Herbal medicine *Cissus sicyoides* as a complement to the treatment of type II Diabetes Mellitus

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ABSTRACT

Diabetes Mellitus (DM) has become a public health issue in recent years. The comorbidities that affect its carriers lead to a reduction in daily activities, worsening of quality of life, and increased mortality because of diseases and complications of the disease. The basic health units, together with their health promotion programs and prevention strategies, have been adapting the protocols for comprehensive care of patients with diabetes mellitus, guiding them to a healthier lifestyle. This study showed the benefits of the complementary use of phytotherapy, specifically Cissus sicyoides in patients with diabetes mellitus, demonstrating hypoglycemic effects in 50% of patients submitted to the use of dry extract. As an adjuvant to the treatment of diabetes mellitus II, there is a need to implement strategies that reinforce the use of herbal therapies and research needs to be carried out for this purpose.

Keywords: Phytotherapy, Diabetes Mellitus, *Cissus sicyoides*.

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INTRODUCTION

At an archaeological site in northwestern Spain, dental plaques from extinct Neanderthals (Homo neanderthalensis) have found microfossils of plants including yarrow (Achillea millefolium) and chamomile (Anthemis arvensis). These herbs lack nutritional value and have a bitter and unpleasant taste. However, they are widely used in traditional medicine. These fossilized teeth date back 49,000 years and are possibly the earliest evidence of the use of medicines.1

The use of medicinal plants in the recovery of health has evolved over time from the simplest forms of treatment to the technologically sophisticated forms of industrial manufacturing used by modern man. Although there is a huge difference between the two ways of use, there is a common factor between them: the active ingredient that causes beneficial reactions in the body, capable of resulting in the recovery of health.[2]

Diabetes mellitus (DM) is a metabolic disease caused by the inability of the pancreas to secrete insulin (type I diabetes) or decreased tissue sensitivity to insulin (type II diabetes). It can also be caused by degeneration or inactivation of the beta cells of the islets of Langerhans.[3] It is a syndrome in the metabolism of carbohydrates, proteins and fats, and can be multifactorial.[4.5]

Due to the deficiency of insulin in the tissues, the metabolism will not have enough glucose to generate energy. Therefore, it uses fat as an energy source and consequently blood glucose levels are altered.[3]

Currently, Diabetes has become a major global public health problem and is growing every year. In 2023, this number reaches the mark of 529 million people worldwide. One in every 350 children has type I diabetes, which is caused by the destruction of insulin-producing cells due to an immune system problem in which antibodies attack the cells that produce insulin. Type II, on the other hand, is the resistance or deficiency of insulin secretion. It is the most common, 90% of cases are acquired throughout life.[6]

The increase in diabetes cases in the world is related to several socioeconomic, demographic, genetic and environmental factors. Where there is an increase in risk factors, such as obesity, lack of physical activity and a healthy diet, among other multifactorial causes. Chronic diseases are one of the biggest public health problems in Brazil and in the world, with high economic costs for society, in addition to the impacts on people's quality of life and life expectancy.[5]

In Brazil, diabetes affects about 7.7% of the Brazilian population, occupying the second place among the chronic diseases with the highest incidence and the fourth place in mortality from chronic diseases in Brazil.[5]

As we can see, Diabetes Mellitus is an important pathology with a high number of carriers and requires continuous care, therefore, we seek to evaluate the benefit of the use of an herbal

medication as a complement to the treatment of these patients. Among the numerous species of plants with hypoglycemic characteristics, we choose *Cissus sicyoides*, better known as "INSULIN".

Nome cientifico – Cissus sicyoides.[2,7]

Popular names – Portuguese: Insulina vegetal, cipó-pucá, indigo climber, uva-brava, cortina de pobre, tinta-dos-gentiles. Spanish: cortina del diablo, insulina vegetal. English: princess vine, toad vine.

Part used: Aerial part.

Distribution habitat: It is distributed in tropical and sub-tropical areas of the Americas, starting from the southern United States and Mexico to Brazil and Argentina.[2]

History of the plant: During the nineteenth century it was used as a laxative, against bruises and in blennorrhagia and as anti-virals.[2]

Therapeutic properties: hypoglycemic, antiinflammatory, antibacterial, bronchodilator, anticonvulsant, antiserotonergic, nervous system depressant, gastroprotective, uterine contraction.[7]

Contraindication: It is contraindicated in case of pregnancy due to the action of uterine contraction. Its use is also contraindicated in cases of hypercalcemia and history of lithiasis due to the presence of calcium oxalate. Its use in cases of asthma attacks is inappropriate.

Adverse Effects: To date, no adverse effects have been reported in humans.[2]

Forms of use: The plant is recommended in the form of decoction of the leaf orally (tea).[2] 2 cups (coffee) or 20 grams of dried leaf in a liter of boiling water. Placing the plant in a container and pour boiling water over it, smother and let it rest for at least 10 minutes and strain before use. drinking 1 cup (tea) 3 times/day (30 min after meals).[2.7]

The objective of this research was to evaluate the use of the medicinal plant insulin – *Cissus sicyoides* as a complement to the treatment of patients with type II diabetes mellitus, based on a qualitative analysis, collected from a group of 12 individuals who agreed to participate in the research, who live in the neighborhood of Jardim Eldorado – Palhoça. A semi-structured questionnaire was applied to the selected research subjects and an evolution form was used to collect glycemic levels before and during the use of tea.

METHODOLOGY

This study is characterized as a descriptive field research, of the exploratory type. Qualitative analysis techniques were used, based on the approximation with the interviewed patients.

For Minayo, qualitative research is characterized by being concerned with reality that cannot be quantified and by deepening its knowledge of human actions and reactions.[8]

The study was carried out at the Jardim Eldorado Basic Health Unit, Palhoça/Santa Catarina. The extension area of the Basic Unit comprises the population living in the Jardim Eldorado neighborhood, which makes up 1,000 families. On average, 48 patients with insulin-dependent type I diabetes mellitus and 120 non-insulin-dependent patients with type II diabetes mellitus are followed.

The interview was conducted with 10% of the population, 12 people, all of whom had type II diabetes mellitus and lived in the coverage area. Patients followed by the Health Unit, both sexes, with a mean glycemic score of 150 to 300 mg/dl were selected.

The research took place from July 12 to December 20, 2008. Data collection was divided into three stages:

After a lecture on diabetes, which discussed the objective of the project to be applied to this population, the active participants of the research were selected, a total of twelve patients with type II diabetes mellitus, who fit the previously established standard and requirement. A home visit was made to sign the free and informed consent form and the history was collected. With these data, clinical conditions and the habits of the individuals in relation to their pathology were evaluated, thus being able to prepare a health education activity. A folder was delivered explaining the pathology (diabetes mellitus) and guiding care regarding diet and physical activity.

2nd moment: For a period of 49 days, weekly, the glycemic rate was evaluated along with eating habits and the practice of physical activities.

3rd moment: After the end of the 49 days, checking the glycemic rate, we make a new home visit to give them the medicinal plant for daily consumption. Delivered properly packaged and dosed, advising on the preparation and therapeutic use of tea through dialogue and an educational folder.

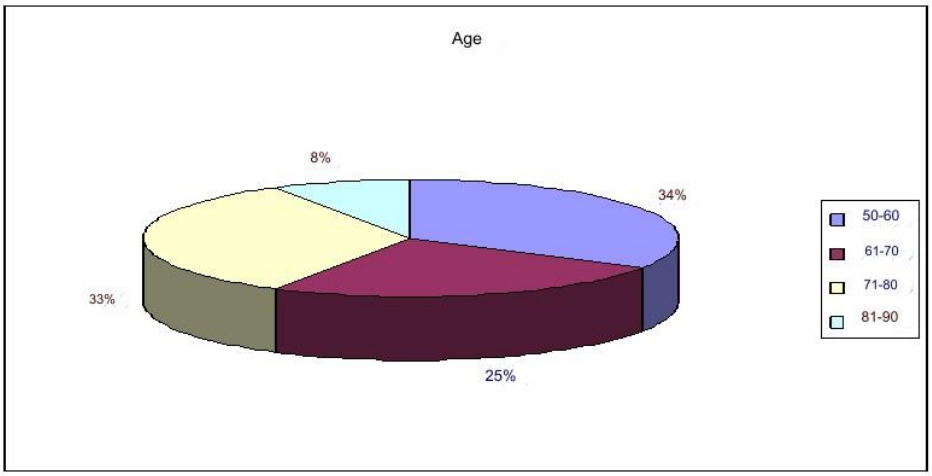
We advise that the use of tea should take place for the next 58 consecutive days, from this we carry out weekly home visits to assess the glycemic rate and eating activities and physical activities, clarifying doubts and verifying the correct use of the tea.

For the development of this research, the recommendations of Opinion 404/2008 of the National Research Ethics Commission were adopted, which determines that the objective of the Research Ethics Committees is to protect the human being in his dignity and integrity and to contribute to scientific development and to be approved by the Ethics Committee of the University of Southern Santa Catarina – UNISUL.[9.10]

RESULTS AND DISCUSSION

Regarding the age of the research participants, it can be seen in graph 01 that 4 (four) were aged between 50 and 60 years representing 34%, 4 (four) between 61 and 70 years (33%), 3 (three) between 71 and 80 years (25%) and 1 (one) between 81 and 90 years (8%), we observed that most of the research subjects have an elderly age group 66% (over 61 years).

Graph 01 – Age range of the research subjects.



Source: The Authors

Diabetes is common and has an increasing incidence. It is estimated that in 1995 it reached 4.0% of the world's adult population and that by 2025 it will reach 5.4%. Most of this increase will occur in developing countries, accentuating the current pattern of concentration of cases in the 45-64 age group. In Brazil, at the end of the 1980s, it was estimated that diabetes occurred in about 8% of the population, aged 30 to 69 years, living in Brazilian metropolitan areas. This prevalence ranged from 3% to 17% between the 30-39 and 60-69 age groups. The prevalence of impaired glucose tolerance was also 8%, ranging from 6 to 11% among the same age groups. Today, it is estimated that 11% of the population is 40 years of age or older, which represents about 5 and a half million carriers.[11]

Regarding the participants' schooling, 9 (nine) 75% had not completed elementary school, 2 (two) 17% were illiterate and 1 (one) 8% had completed high school.

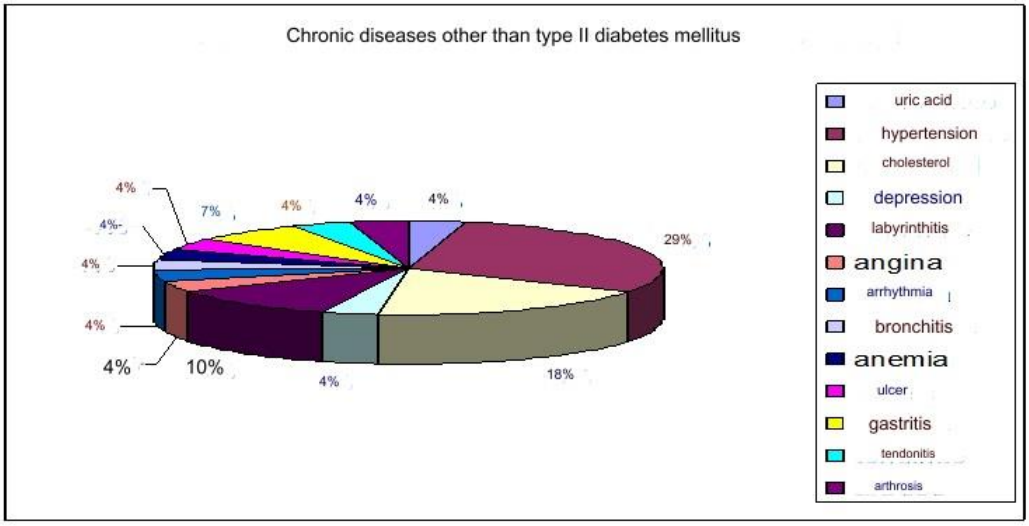
We can see that most of the interviewees had incomplete elementary schooling, based on these data we directed our dialogue in a way that was accessible to them.

Regarding the marital status of the participants, 4 (four) 33% were widowed and 8 (eight) 67% were married.

Due to their advanced age, we noticed that some participants, without a partner, could have this factor related to difficulty in care or lack of family support.

As for chronic diseases, in addition to type II diabetes mellitus, we can see in graph 04 that among the 12 (twelve) participants, most of them had systemic arterial hypertension (SAH) and hypercholesterolemia. (Chart 02)

Graph 02 – Chronic diseases that the research subject has, in addition to type II DM.



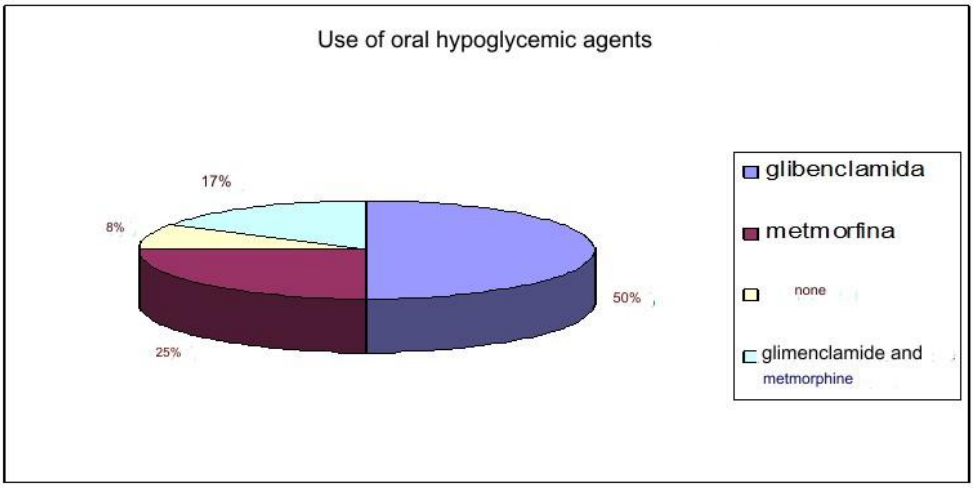
Source: The Authors

The natural history of diabetes is marked by the appearance of chronic complications, generally classified as microvascular – retinopathy, nephropathy, and neuropathy – and macrovascular – coronary artery disease, cerebrovascular disease (CVA) and peripheral vascular disease. All of them are responsible for significant morbidity, with rates of cardiovascular and renal mortality, blindness, limb amputation, loss of function, and quality of life much higher than individuals without diabetes. Ischemic cardiovascular diseases are more frequent and earlier in individuals with diabetes compared to others. In women with diabetes, the protective effect typically recognized for the female gender disappears. The symptomatology of the three major cardiovascular manifestations – coronary heart disease, cerebrovascular disease and peripheral vascular disease. Systemic arterial hypertension affects the majority of patients with diabetes. It is an important risk factor for coronary heart disease and microvascular complications such as retinopathy and nephropathy.[11]

Patients with type II diabetes have a higher prevalence of lipid abnormalities that contribute to higher rates of coronary artery disease (CAD). Therefore, every patient with a risk of coronary artery disease above 20% should receive a statin, regardless of LDL cholesterol level. Monitoring of control (LDL cholesterol, triglycerides, and HDL cholesterol).[11]

Regarding the use of oral hypoglycemic agents, we can see in graph 05, 2 (two) 17% used oral hypoglycemic agents glibenclamide and metformin, 3 (three) 25% used only metformin, which represents 6 (six) 50% used only glibenclamide, which represents and only 1 (one) 8% did not use hypoglycemic medications.

Graph 03 – Oral hypoglycemic agents used by the research subjects.



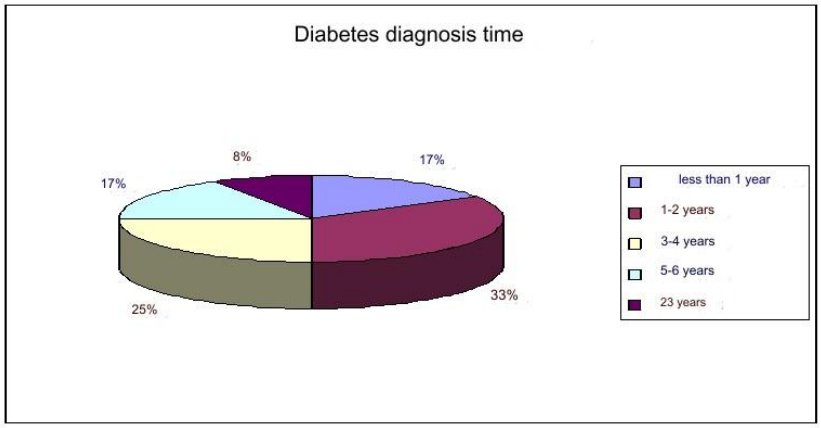
Source: The Authors

Glibenclamide is an oral hypoglycemic agent widely used in type II diabetes mellitus, some pharmacokinetic parameters of glibenclamide are well known: they are rapidly and adequately absorbed by the intestine, distribute in the extracellular fluid, partially bind to plasma proteins; The speed and mode of degradation of these drugs vary. The differences in the duration of action depend on the course of metabolism and the rate of excretion of each.

According to information from the Glibenclamide Leaflet, 45 to 84% are absorbed by the intestines. Of the five metabolites, one is only partially active: the two hydroxylated metabolites are not hypoglycemic and are rapidly and completely eliminated.

Regarding the time of diagnosis of type II diabetes mellitus, we can observe in graph 06 that only 2 (two) 17% had diabetes diagnosed less than 1 (one) year ago, 1 (one) 8% diagnosed 23 years ago, another 2 (two) 17% discovered that they had diabetes mellitus between 5 and 6 years, 3 (three) knew that they were diabetic between 3 and 4 years representing 25%, and 4 (four) had diabetes diagnosed 1 to 2 years ago, representing 33%. (Chart 04)

Graph 04 – Time of diagnosis of diabetes in the research subjects.



Source: The Authors

About 50% of the population with diabetes does not know that they have the disease, sometimes remaining undiagnosed until signs of complications appear. Therefore, screening tests are indicated in asymptomatic individuals who are at higher risk of the disease, although there are no clinical trials documenting the resulting benefit and the cost-effectiveness is questionable. Factors indicative of higher risk are: Age >45 years; Overweight (Body Mass Index, BMI >25); Central obesity (abdominal girdle >102 cm for men and >88 cm for women, measured at the height of the iliac crests); Family history (mother or father) of diabetes; Hypertension (> 140/90 mmHg); HDL cholesterol >35 mg/dL and/or triglycerides >150 mg/dL; Defined cardiovascular, cerebrovascular, or peripheral vascular disease.[11]

Regarding the practice of physical exercises, we can observe in graph 7 that only 3 (three) 25% practiced physical exercise such as walking and dancing, another 9 (nine) equivalent to 75% did not practice any type of physical exercise.

Physical activity and exercise are crucial for preventing complications and managing blood glucose in people with diabetes. They improve glycemic control, reduce cardiovascular risks, promote well-being, and can help with weight loss. Even without weight loss, eight weeks of exercise reduces HbA1c by 0.66 percent. People with diabetes should avoid a sedentary lifestyle by incorporating light activities such as standing or walking.[12th]

The regular practice of physical activity is indicated for all patients with diabetes, as it improves metabolic control, reduces the need for hypoglycemic agents, helps promote weight loss in obese patients, decreases the risks of cardiovascular disease and improves quality of life. Thus, the promotion of physical activity is considered a priority.[11]

Environmental, social and psychological factors may play an important role in the development of type ll diabetes mellitus, and its prevalence is higher in overweight patients than in normal weight patients aged 20 to 75 years. In patients in the age group of 20 to 45 years, the risk is 3.8 times higher. resistance exercise 3 times a week, in the main muscle groups. [G3] Physical

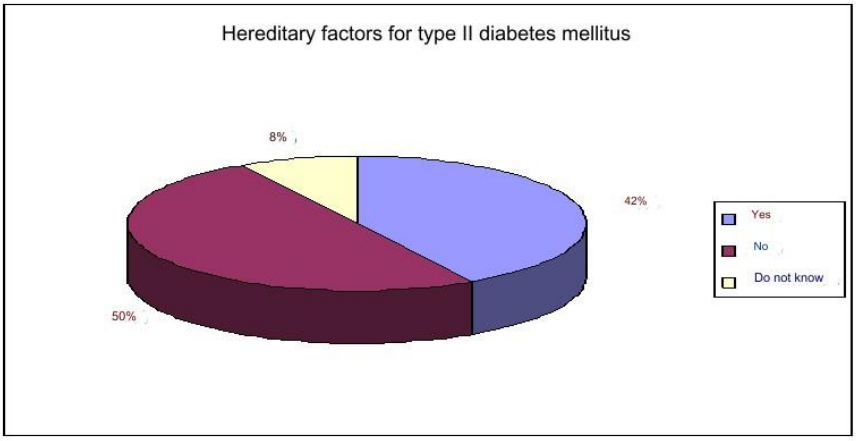
inactivity, in particular, reduces glucose tolerance and favors obesity. With regard to stress, it is stated that it can lead to changes in hormone and neuroregulatory levels, causing deviation from normal blood glucose levels.[14th]

Regarding the use of alternative treatment, among the 12 (twelve) research participants, 7 (seven) equivalent to 58% do not use alternative treatments, another 5 (five) 42% use alternative treatments to help control diabetes mellitus, this treatment being the use of medicinal plants such as Jambolão, Pata de Vaca, Insulina, Espinheira Santa, Sete Sangrias, plants indicated by family or friends or known by people of advanced age.

Although oral antidiabetic drugs and insulin have effective effects in the treatment of DM, they have side effects that hinder their use, in addition to their high cost, even when offered free of charge by the SUS because the government also buys the drug for distribution. The search for plants or natural compounds with antidiabetic activity comes to meet the need for new active compounds, less toxic and possibly more accessible to the population. There are several plants with antidiabetic potential used since ancient times, some of which have proven their effects in the control of DM. More research, including toxicological control, is needed in order to offer the population more accessible medicines, with quality, safety and proven efficacy. There are several plants with potential antidiabetic action in the world, which shows a great chance of discovering new therapeutic possibilities.

As for the hereditary factors for diabetes mellitus Graph 05, 5 (five) 42% subjects had a hereditary factor that would predispose them to develop type II diabetes mellitus, 6 (six) participants equivalent to 50% did not have genetic inheritance and 1 (one) did not know if they had a hereditary factor representing 8%. (Chart 05)

Graph 05 – Participants with hereditary factors for DM.



Source: The Authors

We know that the genetic component is strong, because a patient with a family history is likely to develop the disease in a proportion of 5 to 10 times more than in the general population.

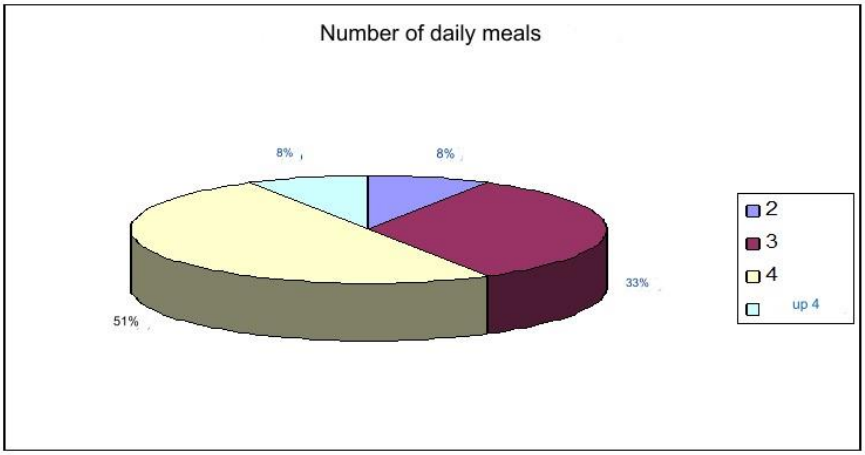
According to Brasil (2024), first-degree relatives of type ll diabetics are several times more likely to develop diabetes than controls without a family history.

Regarding heredity, 50.5% reported having family members with diabetes. The population consisted of 142 people and 49.5% did not report it. Among the former, 20.2% reported having first-degree relatives with the disease. We know that first-degree relatives of type II diabetics are two to six times more likely to develop diabetes than controls without a family history. Also in type II diabetes, the genetic component is strong, which is demonstrated by the five to ten times greater possibility of a patient with a family history developing the disease in relation to the general population, with 90% agreement in identical twins.[11]

Thus, the environmental factors that lead to obesity and sedentary lifestyle have an important interaction with genetic susceptibility, increasing insulin resistance and causing a higher risk for the development of diabetes, which intensifies with advancing age. If the genetic component alone is a relevant factor for the triggering of diabetes mellitus, the situation is more worrying when it is associated with physical inactivity and stress.[11.15 AM]

As for the number of daily meals (graph 06), we have 3 (three), 43% eating an average of three meals a day, the other 4 (four), that is, 57%, had an average of four meals a day, and what we could observe is that many of these meals are rich in carbohydrates, helping to increase their blood glucose rate and, consequently, decompensating diabetes and aggravating clinical conditions.

Graph 06 – Number of daily meals eaten by the research subjects.



Source: The Authors

Nutritional therapy is a fundamental part of the diabetes treatment plan, and can reduce glycated hemoglobin by 1-2%. It is based on the same basic principles of healthy eating.[11.16]

Diabetes mellitus is currently considered one of the main chronic diseases that affect contemporary man and its importance has been growing as a result of several factors. Among these we highlight changes from traditional to modern lifestyles, physical inactivity and obesity. In this direction, mental and physiological anxiety can decrease glucose tolerance, as well as precipitate

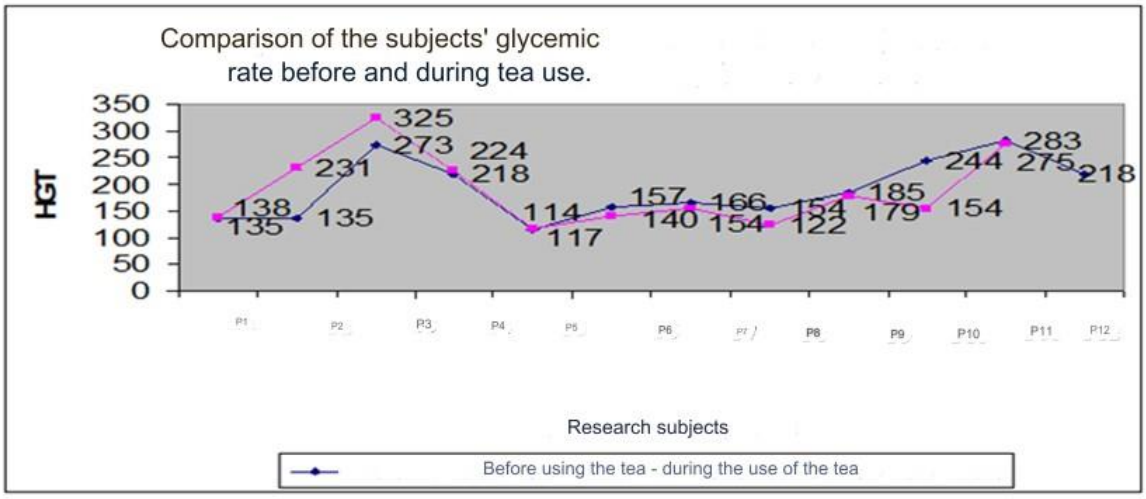
diabetes in people whose tolerance is already declining. Thus, stress in the work environment can contribute to the onset of this disease, requiring institutions to review the guidelines that guide work.[11.16]

When analyzing the most frequent risk factors, it is found that physical inactivity, stress and obesity (BMI) deserve to be highlighted.

ANALYSIS OF SURVEY GLYCEMIC RATE RECORDS

Analyzing graph 07 we can see that among the twelve research patients, six showed a decrease in the glycemic rate with the use of "Insulin" tea and six research patients showed an increase in the glycemic rate, among these five there were factors that may have influenced not to achieve a positive result, such as diseases associated with the administration of unusual medications, stress factors, change of diet during the use of tea, among others.

Graph 07 - Comparison between the glycemic rates of the research subjects before and during the use of tea.



Source: the authors

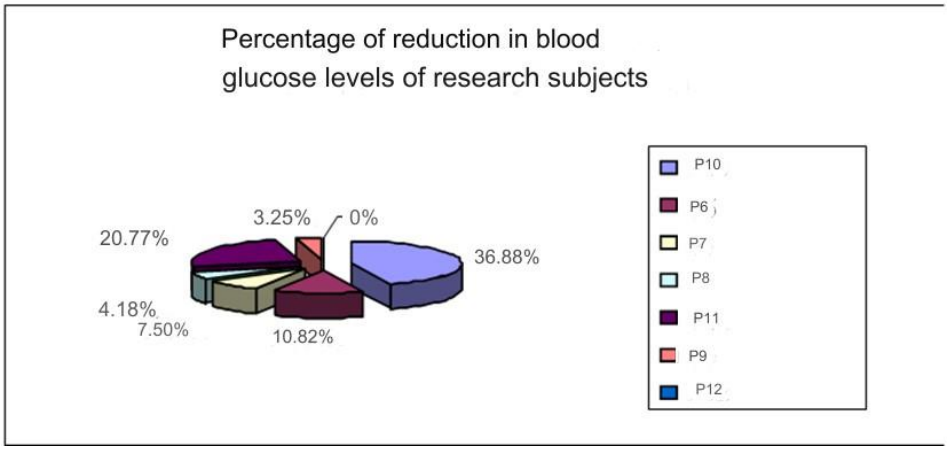
It can be seen in the graph below that the patients submitted to the use of the herbal medicine had a significant reduction in the glycemic rate after use, if compared to the previous rate. However, some factors may have contributed to this result not being even more efficient. For example, stress, anxiety, personal problems, among other problems, including health problems.

According to the Guidelines of the Brazilian Diabetes Society, Environmental, social, and psychological factors may play an important role in the development or worsening of type L diabetes mellitus.

We observed that participant 10 (P10) had the highest glycemic reduction index. This was 38% less when compared to their glycemic level prior to treatment. This can be the result of a balanced routine, with the correct use of herbal treatment.

Therefore, it is believed that this result could also be expanded to others, if the number of participants was more expressive, because taking into account personal issues, the final result suffers interference.

Graph 08 – Percentage of reduction in glycemic levels of the research subjects during the use of tea.



Source: the authors

Phytotherapy has proven to be a great ally of the health and quality of life of the population, promoting health and helping as an adjuvant in various treatments. According to Alonso (2021)[7], the herbal medicine Cissus sicyoide is a plant with hypoglycemic power, capable of helping to reduce blood glucose. It is believed that this effect in the medium term is even more efficient and capable of proving its effects.

The World Health Organization has been increasingly implementing national policies for integrative and complementary practices, and among them, phytotherapy has gained a prominent place, due to the strong evidence and the various training and studies that have been carried out. Since 2006, it has been part of the therapies offered by the SUS. However, their scientific knowledge is still little explored by primary care units and family health strategies. According to Lacerda *et al* (2020), phytotherapy is the most used practice in PHC, and has been accepted by users, promoting a new health paradigm.[18.19]

These herbal medicines, which have been used in primary health care units, have shown beneficial effects. And even though they are medicinal plants, they need to be used carefully and well guided their use, so that the maximum potential of the plant can be used safely.

They are used for various situations, for example, the standardized extract of B. Fortificata (cow's foot), has already proven its hypoglycemic effects, improving metabolic control, in addition to being considered to be understood as drug measures as well.[18th]

Approximately 25% of medicines are derived from plants and produced using modern drug technology, albeit naturalG1. This shows us the great potential that medicinal plants can have in the face of the most diverse diseases of today.

However, these treatments have shown promise. Plants that are still little studied, such as Cissus Sicyoide, having their hypoglycemic effects proven by an experimental study in patients with type II diabetes mellitus, is the beginning of new and future studies in the line of complementary therapies, especially phytotherapy, which has been growing and is already a complementary therapy recognized by the Ministry of Health.

CONCLUSION

In view of this study, it can be concluded that the Cissus Sicyoide plant demonstrated hypoglycemic effects in 50% of the patients submitted to the use of the dry extract. Being an adjuvant to the treatment of diabetes mellitus II, there is still a need to implement strategies that reinforce the use of herbal therapies and research needs to be carried out for this purpose. Since the herbal medicine Cissus Sicyoide has been shown to be a viable option in adjuvant or complementary treatment for patients with Diabetes Mellitus.

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