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Diabetes, Allopathic and Alternative Methods (Kombucha) for Its Treatment

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Abstract

Introduction: Diabetes is a disease characterized by an increase in blood glucose due to disorders in insulin production, this disease is widely distributed throughout the world. **Objective:** to review and systematize the general information on diabetes, as well as the traditional treatments and the findings on kombucha as an alternative method. **Method:** the information retrieval technique or literature review was used on the topics of diabetes, allopathic methods, kombucha, preparation procedures, chemical and microbiological components and pharmacological effects of the drink. **Results:** Various sources of information were found that explain the definition of diabetes and its classification. it commonly presents in four ways depending on the signs, the common ones being type 1, associated with destruction of the β cells of the pancreas and mainly affects minors, and type 2, which is related to genetic and environmental problems and It affects people over 18 years of age, and less frequently gestational diabetes and MODY type. Traditional drugs such as sulfonylureas, glinides and biguanides, thiazolidinediones and α-glucosidase inhibitors are used to control this disease, or alternative therapies are used such as kombucha, a fermented beverage that has its origins in China and is spread worldwide by its beneficial effects in chronic degenerative diseases such as diabetes, due to its chemical and microbiological content. **Conclusion:** The information establishes important data on kombucha as one of the complementary alternatives for the treatment of diabetes.

Keywords

Diabetes Mellitus, Alternative Medicine, Kombucha, Traditional Medicine, Pathophysiology of Diabetes

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1. Introduction

Diabetes is an alteration in the metabolism of carbohydrates, lipids and proteins, characterized by elevated glucose levels, due to failures in the production of insulin secreted by the β cells of the pancreas, or because the body does not respond correctly to this hormone, which is necessary for the body's cells to use glucose and transform it into energy [1].

In this disease, the central disorder is the resistance of all peripheral tissues to the action of insulin, due to defects in its synthesis due to modifications of the receptor, alterations in the intracellular mechanisms of action of this hormone, or because it is produced in low concentrations. The result is that excess glucose is generated in the blood, which causes damage to blood vessels and certain organs [2] such as the eyes, kidney, nerves and heart. Diabetes occurs in two ways, type 1, also called insulin-dependent or juvenile, and type 2. This classification, and the tests used for its diagnosis, were carried out by the National Diabetes Data Group of the United States of America, together with a committee of specialists from the World Health Organization (WHO) between 1979 and 1980 [3].

Diabetes is a disease that affects a large number of people around the world and continues to increase year after year, since according to studies conducted by the World Health Organization [4], the prevalence of this disease has increased in older people 18-year-olds from 108 million in 1980 to 422 million in 2014 and kills 1.5 million people a year. Currently, the number of patients with diabetes ranges between 194 and 246 million worldwide, while in Latin America it is approximately 25 million and in Mexico it is the leading cause of death [5].

Therefore, more effective procedures are sought to treat it through the use of allopathic drugs such as metformin from the biguanide group [6], or with alternative and/or complementary substances that improve the quality of life of patients who suffer from it, among which kombucha can be considered, a fermented drink that forms a zooglea resulting from a consortium of microorganisms (bacteria, fungi and yeasts) [7] and a large number of chemical compounds that give it therapeutic properties in chronic diseases, degenerative diseases such as diabetes and hypertension, among others [8].

The objective of this work was to review and systematize the general information on diabetes, as well as allopathic treatments and kombucha as an alternative method.

2. Diabetes

Diabetes is a disease known since 1535 BC described in the Ebers papyrus [9], but it is Aretaeus of Cappadocia in the 2nd century AD who gave the name to explain the typhoon effect on the water in the organism. Later Thomas Wills, in 1673, added the term honey mellitus for the characteristic taste of urine [10].

This condition is associated with secondary complications [11], such as: alteration in the metabolism of carbohydrates, lipids and proteins. It is one of the most studied diseases today and considered by various authors as a metabolic

problem [12] or metabolic syndrome [13], which is characterized by high blood glucose levels, due to various factors such as failures in the production of insulin secreted by the β cells of the pancreas, resistance of all peripheral tissues to its action [14], defects in its synthesis, due to receptor modifications, alterations in the intracellular mechanisms of insulin action, because it is produced in low concentrations or because the body does not respond correctly to this hormone [15].

Therefore, an excess of glucose in the blood occurs as a result, which causes damage to blood vessels and different organs such as the eyes, kidneys, nerves and heart [2] [5]. mention that insulin is necessary so that the body's cells can use glucose as fuel and transform it into energy [1].

The diagnosis of this disease can be made in two stages: the first is based on signs and symptoms, and for the type 1 diabetes presents: polyphagia, polyuria [16], polydipsia, blurred vision, weakness, weight loss, irritability, while type 2 diabetes manifests with marked weight loss, edema of the feet and hands, coagulation delay, tiredness, sleep, polyphagia, polydipsia and sexual weakness.In a second moment or stage, analyzes of the concentration of glucose, insulin and glycosylated hemoglobin should be performed [17], while, for gestational diabetes, they present some of the same symptoms, plus blood glucose concentrations that are slightly elevated (126 mg/dL) [18].

Diabetes is commonly classified according to the cause that originates it in: diabetes mellitus type 1 (DM1), diabetes mellitus type 2 (DM2), gestational diabetes and type MODY diabetes, the most common being type 1 and 2 [19].

2.1. Diabetes Mellitus Type 1

The diabetes DM1 or type 1 diabetes mellitus is an autoimmune disease in which the immune system attacks the β cells of the pancreas responsible for producing insulin [20], this coupled with a clear interaction of both genetic and environmental factors [21].

It develops as a consequence of the destruction of the β cells of the islets of Langerhans [22], so the affected individual must receive insulin as hormone replacement therapy, it is the main one in infants [20] and only 10% of the total of diabetes cases correspond to this type.

The characteristic symptoms of type 1 diabetes are polydipsia, polyuria [23], weight loss, blurred vision, excessive hunger and fatigue [20], this type of diabetes is subdivided into two [24]: diabetes Mellitus 1A (DM1A), which occurs when there is an autoimmune phenomenon and when autoimmunity is not detected, is called Diabetes Mellitus 1B (DM1B), considering that the rate of destruction of β cells determines the intensity of the clinical picture, it is worth mentioning that people who do not have DM possess a mechanism of anti-apoptosis and regeneration of β cells that in diabetics is stopped [25].

Type 1 Diabetes Pathophysiology

Known as insulin-dependent, type 1 diabetes mellitus is considered a chronic

problem [19]. Although it is essential to mention that it has a great genetic influence manifested in HLA (human leukocyte antigens), environmental factors and the presence of infectious processes such as rubella. In addition to factors related to food such as the ingestion of milk with toxins [22], the above results in an increase in weight of individuals, as well as insulin resistance. Autoimmune cell damage is considered to be manifested by the presence of anti-islet, anti-insulin, anti-glutamate decarboxylase, or anti-decarboxylase antibodies [26].

Insulin synthesis occurs in a pulsatile manner in the β cells of the islets of Langerhans in the pancreas. Depending on glycemia, it is released at the moment when glucose levels can rise due to the presence of stimuli captured by the CNS and by the concentration of glucose in the duodenum [22], this causes a decrease in insulin production, and a blockage of it from the liver. When food is ingested, insulin production rises as a result of an increase in blood glucose, with the aim of maintaining normal levels. If insulin production is insufficient, high blood glucose remains, then the characteristic signs of glucose occur, diabetes such as decreased body mass and loss of body fluids through urine. This is manifested by the difficulty of glucose to enter the cell [22] [27].

2.2. Type 2 Diabetes Mellitus

Type 2 diabetes mellitus, also called idiopathic, is due to genetic or environmental factors or the role played by some glands has now been discovered [28], it is the most frequent. It is usually diagnosed when a series of disorders that occur before hyperglycemia have already occurred.

DM2 has a genetic component that alters insulin secretion through deficient regeneration of β, insulin resistance or both, this type of diabetes represents 85 to 90% of patients with diabetes, being at In general, patients older than 40 years or obese and sedentary, in whom the disease develops gradually.

Its clinical expression can go unnoticed for many years [1] [28], since it goes through different stages before the diagnosis is reached; the first phase is glucose intolerance, something we know as pre-diabetes. In DM2, the individual does not need insulin supply, but could eventually need it throughout its evolution.

Pathophysiology of Type 2 Diabetes

Characterized by an increase in chronic glucose concentration [29], the presence of type 2 diabetes mellitus is mainly manifested by two factors; the former is characterized by insulin resistance in target organs, such as muscle, liver, and adipose tissue [30]; and this has as a consequence a second effect that is the increase in the production of insulin by the β cells of the pancreas, or both, followed one by the other [29], perhaps due to morbid obesity caused by low metabolic activity, hypertension and family inheritance, which forces the pancreas to produce more insulin to keep glucose levels normal.

In this disease it is difficult for the body to adapt to the new insulin requirements, so it presents changes in its function and activates the receptors by signals that allow the activation of the glu4 receptor (glucose transporter) and thus

allow the entry of glucose from the blood to the cell [19].

2.3. Gestational Diabetes

Gestational Diabetes Mellitus (GDM), is a disease that biologically involves the mother, the fetus and the fetal tissues [31], it was first diagnosed in the 50's by OSullivan and Mahan [32]. It is characterized by an elevation of glucose [33], without a history of the presence of type 1 or type 2 diabetes [34], with patient characteristics such as sedentary lifestyle, obesity and lack of physical exercise, its prevalence is between 1% and 14% [31] and is diagnosed in the 2nd or 3rd trimester of pregnancy in about 40% of patients.

Physiopathology of Gestational Diabetes Mellitus

Gestational diabetes is manifested by two factors, the first is insulin resistance and the second is poor response by cells to produce it [33]. During pregnancy, blood glucose concentrations are modified due to the influence of a high amount of reproductive hormones such as progesterone and estrogen, in addition to a placental hormone (placental lactogen), which have a relative effect on insulin production [35], which manifests itself with increased and large metabolic effects on proteins, lipids, and carbohydrates [33].

In the first third of gestation, insulin levels are maintained, which regulates blood glucose, while in the second and third period insulin increases and glucose begins to drop and, subsequently, the influence of estrogens and progesterone cause again a hyperinsulinemia followed by a hyperglycemia near the end of gestation. The placental lactogen hormone and the influence of insulinase generate insulin resistance, which results in hyperinsulinemia and subsequently a balance in blood glucose concentration [35].

As a treatment, it may require administration of insulin during the disorder, it is considered one of the most common complications during pregnancy [34].

Other specific types of diabetes may require insulin administration for treatment [25]: monogenic DM, MODY-type DM, LADA-type DM, exocrine pancreas diseases, drug-induced DM [17].

2.4. Morbidity and Mortality of Diabetes

The prevalence of this disease and its complications in the body causes great economic and health repercussions in the countries [36]. Diabetes is a disease that affects a large number of people around the world [37], reaching epidemic proportions [25] and continues to increase every year. Currently the number of patients with diabetes ranges from 282 million worldwide, while in Latin America it is approximately 62.8 million. In Mexico there are 8.7 million patients, it is the largest cause of death per year [4].

3. Treatments

3.1. Allopathic Medicines

There are a large number of treatments for this disease with the sole objective of

safeguarding the physiological conditions of patients who suffer from it and offering a better quality of life, treatments with traditional medicines consist of the use of drugs hypoglycemic agents, achieving biochemical control to prevent cardiovascular and other organ complications regardless of body conditions [38]. These are made up of four groups of allopathic medications.

3.1.1. Sulfonylureas

They are derivatives of the sulfonylureic, discovered in 1944 [39], they function as insulin secretagogues. To this group belong glibenclamide, glicazide, glimepiride, and glipizide [40].

Sulfonylureas bind to a receptor located on the membrane of the β cell of the pancreas, which are part of the K+ channels, which causes their closure and the Ca++ channels open, this enters the cell cytoplasm and insulin is produced for its release. exocytosis [39].

They are administered orally and are metabolized in the liver, having inactive metabolites as products that are eliminated in the urine or via the bile [41].

Other hypoglycemic drugs are glinides or meglitinides such as repaglinide and nateglinide [40], repaglinide is derived from carbamoylmethyl benzoic acid and nateglinide is obtained from D-phenylalanine [42]. These drugs have a mechanism of action similar to sulfonylureas, since by binding to the membrane they block K^+ receptors causing membrane depolarization, favoring the release of insulin caused by the opening of Ca^{2+} channels [43].

3.1.2. Biguanides

This group includes metformin, phenformin and buformin, they originate from Gaudiniana, an active ingredient obtained from *Galega officinalis*, it was synthesized at the beginning of the 20th century, but it began to be used in the 1950s, the most used is metformin, since phenformin and buformin were withdrawn from the market for causing lactic acidosis [6].

The action of this drug is not carried out on the β cells of the pancreas like the sulfonylureas and glinides. It has been studied that the liver participates in the inhibition of gluconeogenesis and glycogenolysis, it also increases glucose uptake in muscle, it decreases glucose in the digestive tract [6].

In the liver, cation receptors called OCT-1 are located, which allow the entry of metformin into the hepatocyte, causing an inhibition in the respiratory chain of the mitochondria and increasing its concentration in the cytoplasm, this has as a consequence an increase in ATP energy; ADP and AMP, which leads to a decrease in glucose production and at the same time an AMPK protein stimulates insulin action [44]. It is administered orally, its absorption occurs in the small intestine, its half-life is from 1.30 to 5 hours, it is not metabolized and its elimination is renal.

3.1.3. Thiazolidinediones

Also known as glitazones, it is practically one of the newest groups, since they appeared on the market in 1997 [45]. Four drugs belong to this group of hypog-

lycemic agents: troglitazone, rosiglitazone, glitazone and pioglitazone [46], of which only the last two are still used as safe hypoglycemic agents [40], since the other two were withdrawn from the market due to causing hepatotoxicity [47].

These drugs act by increasing the ability of insulin to lower blood glucose levels, in addition to decreasing resistance to it, causing glucose to enter the cell where it is needed. This medicine is administered orally, it is absorbed very quickly, its metabolism is hepatic and it is eliminated by the kidneys.

The action of these drugs is completely different, since they involve a type of receptor known as peroxisome proliferative receptors (PPAR), involved in cell differentiation and gene expression of tissues such as adipocytes, muscle, intestine thick, mammary gland and liver. while in the pancreas they stimulate the synthesis of insulin.

Another effect is that it can cause apoptosis in insulin resistant cells [48]. When thiazolidinediones bind to their PPAR receptor, it causes some cofactors to uncouple from the PPAR promoter region, then transcription of genes that have a role in the glucose transporter (GLUT4) signaling cascade occurs. This causes an increase in insulin receptors 1 and 2 in muscle and fat and as a consequence an increase in the entry of glucose into these tissues, lowering blood glucose.

3.1.4. α-Glucosidase Inhibitors

This last group of hypoglycemic drugs is contemporary with the thiazolidinediones, since they were marketed from 1995 [45]. Its representatives are: acarbose, miglitol and voglibose, these have the function of delaying the conversion of polysaccharides and disaccharides into monosaccharides in the intestine, which results in a lower concentration of glucose entering the blood [38].

The α-glucosidase (glucoside hydrolases) is an enzyme that acts by hydrolysis to reduce carbohydrates to smaller sugars so that they are subsequently absorbed [49]. These drugs work by competitive inhibition with digestive enzymes and their function is to delay the absorption of carbohydrates. carbohydrates, which causes the elevation of glucose concentrations after eating not to be as marked [45].

3.2. Alternative Medicines

The use of alternative medicines is not new, since since ancient times Hippocrates affirmed that the herb was useful for health and Confucius used ginger in all his meals [50]. Alternative and/or complementary therapies constitute a therapeutic group not integrated in the practice of medicine supported by the scientific method and include traditional medicine based on the use of natural products (PN).

Some specialists mention that it is difficult to calculate the percentage of the population that uses them due to their unconventional distribution, but it is considered to be growing, both in the developing world and in the West [51]. According to the WHO, 80% of the world's population, that is, more than four

billion people, use plants as their main medicinal remedy and this has continued to increase in recent years in the general population, as well as in patients with chronic diseases such as diabetes mellitus [52] [53].

3.2.1. Alternative Medicine Preparation

The proper use and preparation of alternative and/or complementary medicines benefit the body by purifying and healing. A large number of plants are used, among which we can highlight, to mention a few: nopal, chaya, aloe, as well as various fruits such as pineapple, lemon [54]. Preparations in the form of infusions, teas, decoctions, juices, macerations or ferments are also used [55] [56].

3.2.2. Fermentation

Fermentation is understood as the chemical process that occurs in a solution by the action of an enzyme or set of enzymes synthesized by microorganisms for the purpose of using it as a healing substance [57]. In the case of kombucha, a period of time of at least 3 days and up to 60 days is required, depending on the temperature and sucrose concentration [58]. Fermented beverages are also considered as alternative medicines and have been used from ancient times to the present, since they contain a large number of microorganisms with probiotic properties and prebiotic compounds, as in kombucha [59].

4. Kombucha

Kombucha is a fermented beverage, the result of a group of bacteria and yeasts, sweetened with sucrose to which 20% of an infusion is added [7], with a pH of 2.7-3 [60], with a history of thousands of years in the East and yet it is quite popular today in the West.

It is traditionally prepared by fermenting sweetened black or green tea [61], which is inoculated with a film formed during previous cultivation (zooglea), popularly known as tea fungus, and incubated statically under aerobic conditions for 7 - 10 days [62], a period in which it begins with a thin and transparent layer, later it takes on a whitish gelatinous appearance [63].

4.1. Composition of Kombucha

Kombucha is a drink composed of two main elements, on the one hand, it contains a group of bacteria and yeasts [8], while on the other there are a large number of chemical components, both elements depend on different factors such as; the tea with which the kombucha is prepared, either black or green; the fermentation time, since the longer the fermentation lasts, the more acidic the solution becomes; or the source of the inoculum with which the kombucha is made [61].

4.2. Microbiology of Kombucha

The bacteria that are part of the fungus belong to the order *Acetobacter xylinum*, *Acetobacter xylinoides*, *Bacterium gluconicum*, *Acetobacter aceti*, *Acetobacter*

pasteurianus and *Gluconobacter oxydans*, *Lactobacillus sp.*, *Lactococcus sp.*, *Leuconostoc sp.*, *Bifidobacterium sp.*, *Thermus sp.*, *Allobacullum sp.*, *Ruminococcaceae Incerate Sedis*, *Propionilbacterium sp.*, *Enterococcus sp.* [58].

The fermentation process of these microorganisms consists of converting sucrose into glucose, fructose, ethyl alcohol, carbon dioxide and acetic acid [61]. In addition to bacteria, there are many species of yeast. including species of *Saccharomyces*, *Saccharomycodes*, *Schizosaccharomyces*, *Zygosaccharomyces*, *Brettanomyces*, *Candida*, *Torulospora*, *Koleckera*, *Pichia*, *Mycotorula*, and *Mycoderma.*

Of the Saccharomyces species, *Saccharomyces sp. Saccharomyces cerevisiae*, *Saccharomyces bisporus*, *Saccharomycoides ludwigii*, *Schizosaccharomyces pombe*, *Zygosaccharomyces rouxii*, *and Zygosaccharomyces bailii. From the species Brettanomyces intermedius*, *they isolated Brettanomyces bruxellensis*, *B. claussenii. Brettanomyces*, *Zygosaccharomyces and Saccharomyces spp. Zygosaccharomyces and S. cerevisiae*, *Zygosaccharomyces kombuchaensis sp. Z. kombuchaensis sp.* and *Zygosaccharomyces lentus.*

From the Candida species, *Candida sp*, *Candida famata*, *Candida guilliermondii* and *Candida species. C. fameta*, *Candida stellata. Candida guilliermondi*, *Candida colleculosa*, *Candida kefyr* and *Candida krusei*, were isolated. As for the Torula species, the following were found: *Torulopsis*, *Torulaspora delbrueckii*, *Mycotorula*, *Mycoderma*, *Pichia*, *Membrana faciens de Pichia*, *Kloeckera apiculata and Kluyveromyces africanus.*

The Russian researchers Barbancik in 1958 and Konovalow in 1959 discovered that the presence of antibiotics, organic acids, alcohol and carbonic acid as a product of fermentation give it a protective property, which prevents bacteria or yeasts that are not part of the fermentation from adhering. of the zooglea (Gram negative) [57]. The kombucha fermentation process gives rise to different chemical compounds such as: acids (lactic, acetic, gluconic and glucuronic), ethanol and glycerol, vitamins, antibiotics and amino acids. The concentration of these products will depend on the time and the equipment in which it is fermented [8].

4.3. Chemical Components of Kombucha

Chemical tests of the kombucha beverage have indicated the presence of a variety of compounds, including organic acids, mainly acetic, gluconic and glucuronic acid (GlcUA), citric, L-lactic, malic, tartaric, malonic, oxalic, succinic, pyruvic and usnic acids can also be found [64].

Regarding the vitamin content of this drink, the B vitamins: B1, B6 and B12 and vitamin C. The minerals present in kombucha tea are copper, iron, manganese, nickel and zinc. In addition, traces of lead were detected, which are minerals that increase due to the metabolic activity of kombucha [58]. Another of the substances found are polyphenols, considered as antioxidants and preventive of chronic degenerative diseases. The polyphenols found are: epicatechin (EC), ep-

icatechin gallate (ECG), epigallocatechin (EGC), epigallocatechin gallate (EGCG) and theaflavin (TF). Elements that increase with fermentation time [65]. Unlike the side effects caused by allopathic medicine, the active ingredients of kombucha have the ability, due to their metabolic characteristics, to restore cell membranes without any side effects, thus promoting bodily well-being [66].

4.4. Therapeutic Properties of Kombucha

Kombucha or kombucha tea has been widely used for its healing properties due to the aforementioned components, and each of the metabolites provides therapeutic effects, since liver-protective properties have been observed [67], as an alternative method in arteriosclerosis [68], to mention a few examples.

Usnic acid has an important role as one of the main elements of kombucha, it acts on mitochondrial respiration by decreasing its energy efficiency and consuming more calories than normal to perform a certain physiological function in the presence of obesity [69].

Polyphenols exert antidiabetic actions, whose main mechanism in the gastrointestinal tract is to inhibit or slow down the digestive process of carbohydrates. While, at the systemic level, some compounds that promote insulin sensitivity, decrease oxidative stress, promote insulin secretion [70], these substances prevent damage to the β cells of the pancreas or stimulate the regeneration of this type of cells in rats in which diabetes was induced and thus preserve the concentration of insulin [71].

Another important compound in the antidiabetic effect is acetic acid, which can reduce blood glucose by preventing the complete digestion of carbohydrates that is carried out by gastric emptying, inactivating some of the digestive enzymes that break down carbohydrates into sugar, which slows down the conversion of complex carbohydrates into sugars for the bloodstream, which causes a decrease in blood glucose, avoiding its elevation [8].

Another type of substance found in kombucha is a set of enzymes such as: invertase, amylase, and catalase, whose function is to degrade food molecules, making them smaller, facilitating their assimilation by the body. For example, invertase converts sucrose to glucose and fructose. Lactase hydrolyzes lactose, converting it into glucose and galactose. An analysis carried out in 1993 by the University of Stuttgart also showed the presence of a significant amount of choline, in addition to containing a large proportion of volatile compounds that are the ones that partly give it its flavor and particular aroma [72].

The presence and quantity of the chemical components depends on the microorganisms in the culture for fermentation, fermentation temperature, sucrose content, and type of tea used [58].

4.5. Beneficial Effects of Kombucha

The health benefits of kombucha consumption have been extensively studied [73] in a large number of ailments, mainly those considered chronic degenera-

tive such as arteriosclerosis [68], hypertension, hyperlipidemia and diabetes, for lower glucose levels [8], among others.

Zubaidah *et al.* (2019) induced diabetes in Wistar rats with streptozotocin and subsequently administered kombucha made from snake fruits, the drink had a pH of 3.2. A decrease in blood glucose level, normal cells of the pancreas, and an adequate lipid profile were identified. The authors point out that the organic and phenolic acid content of Kombucha could explain its antidiabetic activity [74].

Dashti and Morshedi (2000) carried out a comparative study between the effect of black tea and kombucha tea on blood glucose levels in diabetic rats in which diabetes was induced with a dose of 60 mg/kg of streptozotocin administered daily. IP form, from which it was obtained that the blood glucose levels of animals that received both black tea and kombucha tea decreased in relation to the animals in the control group and did not show a significant difference between the treatment groups [50].

Aloulou *et al.* (2012) carried out a comparative study between black tea and kombucha tea at doses of 5 ml, orally, to evaluate the hypoglycemic effect in diabetic rats induced with alloxan for a period of 30 days. Kombucha was shown to have better hypoglycemic effects than black tea in blood samples obtained from rats, concluding that this substance can be used as a hypoglycemic agent [37].

Bhattacharya *et al.* (2014) used fermented kombucha tea and compared with the use of unfermented black tea in rats with alloxan and the results first showed a decrease in insulin production and an increase in glucose and after treatment a decrease in insulin production was presented. better recovery with kombucha tea than black tea, which could be due to the formation of some antioxidant molecules during the fermentation period [70].

Olinda *et al.* (2016) carried out a comparative study between kombucha and glibenclamide to measure the protective effect on the kidney of rats with diabetes induced with streptozotocin, in which glycemia was also measured, both in the control group and in the rats treated with kombucha. and glibenclamide, showing a significant difference between treatment groups in relation to the control group [11].

4.6. Proposed doses of Kombucha

In relation to the dose of kombucha, it is necessary to consider the pH of the drink that fluctuates in the range of 2.5 - 3.5 [7], the studies carried out by researchers do not differ much in therapeutic recommendations, both in experimental animals and larger animals, or in humans, although it is important to point out that not all patients can use it.

Olinda *et al.* (2016) used kombucha in rats at a dose of 1.71 ml/kg orally for a period of 14 days of treatment [11]. Stevens recommends 100 ml in humans for the first week and 200 ml for the second and 300 ml for the third week [63]. While Günter (2005), made therapeutic recommendations of 500 to 750 ml of

kombucha per day [57]. On the other hand, in the trials carried out by our work team, kombucha was used at a dose of 324 mg/kg orally for a period of 21 days of treatment to observe the hypoglycemic effects [75].

5. Conclusion

There is evidence that alternative medicines, including kombucha, for the treatment of diabetes mellitus represent an option to avoid the side effects caused by conventional drugs. The decision to carry out a review on the effects of kombucha is based on the results obtained by several researchers in the field of medicine, both human and animal, establishing its beneficial effects. It is important to emphasize that, according to this review, a series of factors such as the species in which the kombucha is used, the fermentation time, the dose to be used, since it is verified that there are differences in the concentration of the chemical and microbiological components.

Documentary Research Approach

This research only intends to present the findings on the use of kombucha as an alternative and/or complementary medicine in the treatment of diabetes.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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