending on its concentration.(STASIAK; BŁAJEK, 2009) As mentioned, the microbiota and metabolic composition of kombucha vary based on the exact composition of the SCOBY, the type and concentration of tea and sugar,(FU, C. *et al.*, 2014; GAGGIÀ *et al.*, 2018) oxygen concentrations, fermentation time, temperature, and storage duration.(FILIPPIS, DE *et al.*, 2018; FU, C. *et al.*, 2014)

During the fermentation process, invertase and saccharase, enzymes present in the yeast of the SCOBY, hydrolyze sucrose from the base ingredient into glucose and fructose.(DIMIDI *et al.*, 2019; JAYABALAN, Rasu *et al.*, 2014) These sugars are prerequisites for ethanol and, consequently, for the production of organic acids throughout the kombucha fermentation process. Other components of kombucha, such as Acetobacter bacteria, can produce acetic acid from ethanol. This process is carried out by alcohol dehydrogenase and aldehyde dehydrogenase enzymes, which produce acetic acid, generating water and carbon dioxide as the final products of the Krebs cycle.(MARTÍNEZ LEAL *et al.*, 2018; YAVARI *et al.*, 2017)

Glucuronic acid (GlcUA) in kombucha has a detoxifying effect by promoting essential lipid-soluble metabolism—a mechanism of hepatic detoxification that makes liposoluble compounds more polar and water-soluble, facilitating their transport and excretion from the body.(VINA *et al.*, 2013; YAVARI *et al.*, 2017) This process, called glucuronidation, is one of the main pathways for the biotransformation and excretion of potentially toxic endobiotics and xenobiotics in mammals.(BELLO; FALLER, 2016; KOVACEVIC *et al.*, 2014; VINA *et al.*, 2014)

Other phenolic compounds in the beverage confer potent antioxidant properties, reducing lipid oxidation.(VINA *et al.*, 2014) Antioxidants can prevent many metabolic disorders and diseases caused by free radicals, such as degenerative diseases, diabetes, cancer, and heart diseases.(BIANCHI; ANTUNES, 1999; SUFFI *et al.*, 2024; VINA *et al.*, 2014) These free radicals catalyze enzymes during cellular metabolism electron transfer processes and increase the body's vulnerability to exogenous factors. The result is the induction of cellular damage through oxidative stress.(BIANCHI; ANTUNES, 1999)

Camellia sinensis, the base herb of the beverage, contains high amounts of catechins. Recent studies indicated antibiotic properties of catechins, inhibiting the simultaneous proliferation of gram-positive and gram-negative bacteria, such as *Helicobacter pylori*, *Escherichia coli*, *Yersinia enterocolitica*, and *Staphylococcus aureus*, for example.(WATAWANA *et al.*, 2015) These catechins also act as antioxidants, eliminating

radicals and even metals such as copper and iron, which, when found in a free state or not bound to proteins, have a pro-oxidant effect that can damage lipids, proteins, and nucleic acids. Additionally, it has been demonstrated that polyphenols in green tea have significant tumor-suppressive effects in experimental conditions in cell lines,(ALAEI; DOUDI; SETORKI, 2020) animal models,(ALAEI; DOUDI; SETORKI, 2020) and clinical trials,(ALAEI; DOUDI; SETORKI, 2020; GONZÁLEZ ARBELÁEZ *et al.*, 2018; GOSZCZ *et al.*, 2017; VENKATAKRISHNAN *et al.*, 2018) suggesting their therapeutic potential in combating cardiovascular diseases.

The herbal remedy also regulates intestinal transit through its prebiotic and probiotic properties, influencing human intestinal microbiota.(ALAEI; DOUDI; SETORKI, 2020) The bacteria and yeasts in kombucha compete against pathogenic microorganisms, hindering infection. Furthermore, probiotics' ability to modulate digestion by binding to the surface cell receptors of intestinal enterocytes favors the synthesis of cytokines, which, in turn, amplifies the activity of natural killer (NK) cells or immunoglobulins as a whole, impacting the immune system cautiously without triggering an exaggerated inflammatory response.(SAAD, 2006) A reduction in hypersensitivity reactions in individuals susceptible to food allergies may also occur (SAAD, 2006) along with the crucial role in the balance of various bodily systems, including the central nervous system. Intestinal dysbiosis is also considered a risk factor for the development of Parkinson's disease, and research indicates that probiotics may offer a potential therapeutic solution. (MENEZES *et al.*, 2024)

2 METHODS

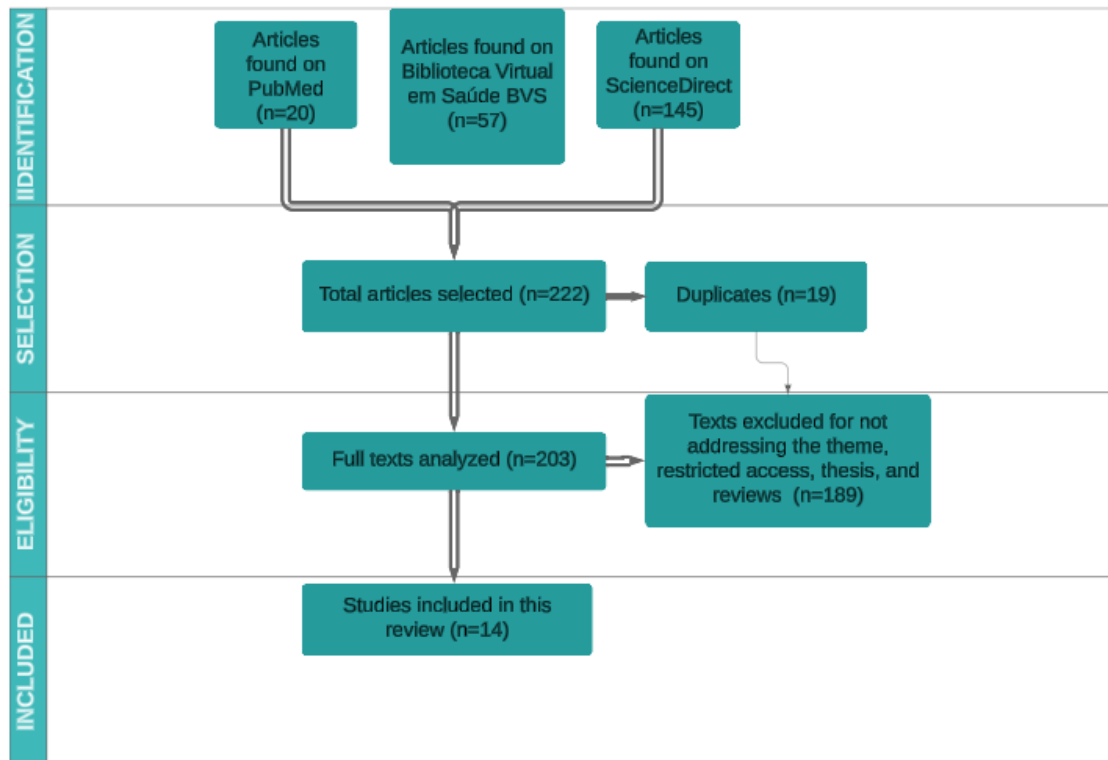
This study was characterized as an integrative literature review, providing a comprehensive understanding of the topic of interest. Thus, this research aimed to synthesize, from scientific journals and databases in the field, what has been empirically studied regarding the benefits of kombucha for the control of Type 2 Diabetes (DM2).

Searches were conducted in various databases; however, only three of these bibliographic sources yielded relevant results — PubMed, ScienceDirect, and the Virtual Health Library (BVS). The descriptors kombucha, cholesterol, and diabetes were used with Boolean operators AND/OR. Search filters were applied to limit the publication time frame from 2012 onwards, totaling approximately 10 years until the date this work was written.

The Figure 1 shows a result of this search, 119 articles were obtained. After reviewing the titles, articles that did not address the proposed theme, as well as duplicates and reviews,

were excluded. All original articles indexed between January 1, 2012, and December 31, 2022, with experimental designs (clinical trials, randomized or non-randomized) or observational designs (case-control studies, cohort studies, and before-and-after studies) were included. At the end of the selection process, the results and discussions of this work were based on the in-depth reading of 11 articles that were relevant to the research.

Figure 1 - Flowchart of the study selection process, adapted from PRISMA



Source: Elaborated by the authors.

3 RESULTS

3.1 HYPOGLYCEMIC PROPERTIES

Given the global prevalence of this disease (SAEEDI et al., 2019), there is a need to explore alternatives to oral hypoglycemic agents that are effective not only in reducing glycemic levels but also in mitigating the mechanisms secondary to persistent hyperglycemia that cause harm to the patient. In this context, functional foods attract special attention for their potential to provide health benefits while being mostly free of adverse effects.(FERNANDES et al., 2007; MUKHERJEE; VENKATESH; PONNUSANKAR, 2010; RAO; NAMMI, 2006)

In in vivo studies conducted with animals, the administration of kombucha has demonstrated significant health benefits, including the reduction of oxidative stress and inflammation, prevention of cardiovascular diseases, stimulation of gastrointestinal and immune function, as well as hypoglycemic and hypolipidemic actions. (ALOULOU *et al.*, 2012; BHATTACHARYA; GACHHUI; SIL, 2013; CARDOSO *et al.*, 2021; DIPTI *et al.*, 2003; XU *et al.*, 2022)

The analysis of previously conducted studies addressing the hypoglycemic effects of supplementing diabetic rats with kombucha points to three main mechanisms underlying the reduction in serum glucose: enzymatic inhibition, reduction of oxidative stress, and regulation of intestinal microbiota. (ALOULOU *et al.*, 2012; BHATTACHARYA; GACHHUI; SIL, 2013; CARDOSO *et al.*, 2021; XU *et al.*, 2022)

Regarding enzymatic inhibition, Aloulou *et al.* (2012) evaluated the effect of kombucha on the activity of two pancreatic enzymes contributing to the hyperglycemic and dyslipidemic state of diabetic individuals, lipase, and alpha-amylase. Lipase is responsible for lipid digestion and absorption, also influencing postprandial glucose levels. Alpha-amylase is associated with carbohydrate digestion and assimilation. For this analysis, adult Wistar rats had diabetes induced by alloxan, a toxin inducing damage and death of pancreatic beta cells, leading to endocrine pancreas failure. Subsequently, these experimental rats received kombucha or black tea for one month for laboratory and histopathological evaluation.

In diabetic rats, a significant increase in plasma and pancreatic alpha-amylase activity was observed. However, supplementation with both kombucha and black tea led to a reduction in this enzyme's activity, accompanied by a decrease in serum glucose levels. This reduction in enzyme activity results in lower levels of absorbable monosaccharides produced from starch digestion in the diet. When comparing the results obtained with the use of both beverages, the effects were more pronounced in rats whose diet was supplemented with kombucha. (ALOULOU *et al.*, 2012)

It was also observed that there was an increase in plasma lipase activity (about 194%) and pancreatic lipase activity (about 220%) in diabetic rats. Consequently, plasma levels of triglycerides and LDL also experienced considerable increases (194 +/- 50% and 404 +/- 107%, respectively). The use of black tea or kombucha led to a reduction in enzyme activity, consequently reducing the hydrolysis of triglycerides to monoglycerides and free fatty acids, thereby attenuating serum levels of triglycerides and LDL significantly. The effect of supplementation with kombucha was superior to that observed with the use of black tea. It is essential to note that there was also an increase in plasma HDL levels with the use of both

supplements, 137 +/- 18% in black tea supplementation and 157 +/- 30% in kombucha use.(ALOULOU *et al.*, 2012)

This inhibitory effect exerted by kombucha is believed to be due to the presence of polyphenols resulting from fermentation in its preparation process. The effect of polyphenols in reducing the activity of alpha-amylase in both saliva and the intestine had been previously reported. Furthermore, previous *in vitro* experiments reported that polyphenols can inhibit pancreatic lipase.(NAKAI *et al.*, 2005)

Beyond the specific action of these functional beverages on enzymatic activity, the observed hypoglycemic and hypolipidemic effects may be due to the attenuation of oxidative stress present in diabetes, where there is depletion of antioxidant defenses and an increase in Reactive Oxygen Species (ROS) levels.(ALOULOU *et al.*, 2012; BHATTACHARYA; GACHHUI; SIL, 2013; CARDOSO *et al.*, 2021) This oxidative stress in DM can be partly caused by the auto-oxidation of glucose itself and/or the non-enzymatic glycosylation of certain proteins due to hyperglycemia, leading to the production of free radicals.(BHATTACHARYA; GACHHUI; SIL, 2013)

This potential mechanism underlying the hypoglycemic effect of both beverages was suggested in the study by Bhattacharya, Gachhui, and Sil (2013), where the administration of kombucha and black tea to alloxan-induced diabetic rats over a period of 14 days demonstrated the ability to reduce serum glucose by 56.4% with kombucha supplementation and 48.5% with black tea use. Other typical findings in diabetic rats, such as loss of body weight and levels of glycated hemoglobin, also showed a significant improvement in the intervention group.(BHATTACHARYA; GACHHUI; SIL, 2013)

The antioxidant capacity observed in both black tea and kombucha is primarily due to their rich composition of phenolic acids, organic acids, and flavonoids.(ALOULOU *et al.*, 2012; BHATTACHARYA; GACHHUI; SIL, 2013; YANG, Z.-W. *et al.*, 2009) However, the fermentation process involved in the preparation of kombucha confers a higher concentration of these components.(BHATTACHARYA; GACHHUI; SIL, 2013)

The superior antioxidant power of kombucha has been confirmed in various comparative studies.(ALOULOU *et al.*, 2012; BHATTACHARYA; GACHHUI; SIL, 2013; CARDOSO *et al.*, 2021) Previous analyses of kombucha composition identified 127 phenolic compounds, with 70.2% belonging to the flavonoid class.(CARDOSO *et al.*, 2021) Comparative evaluation of kombucha produced from green tea or black tea by Cardoso *et al.* (2021) indicated a higher antioxidant effect in supplementation with black tea-based kombucha,

surpassing the total antioxidant capacity observed in the control group and reaching levels similar to the green tea-based kombucha supplementation group.

In Bhattacharya, Gachhui, and Sil's study (2013), diabetic rats induced by alloxan received supplementation with kombucha and black tea for 14 days, and the results were compared with the reference hypoglycemic treatment, glibenclamide. Kombucha demonstrated superior antioxidant capacity to black tea, as evidenced by the clearance activity on important oxidant radicals (DPPH, hydroxyl, and superoxide), surpassing black tea by 18.9%, 17.2%, and 14.97%, respectively. The analysis also revealed the presence of d-saccharic acid 1,4-lactone in kombucha, an important substance with high antioxidant power, protecting plasma proteins and platelets against oxidative damage, not found in black tea. Kombucha also contains specific organic acids, such as glucuronic acid, capable of conjugating and solubilizing toxins, facilitating their elimination.

The antioxidant effect of both beverages was further investigated by analyzing the activity of key antioxidant enzymes, such as superoxide dismutase and catalase. (BHATTACHARYA; GACHHUI; SIL, 2013; CARDOSO *et al.*, 2021) Bhattacharya, Gachhui, and Sil (2013) observed an increase in superoxide dismutase levels in the hepatic and cardiac tissues and a reduction in pancreatic and renal tissues of diabetic rats. Kombucha had a more prominent effect compared to black tea, comparable to the synthetic drug considered the standard (glibenclamide). Cardoso *et al.* (2021) found a considerable increase in enzyme activity with kombucha supplementation in the liver, contributing to a significant reduction in nitric oxide levels and enhancing the total antioxidant capacity.

The improved total antioxidant capacity resulting from kombucha consumption, as demonstrated in Cardoso *et al.*'s study (2021), led to diabetic experimental groups having insulin sensitivity results similar to the control group. A similar effect was observed in Xu *et al.*'s study (2022), showing significant reductions in fasting glucose levels and caloric intake, along with recovery of body weight after 4 weeks of kombucha intervention.

Additionally, kombucha supplementation led to significant improvements in glucose regulation, insulin resistance, and pancreatic beta-cell function, as assessed by the Oral Glucose Tolerance Test (OGTT) and Homeostatic Model Assessment of Beta-cell function (HOMA-beta) (XU, S. *et al.*, 2022). Kombucha was effective in reducing resistance to insulin, promoting insulin secretion, and increasing hepatic glycogen content, indicative of improved insulin sensitivity.

The increased antioxidant capacity of kombucha also translated into reduced damage to hepatic, pancreatic, renal, and cardiac tissues. (ALOULOU *et al.*, 2012; CARDOSO *et al.*,

2021) Aloulou et al. (2012) assessed the effect of kombucha on the hepatic and renal functions of alloxan-induced diabetic rats. Diabetic rats showed significant increases in serum AST, ALT, GGT, urea, and creatinine levels. Kombucha and black tea administration reversed these increases to normal levels, as confirmed by histological analysis of tissues from experimental group rats. Bhattacharya, Gachhui, and Sil (2013) and Cardoso et al. (2021) also reported similar reductions in liver enzyme levels, indicating potential hepatoprotective effects.

Bhattacharya, Gachhui, and Sil (2013) investigated the hepatoprotective effects of kombucha by assessing DNA fragmentation and apoptosis induced by the accumulation of reactive oxygen species (ROS). Kombucha, similar to black tea, led to rearrangement of cells and a reduction in apoptotic bodies in the liver of diabetic rats. Furthermore, kombucha exhibited protective effects on kidney tissues, attenuating typical alterations observed in diabetic rats.(BHATTACHARYA; GACHHUI; SIL, 2013)

Finally, it is believed that the components resulting from the fermentation of teas by the SCOBY (Symbiotic Culture of Bacteria and Yeast), involved in kombucha preparation, also have regulatory effects on intestinal microbiota.(HU *et al.*, 2019; LI, Y. *et al.*, 2020) Previous studies suggest three main pathways that may explain the possible association between dysbiosis and the pathophysiology of type 2 diabetes.(XU *et al.*, 2022) Two of these pathways will be discussed more in-depth in this review.

The first pathway is associated with short-chain fatty acids (SCFAs).(ANHÊ *et al.*, 2020; AOKI *et al.*, 2017) These compounds are continuously produced by gastrointestinal probiotics and can activate L cells to secrete gastrointestinal hormones such as GLP-1 and PYY, regulating glucose metabolism and energy balance. Diets rich in fat and sugar can disrupt the intestinal microbiota, inhibit SCFA production, and promote the growth of gram-negative or pathogenic bacteria, leading to increased intestinal content of lipopolysaccharides (LPS) that damages the intestinal mucosa. This explains the second pathway linking dysbiosis and type 2 diabetes, where the inflammatory response triggered by mucosal and pancreatic islet damage can not only lead to insulin resistance through inflammation but also reduce insulin production.(HU *et al.*, 2019)

In this context, the study by Xu et al. (2022) aimed to evaluate the effect of dietary supplementation with kombucha on the type 2 diabetes condition in experimental rats by monitoring fasting glucose levels, analyzing the microbiota, and assessing intestinal mucosa integrity. Regarding dysbiosis, diabetic rats exhibited a significant reduction in intestinal microbiota diversity and a substantial increase in the population of gram-negative and pathogenic bacteria, including Proteobacteria and Bacteroides, markers.

3.2 HYPOLIPIDEMIC PROPERTIES

Furthermore, kombucha also possesses properties that have proven beneficial in terms of hypercholesterolemia, as demonstrated in studies with mice. Research has shown that the beverage is a more effective inhibitor of alpha-amylase and lipase activities, both in plasma and pancreas, compared to black tea. It also exhibits a promising effect in preventing the increase in blood glucose levels.(ALOULOU *et al.*, 2012) This effect extends to lipid absorption, with kombucha significantly delaying the absorption of LDL cholesterol and triglycerides (TG), while simultaneously increasing HDL cholesterol.(BELLASSOUED *et al.*, 2015)

Similar findings were reported by Permatasari *et al.* (2022), demonstrating that these effects are more pronounced in the variant of the beverage produced from sea grapes. Furthermore, kombucha showed important antioxidant properties attributed to compounds generated during fermentation, such as polyphenols and catechins. These substances helped reduce lipid peroxidation and strengthened the antioxidant defense system in the body. Superoxide dismutase (SOD) activity increased after consuming sea grape kombucha, contributing to neutralizing free radicals and reducing oxidative stress. This effect is particularly beneficial for obese patients, as excess fat accumulation can lead to increased release of reactive oxygen species (ROS) and trigger chronic inflammation. A significant decrease (50%) in cholesterol levels was also observed, attributed to the high level of palmitic acid (around 80%) in the beverage, a saturated fatty acid present in sea grapes.(PERMATASARI *et al.*, 2022)

Moreover, kombucha consumption positively affected lipid metabolism and body composition in animals, including reductions in total adipose tissue. It is worth noting that catechins play a crucial role in reducing lipid vesicles in the liver, improving organ health without affecting its weight, for instance, or other related parameters, thus implying an extension of hepatic steatosis.(ALOULOU *et al.*, 2012) In a parallel study, Cardoso *et al.* (2021) demonstrated that a high-fat and fructose diet led to increased vesicle accumulation in the livers of experimental rats, progressing to grade 2 hepatic steatosis. This condition was reversed to grade 1 through kombucha supplementation, similar to the control group.(CARDOSO *et al.*, 2021)

In addition to lipid-metabolic changes, there was an increase in total antioxidant capacity, along with the activation of superoxide dismutase (SOD) and catalase (CAT) enzymes in the liver.(CARDOSO *et al.*, 2021) Also, the hepatoprotective effect provided by kombucha, as evidenced by the reduction in alanine transaminase (ALT) enzyme activity, an indicator of

liver damage. There were no changes in aspartate transaminase (AST) and uric acid values, indicating preserved liver function.

The study by Permatasari et al. (2022) supported this hypothesis, as histological findings showed that kombucha had an improved effect on the pancreas and effectively protected liver and kidney function in diabetic rats. The hepatoprotective effect exerted by kombucha is extensive, reducing fat accumulation, lipogenesis, and increasing beta-oxidation, protecting the liver from lipotoxicity. Cardoso et al. (2021) also demonstrated that the use of kombucha can reduce hepatocyte apoptosis. These benefits were confirmed by the reduction in the expression of genetic markers of beta-oxidation and the reduction of lipogenesis markers, such as SREBP1c, a transcription factor that controls the expression of enzymes necessary for triglyceride synthesis and storage. Additionally, the lipolytic effects of kombucha can be attributed to its influence on the sympathetic nervous system (SNS), linked to increased energy expenditure, changes in appetite, positive regulation of enzymes involved in hepatic fat oxidation, and reduced nutrient absorption.(ALOULOU *et al.*, 2012)

Kombucha also demonstrated the ability to modulate the microbiota in mice with non-alcoholic fatty liver disease (NAFLD), characterized by fat accumulation in the liver in individuals with no significant history of alcohol consumption, intrinsically linked to obesity.(BELLASSOUED *et al.*, 2015) This study showed that NAFLD is influenced by both diet and intestinal microbiota. Therefore, diets high in fat promote changes in the microbiota and increase intestinal permeability, leading to the absorption of bacterial metabolites.(URRUTIA *et al.*, 2021) These factors can trigger tissue inflammation, possibly leading to hepatocyte inflammation and progression from steatosis to hepatitis.(MURUGESAN *et al.*, 2009)

On the other hand, the beverage demonstrated the ability to modulate the microbiota in mice with this pathology, reducing lipid and collagen deposition in hepatocytes and regulating the expression of the hepatic FXR gene.(MOREIRA, G. V. *et al.*, 2022) The supplementation increased the expression of CPT-1 to levels similar to the control group in the study by Mello, Materozzi, and Galli (2016). This protein is involved in mitochondrial pathways of beta-oxidation and fat transport, playing a crucial role in fatty acid oxidation and triglyceride reduction.(CARDOSO *et al.*, 2021) This supplementation also contributed to reducing PFK activity, an enzyme associated with glucose and lipid metabolism, maintaining a balance between glycolysis and intensifying both hepatic lipogenesis and lipolysis.(MELLO; MATEROZZI; GALLI, 2016; MOREIRA, G. V. *et al.*, 2022)

In conclusion, kombucha also demonstrates an increase in Adipo-R2 expression, a receptor for adiponectin, a hormone secreted by adipose tissue with a protective effect against inflammation and a positive modulator of the endocrine system. This is achieved through increased insulin sensitivity, reduced lipogenesis, glycogenolysis, gluconeogenesis, and increased fat oxidation. Another important factor observed was the reduction in ferric levels in the bloodstream of guinea pigs, contributing to a decrease in oxidative stress and potential atherosclerotic lesions.(ALAEI; DOUDI; SETORKI, 2020)

Thus, *in vivo* studies suggest that dietary supplementation with kombucha can provide numerous health benefits through various intricately interconnected mechanisms that still require further elucidation.

4 CONCLUSION

The present study aimed to synthesize the main scientific impressions regarding kombucha supplementation and its hypoglycemic and antilipidemic activities. Despite the limited literature available on this subject, the findings suggest significant therapeutic potential for combating diabetes in humans.

The literature uniformly indicates that the dietary effect of kombucha is presumably attributed to its potent antioxidant properties. However, given the scarcity of studies produced on this topic up to the present moment, it is evident that more research needs to be conducted to capitalize on the protective effects of kombucha in humans and establish its appropriate use as an effective functional food with therapeutic potential for the treatment of type 2 diabetes.

With confirmation of the therapeutic effects of kombucha, opportunities arise for the scientific community to explore and study non-pharmacological therapeutic alternatives for treating other diseases as well, utilizing these herbal and natural properties.

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