



Cissus sicyoides phytotherapy as complementary to the treatment of type II diabetes mellitus

Fitoterápico *Cissus sicyoides* como complementar ao tratamento de diabetes mellitus tipo II

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ABSTRACT

Diabetes Mellitus (DM) has become a public health issue in recent years. The comorbidities that affect their sufferers lead to a reduction in daily activities, a worsening of quality of life and an increase in mortality because of illnesses and complications of the disease. Basic health units, together with their health promotion programs and prevention strategies, have been adapting protocols for comprehensive care for patients with diabetes mellitus, guiding them towards a healthier lifestyle. This work 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 the dry extract. As an adjunct 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*.

INTRODUCTION

At an archaeological site in northwestern Spain, microfossils of plants including yarrow (*Achillea millefolium*) and chamomile (*Anthemis arvensis*) were found in the dental plaques of extinct Neanderthals (*Homo neanderthalensis*). These herbs lack nutritional value and have a

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bitter, 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 medicine .¹

The use of medicinal plants in health recovery 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. ^{two}

Diabetes mellitus (DM) is a metabolic disease caused by the inability of the pancreas to secrete insulin (type I diabetes) or by decreased tissue sensitivity to insulin (type II diabetes). It may also be caused by degeneration or inactivation of beta cells in the islets of Langerhans. ³ It is a syndrome in the metabolism of carbohydrates, proteins and fats, and may be multifactorial. ^{4,5}

Due to insulin deficiency in 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 will reach 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 a problem with the immune system in which antibodies attack the cells that produce insulin. Type II is resistance or deficiency in insulin secretion. It is the most common, 90% of cases are acquired throughout life. ⁶

The increase in Diabetes cases worldwide 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 the world, having high economic costs for society in addition to the impacts on a person's quality of life and life expectancy. ⁵

In Brazil, Diabetes affects around 7.7% of the Brazilian population, ranking second among the chronic diseases with the highest incidence and 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 sufferers and requires continuous care. Given this, we sought to evaluate the benefit of using herbal medication as a complement to the treatment of these patients. Among the countless species of plants with hypoglycemic characteristics, we chose *Cissus sicyoides* , better known as



“INSULIN”.

- **Scientific name** – *Cissus sicyoides*.^{2,7}
- **Popular names** – Portuguese: Vegetable insulin, cipó-pucá, climbing indigo, wild grape, poor man's curtain, gentile ink. Spanish: Cortina del Diablo, vegetable insulin. English: princess vine, toad vine.
- **Part used:** Aerial part.
- **Distribution habitat** : It is distributed in tropical and sub-tropical areas of America, starting from the south of the USA and Mexico to Brazil and Argentina.^{two}
- **History of the plant:** During the 19th century it was used as a laxative, against bruises and blenorrhagia and as an antiviral.^{two}
- **Therapeutic properties:** hypoglycemic, anti-inflammatory, 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 a 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.^{two}
- **Instructions for use** : The plant is recommended in the form of an oral leaf decoction (tea).² cups (coffee) or 20 grams of dry leaf in a liter of boiling water. Place the plant in a container and pour boiling water over it, simmer and leave to rest for at least 10 minutes and strain before using. taking 1 cup (tea) 3 times/day (30 minutes after meals).^{2,7}

This research aimed 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 Jardim Eldorado – Palhoça neighborhood. A semi-structured questionnaire was applied to the selected research subjects and a progress form was used to collect glycemic rates before and during the use of tea.

METHODOLOGY

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



For Minayo, qualitative research is characterized by being concerned with reality that cannot be quantified and by delving deeper into understanding human actions and reactions.⁸

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

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

The research was carried out from July 12th to December 20th, 2008. Data collection was divided into three moments:

After a lecture on diabetes in which the objective of the project to be applied to this population was discussed, active research participants were selected, a total of twelve people with type II diabetes mellitus, who met the previously established standard and requirement. A home visit was carried out to sign the informed consent form and collect the history. With these data in hand, the clinical conditions and habits of individuals in relation to their pathology were assessed, thus being able to prepare a health education activity. A folder was delivered explaining the pathology (diabetes mellitus) and guidance regarding nutrition 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 of checking the glycemic rate, we carried out a new home visit to give them the medicinal plant for daily consumption. Delivered properly packaged and dosed, providing guidance on the preparation and therapeutic use of tea through dialogue and an educational folder.

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

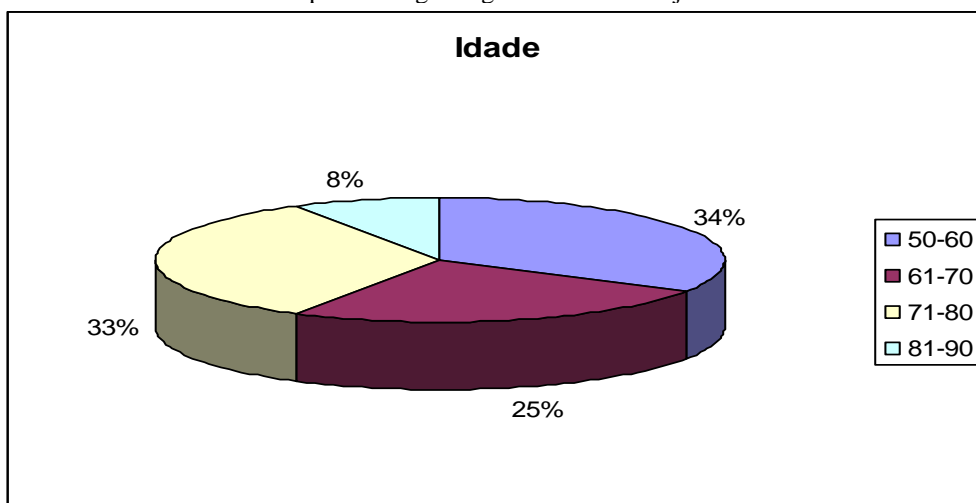
For the development of this research, the recommendations of opinion 404/2008 of the National Research Ethics Committee were adopted, which determines that the objective of Research Ethics Committees is to protect human beings in their dignity and integrity and contribute to scientific development and 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 between 50 and 60 years old, representing 34%, 4 (four) were between 61 and 70 years old (33%), 3 (three) between 71 and 80 years old (25%) and 1 (one) between 81 and 90 years old (8%), we observed that the majority of research subjects are elderly, 66% (over 61 years old).

Graph 01 – Age range of research subjects.



Source: The authors

Diabetes is common and of increasing incidence. It is estimated that, in 1995, it reached 4.0% of the world's adult population and that, in 2025, it will reach the figure of 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 these countries. In Brazil, at the end of the 1980s, it was estimated that diabetes occurred in around 8% of the population, aged 30 to 69, residing 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%, varying from 6 to 11% among the same age groups. Today it is estimated that 11% of the population is aged 40 or over, which represents around 5 and a half million people with it. ¹¹

Regarding the participants' education, 9 (nine) 75% had incomplete primary education, 2 (two) 17% were illiterate and 1 (one) 8% had completed secondary education.

We can see that the majority of those surveyed had incomplete primary education, based on this data we direct our dialogue in a way that is accessible to them.

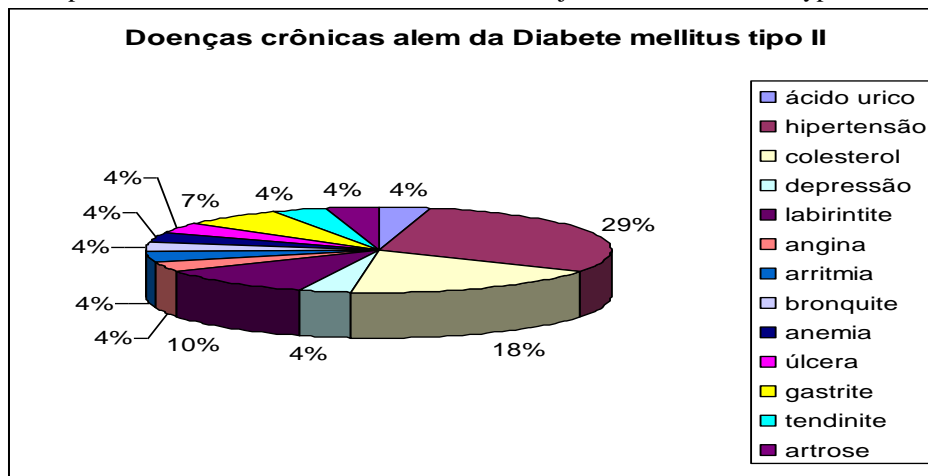
Regarding the marital status of the participants, 4 (four) 33% were widowed and 8 (eight)

67% were married.

Due to their advanced age, we realized 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, 47% had systemic arterial hypertension (SAH) and hypercholesterolemia. (Graph 02)

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



Source: The authors

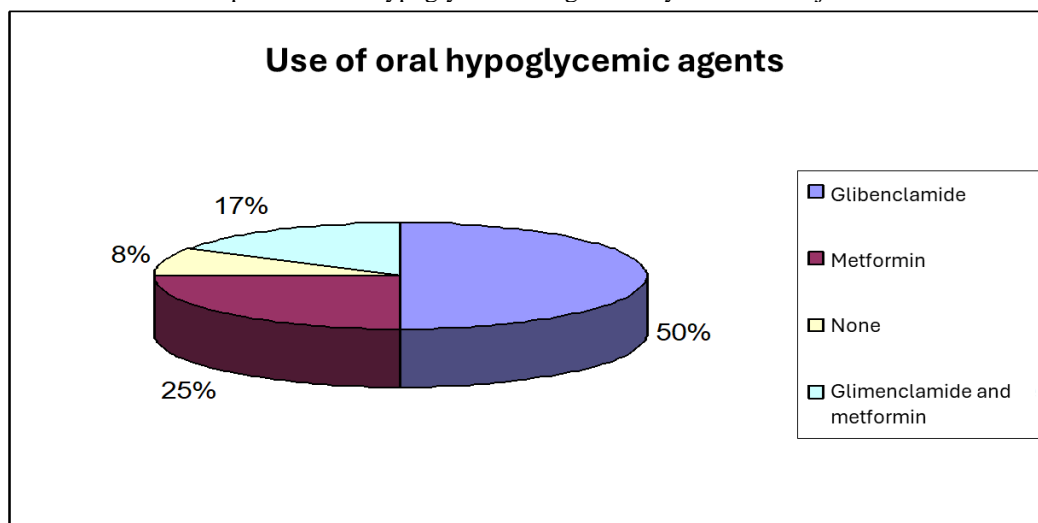
The natural history of diabetes is marked by the appearance of chronic complications, generally classified as microvascular – retinopathy, nephropathy and neuropathy – and macrovascular – coronary artery disease, cerebrovascular disease (CVA) and peripheral vascular disease. All are responsible for significant morbidity, with rates of cardiovascular and renal mortality, blindness, limb amputation, loss of function and quality of life much higher than that of individuals without diabetes. Cardiovascular ischemic diseases are more frequent and earlier in individuals with diabetes, compared to others. In women with diabetes, the protective effect typically recognized for females disappears. The symptoms of the three major cardiovascular manifestations – coronary disease, cerebrovascular disease and peripheral vascular disease. Systemic arterial hypertension affects the majority of people with diabetes. It is an important risk factor for coronary 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. Control monitoring (LDL cholesterol, triglycerides, and HDL cholesterol).¹¹

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

Graph 03 – Oral hypoglycemic drugs used by research subjects.



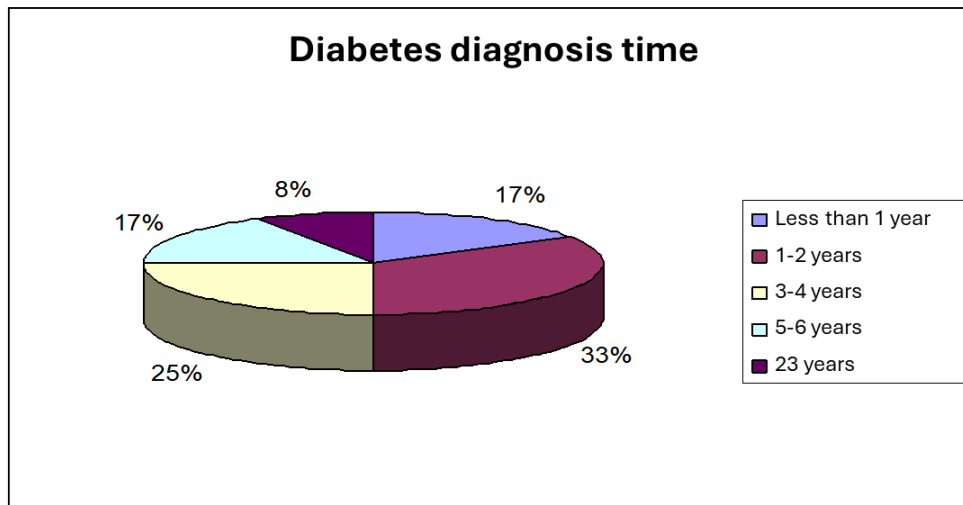
Source: The authors

Glibenclamide is an oral hypoglycemic agent widely used in type II diabetes mellitus. Some pharmacokinetic parameters of glibenclamide are well known: they are quickly and adequately absorbed by the intestine, distributed throughout the extracellular fluid, partially bound to plasma proteins; the speed and mode of degradation of these drugs vary. Differences in duration of action depend on the course of metabolism and the speed of excretion of each of them.

According to information in 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 quickly and eliminated.

Regarding the time of diagnosis of type II diabetes mellitus, we can see 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 old, 3 (three) discovered that they were diabetic between 3 and 4 years old, representing 25%, and 4 (four) had diabetes diagnosed 1 to 2 years ago years representing 33%. (Graph 04)

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



Source: The authors

Around 50% of the population with diabetes is unaware 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 that document the resulting benefit and the cost-effectiveness relationship is questionable. Factors indicating greater risk are: Age >45 years; Overweight (Body Mass Index BMI >25); Central obesity (waistline >102 cm for men and >88 cm for women, measured at the height of the iliac crests); Family history (mother or father) of diabetes; Arterial 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 exercise, we can see 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 sugar 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%. People with diabetes should avoid a sedentary lifestyle, incorporating light activities, such as standing or walking. ¹²

Regular physical activity is recommended for all patients with diabetes, as it improves metabolic control, reduces the need for hypoglycemic drugs, helps promote weight loss in obese patients, reduces the risk of cardiovascular disease and improves quality of life. Therefore, promoting physical activity is considered a priority. ¹¹



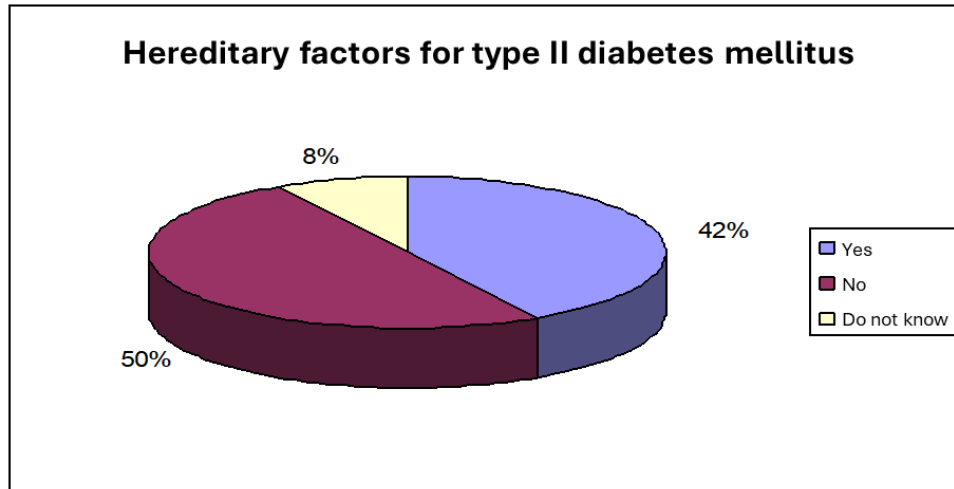
II diabetes mellitus, with its prevalence being higher in overweight patients than in normal weight patients aged 20 to 75 years. In patients aged 20 to 45 years the risk is 3.8 times higher. resistance exercise 3 times a week, in the main muscle groups. ^{G3} Physical inactivity, in particular, reduces glucose tolerance and favors obesity. With regard to stress, it is stated that it can lead to changes in hormonal and neuroregulatory levels, causing a deviation from normal blood glucose levels. ¹⁴

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 recommended by family or friends or knowledge of elderly people.

Although oral antidiabetics and insulin have effective effects in DM therapy, they have side effects that make their use difficult, in addition to their high cost, even when offered free of charge by the SUS as the government also purchases the medication for distribution. The search for plants or natural compounds with antidiabetic activity meets the need for new active compounds, less toxic and possibly more accessible to the population. There are several plants with antidiabetic potential that have been used since ancient times, with some having already proven effects in controlling DM. More research is needed, including toxicological control, so that the population can be offered more accessible medicines of proven quality, safety and efficacy. There are several plants with potential antidiabetic action in the world, which shows a great chance of discovering new therapeutic possibilities.

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

Graph 05 – Participants with hereditary factors for DM.



Source: The authors

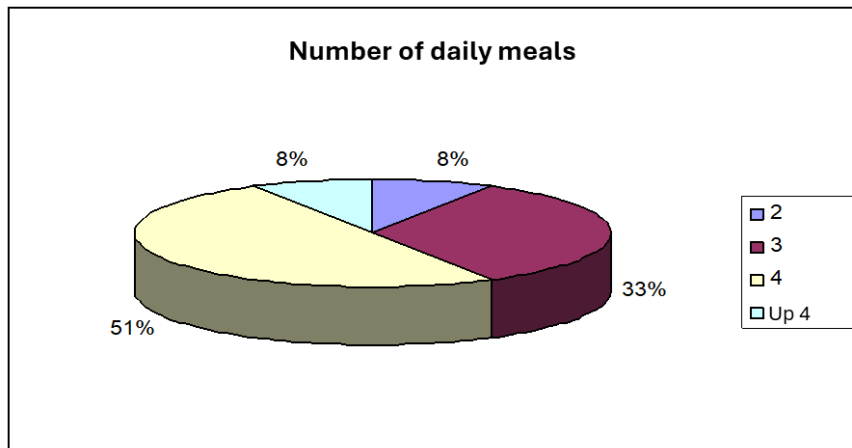
We know that the genetic component is strong, as a patient with a family history is 5 to 10 times more likely to develop the disease compared to the general population. According to Brasil (2024), first-degree relatives of type II diabetics are several times more likely to develop diabetes than controls without a family history.

Regarding heredity, 50.5% said they had family members with diabetes. The population consisted of 142 people and 49.5% did not report. Among the former, 20.2% report having first-degree relatives who have 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 higher possibility of a patient with a family history of developing the disease compared to the general population, with a 90% agreement in identical twins.¹¹

Thus, the environmental factors that lead to obesity and a sedentary lifestyle have an important interaction with genetic susceptibility, increasing insulin resistance and causing a greater risk of developing diabetes, which intensifies with advancing age. If the genetic component alone is a relevant factor in triggering diabetes mellitus, the situation is more worrying when it is associated with physical inactivity and stress.^{11,15}

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% eating 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 your blood glucose level and consequently causing diabetes decompensation and worsening of clinical conditions.

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



Source: The authors

Nutritional therapy is a fundamental part of the diabetes therapeutic plan and can reduce glycated hemoglobin by 1-2%. It is based on the same basic principles as healthy eating. ^{11.16}

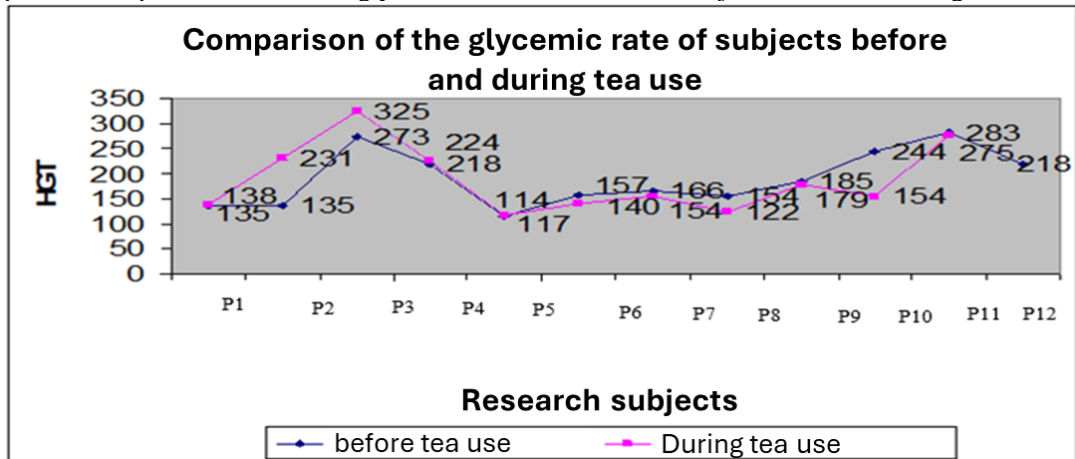
Diabetes mellitus is currently considered one of the main chronic diseases that affect contemporary men and its importance has been growing due to several factors. Among these we highlight changes from traditional to modern lifestyle, physical inactivity and obesity. In this sense, mental and physiological anxiety can decrease glucose tolerance, as well as precipitate diabetes in people whose tolerance is already declining. Therefore, stress in the work environment can contribute to the onset of this disease, requiring institutions to review the guidelines that guide their work. ^{11.16}

When analyzing the most frequent risk factors, it appears that physical inactivity, stress and obesity (BMI) deserve attention.

ANALYSIS OF RESEARCH GLUCEMIC RATE RECORDS

Analyzing graph 07 we can see that among the twelve research patients, six demonstrated 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 the non- achieve a positive result, such as illnesses associated with the administration of unusual medications, stress factors, changes in diet while using tea, among others.

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



Source: The authors

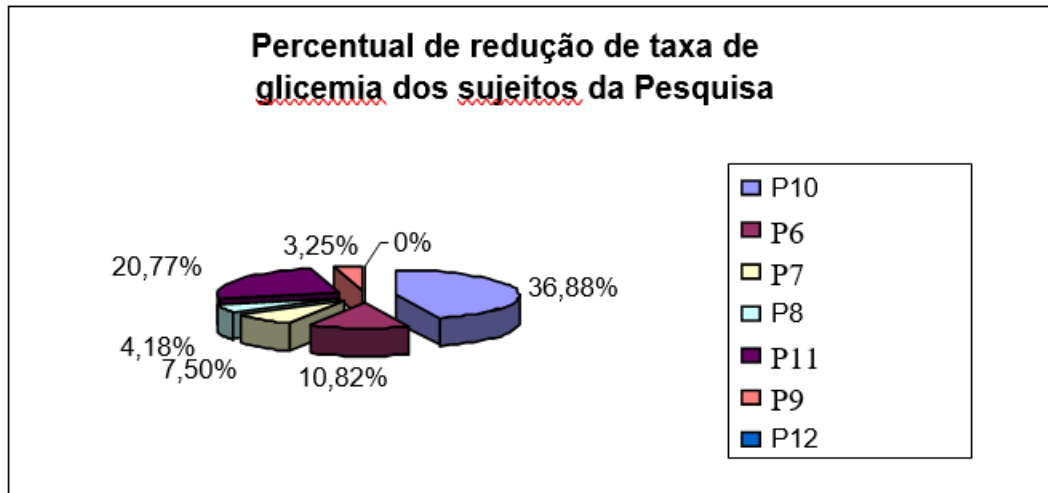
It can be seen in the graph below that patients undergoing the use of herbal medicine had a significant reduction in their glycemetic rate after use, compared to the previous rate. However, some factors may have contributed to this result not being even more efficient. For example, stress, anxiety, personal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

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

We observed that participant 10 (P10) had the highest rate of blood glucose reduction. This is 38% less when compared to your glycemetic rate prior to treatment. This may be the result of a balanced routine, with the correct use of herbal treatment.

Therefore, it is believed that this result could also be extended to others, if the number of participants were more significant, as taking into account personal issues, the final result suffers interference.

Graph 08 – Percentage of reduction in glyceimic rates of research subjects while using tea.



Source: The authors

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

The World Health Organization has increasingly implemented national policies on integrative and complementary practices and among them, herbal medicine gains 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 SUS. However, its scientific knowledge is still little explored by basic units and family health strategies. According to Lacerda *et al* (2020), phytotherapy is the most used practice in PHCs, and has been accepted by users, promoting a new health paradigm.^{18,19}

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

They are used for different situations, for example, the standardized extract of *B. Fortificata* (cow paw), has already proven its hypoglycemic effects, improving metabolic control, in addition to being considered to be also understood as medicinal measures.¹⁸

Approximately 25% of medicines are derived from plants and produced using modern technology, although natural^{G1}. This shows us the great potential that medicinal plants can have, facing the most diverse diseases of today.



However, these treatments have shown promise. Plants that are still little studied, such as *Cissus Sicyoid*, with its hypoglycemic effects proven by an experimental study on 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

Given this study, it can be concluded that the *Cissus* plant *Sicyoid* demonstrated hypoglycemic effects in 50% of patients submitted to the use of the dry extract. Being an adjunct 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 to this end. Since, the herbal medicine *Cissus Sicyoid*, proved to be a viable option in adjuvant or complementary treatment for patients with Diabetes Mellitus.



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