Pharmacogn J. 2025; 17(1): 63-70
A Multifaceted Journal in the field of Natural Products and Pharmacognosy
www.phcogj.com

Research Article

Effect of the Ethanolic Extract of *Chuquiraga weberbaueri* Tovar on Glycemia in BALB/c Mice

Angel Armando Marin Raico[1], Rosa Isabel Florez Carrasco[1], Jesús Eduardo Rojas Jaimes[1,2], Juana Elvira Chávez Flores[3], José Arenas Gamio[4]

ABSTRACT

Background: Diabetes mellitus is one of the most prevalent diseases worldwide and is associated with many complications. While there are many drugs available to control blood glucose levels, many people cannot access them due to economic reasons. **Object***:* The aim of this study was to determine the hypoglycemic effect of the ethanolic extract of *Chuquiraga weberbaueri* in mice induced with hyperglycemia. **Methods***:* The mice were divided into 6 groups: the first group served as a control group and was administered only physiological saline solution; the second group was induced to hyperglycemia with Alloxan. The following three groups were induced with Alloxan and additionally administered ethanolic extract of *Chuquiraga weberbaueri* at different concentrations of 100 mg/kg, 250 mg/kg, and 500 mg/kg respectively. The last group was administered Alloxan and glibenclamide. The glucose levels were measured for each group at 2, 4, and 24 hours after administering the extracts. **Results***:* The phytochemical analysis of the ethanolic extracts of the leaves of *Chuquiraga weberbauei* showed the presence of flavonoids, tannins, alkaloids and steroids. The ethanolic extracts (100 mg/kg at 2 hours and 250 mg/kg at 2 and 4 hours) demonstrated a decrease in blood glucose compared to the control group. In the toxicity test, the comparison between the control group and the "extract" treatment group showed that no conclusive results were observed with respect to the *chuquiragua* extract. **Interpretation***:* The results of the study showed that the ethanolic extract of *Chuquiraga weberbaueri* showed the effect of reducing blood glucose in BALB/c mice.

Keywords: Plant Extracts, Hypoglycemic Agents, Mice.

Angel Armando Marin Raico[1], Rosa Isabel Florez Carrasco[1], Jesús Eduardo Rojas Jaimes[1,2], Juana Elvira Chávez Flores[3], José Arenas Gamio[4]

[1]Escuela de Medicina Humana, Universidad Científica del Sur, Lima-PERÚ.

[2]Facultad de Ciencias de la Salud, Universidad Privada del Norte, Lima-PERÚ.

[3]Escuela de Farmacia y Bioquímica, Universidad Norbert Wiener, Lima-PERÚ.

[4]Departamento de Patología Clínica, Hospital Guillermo Almenara Irigoyen, Lima-PERÚ.

Correspondence

Jesús Rojas Jaimes

Escuela de Medicina Humana, Universidad Científica del Sur; Facultad de Ciencias de la Salud, Universidad Privada del Norte, Lima-PERÚ.

E-mail: jesus.rojas.jaimes@gmail.com

History

- Submission Date: 12-09-2024;
- Review completed: 17-12-2024;
- Accepted Date: 07-01-2025.

DOI : 10.5530/pj.2025.17.8

Article Available online

http://www.phcogj.com/v17/i1

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the metabolic diseases that has gained relevance in recent years. According to the WHO, the number of people with diabetes increased by 314 million cases from 1980 to 2014, reaching a total of 422 million cases to date [1]. En Peru, in 2018, 3.6% of every 100 people over the age of 15 were reported to have T2DM, according to MINSA [2]. This figure increased by 0.3% in 2019, according to the Demographic and Family Health Survey (ENDES) [3]. As is well known, T2DM leads to multiple complications in affected individuals, putting their health and quality of life at risk. Some of these complications include stroke, kidney failure, myocardial infarction, blindness, and lower limb amputation [4, 5].

The use of plants for disease treatment is an ancient practice that continues to be employed today and is an important pillar in human health. For example, plants can be used in the development of pharmaceuticals, using the whole plant or its parts to extract compounds for active ingredient production [6]. The *Chuquiraga* species is found in various Latin American countries and is used for its medicinal properties. It belongs to the Asteraceae family [7], and there are around 150 species of *Chuquiraga*, of which only 22 have been accepted by The Plant List, an organization that collaborates with the Royal Botanic Gardens, Kew, and the Missouri Botanical Garden [8]. One of these accepted species is *Chuquiraga weberbaueri*, which is found in the northern region of Peru at an altitude of 3000 to 4500 meters above sea level [9]. It is a spiny shrub that grows on rocky slopes and is locally scarce. It is used for medicinal purposes to combat cough, bronchitis, asthma, liver diseases, and it is colloquially known as "Amaro Amaro" or "Amaro" [10,11].

In recent times, various researchers have focused their attention on the study of medicinal plants due to their potential role as antidiabetic agents. In vivo tests have been carried out on animal models such as rats and mice to evaluate their effectiveness in treating complications associated with the disease. The results obtained indicate that numerous plants have the ability to reduce blood glucose levels and contribute to improving other diabetes-related complications. Since the use of plants is a cost-effective way to prevent or treat diseases and they are more accessible than drugs [12]. The majority of plants used have not yet been studied or their effectiveness has not been proven. For example, in the northern region of the country (Cajamarca-Peru), the population uses *Chuquiraga weberbaueri* to control diabetes, believing that this plant has the ability to reduce blood glucose levels. However, there are no previous studies confirming that this specific species has hypoglycemic effects. Additionally, there is a study on another species from the same family, *Chuquiraga jussieui*, which demonstrated its hypoglycemic effectiveness in a murine model in rats in a 2019 study conducted in Ecuador [13]. In the global transition there is a tendency to use natural resources, such as plants, and thus discover new low-cost and widely available therapeutic substances.

Cite this article: Raico AAM, Carrasco RIF, Jaimes JER, Flores JEC, Gamio JA. Effect of the Ethanolic Extract of *Chuquiraga weberbaueri* Tovar on Glycemia in BALB/c Mice. Pharmacogn J. 2025;17(1): 63-70.

Currently, alternatives are being sought to control high blood glucose levels in diabetic patients, and for this purpose, plants with glucose-lowering capabilities are used. For example, Inocente-Camones et al. 2015, studied the hypoglycemic effect of aqueous and ethanolic extracts of *Psidium guajava* L. (Guava) in Alloxan-induced diabetic rats, and it was found that both extracts, especially the aqueous extract at a dose of 250 mg/kg, significantly reduced glucose levels compared to the ethanolic extract at a dose of 500 mg/kg, which only showed a slight decrease in glucose levels [14]. Herrera-Calderon et al. 2015, evaluated the hypoglycemic effect of the ethanolic extract of *Geranium ruizii Hieron*. (Pasuchaca) in Alloxan-induced hyperglycemia in rats, and it was found that the ethanolic extract of *Geranium ruizii Hieron* has a hypoglycemic effect at doses of 50 and 150 mg/kg [15]. Nawel H et al. 2019, conducted a review of Algerian medicinal plants used in the treatment of diabetes [16]. However, there is no study demonstrating this hypoglycemic effect in the species *Chuquiraga weberbaueri*. If the hypoglycemic effects are proven, the use of this plant could be used as complementary therapy in diabetes control. Furthermore, as mentioned earlier, there are people who already use this plant for this purpose, so it is important to provide accurate information about its effects on blood glucose levels. Therefore, the aim of this study was to determine the hypoglycemic effect of the ethanolic extract of *Chuquiraga weberbaueri* in mice induced with hyperglycemia.

METHODS

Plant Material Collection

The plants were collected in the district of Namora, Cajamarca region, Peru, with the geographical coordinates:

Latitude South: 7°10'43.9" S, Longitude West: 78°13'44.9" W, at an altitude of 3755 meters above sea level. A total of 4.8 kilograms of branches of *Chuquiraga weberbaueri* were collected. The plants were cleaned with water and disinfected in 96% ethanol, then packed in paper and transported to Lima-Peru for metabolite extraction in the laboratory and taxonomic identification at the Museum of Natural History of the National University of San Marcos, where taxonomic identification using the flower and leaves was carried out.

Extraction of metabolites

The leaves of *Chuquiraga weberbaueri* were used for extraction. The leaves were separated from the stems and then dried in the oven, resulting in 2 to 2.5 kilograms of dry leaves. Once the leaves were dry, they were manually crushed using a blade shredder. For every 300 grams of crushed dry leaves, 2 liters of 70% alcohol were added to a glass container, which was externally wrapped with dark plastic bags. The mixture was then allowed to macerate for 7 days, and the container was shaken daily for 10 minutes. Each macerate was subjected to 9 successive filtrations using rough filter paper with a porosity of 12µm. The filtrate was then placed in Pyrex containers for drying and obtaining pastes. The filtrate was left to rest in an extraction hood until the volume decreased to approximately one-third of the initial volume. Finally, it was placed in an incubator at 40°C until the presence of a paste without liquid content around it was observed. Once the paste was obtained, it was removed from the Pyrex container using a sterile palette instrument and stored in glass jars in an incubator at room temperature. The dry paste was weighed on an analytical balance and diluted in sterile distilled water using a magnetic stirrer with a magnetic pellet. The stirring temperature was 40°C, and the speed was set to 300 revolutions per minute (RPM). This procedure lasted for 30 minutes to obtain the extract. The ethanolic extracts were administered orally at doses of 100 mg/kg, 250 mg/kg, and 500 mg/kg. Approximately 0.2 mL of extract was given to each mouse weighing 30-40 grams, and they were refrigerated for preservation [17,18].

Qualitative phytochemical analysis of *Chuquiraga weberbaueri*

A preliminary phytochemical analysis was performed on the leaves of *Chuquiraga weberbaueri* using the ethanolic extract of the plant. The analysis was based on coloration and precipitation tests according to Olga Luck de Ugaz [19], with the aim of confirming the presence or absence of metabolites. Five milligrams of *Chuquiraga weberbaueri* sample were diluted in ethanol, to which 1 mL of reagent for the determination of alkaloids, flavonoids, and steroids was added. This analysis was performed because the presence of flavonoids in the extract was expected, as many studies have shown that this secondary metabolite has various activities on the metabolism of different human cells, including reducing glucose levels. This was the basis for further research. The following reagents were used to perform phytochemical assays on the ethanolic extract of *Chuquiraga weberbaueri*: aluminum chloride ($AlCl_3$), iron chloride ($FeCl_3$), Shinoda, sodium hydroxide (NaOH) for tannins, Liberman Burchand, Salkowski, sulfuric acid (H_2SO_4) for steroids, Bertrand, Dryendorff, Mayer, Popoff, Sonnepschen, and Wagner for alkaloids.

Experimental animal

Male BALB/c mice were used [20]. They were acquired from a bioterium at the National Institute of Health, with an average weight of 30-40 grams. The animals were acclimated for seven days in groups of five mice in cages, at room temperature and under natural light. The mice were fed pellet feed [21], obtained from a balanced food production center at the agricultural university, and water was provided ad libitum [22].

To determine the sample size, the findings obtained by Fiaz Alam et al. 2018 and H Chen 2001 were considered, where mice induced with hyperglycemia were used to demonstrate the hypoglycemic effects of the plant extracts under study [23,24]. The sample size was calculated using the statistical software OPENEPI (https://www.openepi.com/Menu/OE_Menu.htm) [25], considering a significance level of less than 0.05 and a power of 80%. To estimate a difference in means, a minimum of 4 mice per group was obtained, with an additional 20% to account for potential losses, resulting in a total of 5 mice per group.

Induction of experimental diabetes

Because Alloxan destroys pancreatic cells and this effect does not allow the proper metabolism of blood glucose, blood glucose increases, which is the phenomenon observed in both type I and type II diabetes. Therefore, this methodology can be used in animal models in which diabetes is intended to be generated [14,26].

Diabetes was induced by intraperitoneal administration of 100 mg/kg of Alloxan dissolved in physiological saline at a concentration of 10 mg/mL, multiplied by the dose of Alloxan (100 mg/kg) [14, 26]. After 24 hours, blood glucose was measured with a 12-hour fasting period before the treatment with Alloxan, using an Accu-Chek Instant handheld glucometer [27]. Mice with glucose levels above 150 mg/dL were selected for further experiments [28]. After 24 hours of the Alloxan supply, the treatments were given using the extracts of *Chuquiraga weberbaueri.*

Experimental design

A total of 30 mice were used, distributed into groups of five mice in each cage:

Group 1: Blank control group - received 2 mL of physiological saline orally.

Group 2: Hyperglycemic control group - received only 100 mg/kg of Alloxan intraperitoneally and no treatment.

Group 3: Hyperglycemic group - received 100 mg/kg of ethanolic extract orally using an orogastric tube.

Group 4: Hyperglycemic group - received 250 mg/kg of ethanolic extract orally using an orogastric tube.

Group 5: Hyperglycemic group - received 500 mg/kg of ethanolic extract orally using an orogastric tube.

Group 6: Hyperglycemic group - received 5 mg/kg of glibenclamide (gliburide) orally using an orogastric tube [14].

Measurement of blood glucose

Blood samples were taken from the tail of the mice for glucose determination using a Roche Accu-Chek Instant digital glucometer [27]. Blood glucose measurements were taken before the treatment with Alloxan and at 24 hours after Alloxan administration [14]. Mice with blood glucose levels exceeding 150 mg/dL [16], were administered the ethanolic extracts and glibenclamide (gliburide). Glucose levels were measured in all groups at 2 hours, 4 hours, and 24 hours after administration of the ethanolic extract and glibenclamide.

Toxicity assay

To evaluate the toxicity of the ethanolic extract, 18 additional mice were used, which were divided into two groups of 9 mice. Group 1 was administered the ethanolic extract of 2000 mg/kg in a single dose, group 2 was administered physiological saline. These groups were subdivided into three groups of three. Each subgroup of three was sacrificed at 24 hours, 7 days and 14 days after administration of the extract. Each group was sacrificed to take samples and fixed in 10% formalin to make histological slides in paraffin, and the liver, kidney and brain samples were analyzed pathologically [29].

Ethical Aspects

The guidelines of the "Guide for the Management and Care of Laboratory Animals" of the National Center for Biological Products of the National Institute of Health were followed. Following the principle of the three Rs, Reduce, Replace and Refine. In addition to providing the best care for the animals during the experiment, allocate a suitable and clean place, as well as water and food [30, 31]. The study was approved by the academic directorial resolution of Universidad Científica del Sur university with resolution number 728. The experimental trial was register with N° 994-2021-PRE15 number.

Euthanasia

The pharmacological method was used for euthanasia. Consequently, Pentobarbital was used intraperitoneally at a dose of 150 mg/kg, which induced depression of the central nervous system leading to anesthesia and subsequently death. This method was used because it is the fastest and least painful [32-34].

Processing and statistical analysis

The SPSS 18 software [35], was used for data processing and statistical analysis. Descriptive analysis was performed, considering means, standard deviations (SD), and percentages, depending on the type of study variable. The Shapiro-Wilk parametric test was used to analyze the normality of numerical variables ($p<0,05$). We used an ANOVA and additionally, the Bonferroni analysis of variance test was used to determine the specific significant difference between groups.

RESULTS

The phytochemical analysis of the ethanolic extracts of the leaves of *Chuquiraga weberbaueri* showed the presence of various secondary metabolites such as: flavonoids, tannins, alkaloids and steroids in abundant form, as shown. in table 1

Table 1. Results of Phytochemical Assays Applied to the Ethanolic Extract of *Chuquiraga weberbaueri*.

Flavonoids	AlCl3 Aluminum chloride	+++
	FeCl3 (Iron chloride)	+++
	SHINODA	+++
Tannins	H2SO4 (Sulfuric acid)	+++
	NaOH (sodium hydroxide)	+++
Alkaloids	BERTRAND	+++
	DRAYENDORFF	+++
	MAYER	+++
	POPOFF	+++
	SONNEPSCHEN	+++
	WAGNER	+++
Steroids	LIBERMAN BURCHAND	+++
	SALKOWSKI	+++

++++ VERY ABUNDANT +++ ABUNDANT ++ REGULAR + SCARCE- ABSENCE

Legend

$^{a, b, c, d}$ =p< 0,05.

It was observed that the best treatment regarding the decrease in glucose compared to the blank control "saline solution" with values of 139.40 ± 12.46 mg/ dL, at 2 hours and 139.20 ± 8.16 mg/ dL at 4 hours, the ethanolic extract of 250 mg/kg was worth 133.20 ± 10.23 mg/ dL at 2 hours and 134.00 ± 25.61 mg/ dL at 4 hours. Post Bonferroni analysis of variance test was used to determine the specific significant difference between groups.

With respect to the sheets of liver tissue, portal inflammatory infiltrate was found in the mice that were sacrificed seven days after receiving the ethanolic extract and hepatic steatosis with perivascular inflammatory infiltrate in the mice that were sacrificed 24 hours after receiving the ethanolic extract. ethanolic extract. In the kidney sections, a mild perivascular inflammatory infiltrate was observed in the mice that only received saline, in those that received the extract and were sacrificed at 24 hours a congestive kidney was found, and in those that were sacrificed at seven- and fourteen-days, a moderate perivascular inflammatory infiltrate was found. The comparison between the blank control group and the "extract" treatment group demonstrated that no conclusive results were observed with respect to the *chuquiraga* extract.

DISCUSSION

It was possible to corroborate that the extracts of *Chuquiraga weberbaueri* at doses of 100 mg/ kg, 250 mg/kg were the treatments that lowered blood glucose the most compared to the 500 mg/ kg extract that lowered blood glucose slightly. This decrease occurred between 2 hours to 24 hours for the concentrations of 100 mg/kg and 250 mg/kg and between 2 to 4 hours for the concentration of 500 mg/kg after being administered to the mice induced to hyperglycemia (figure 1). However, these values were not statistically significant compared to the blank control (0.9% saline solution) or the positive control (Glibenclamide). The hypoglycemic effect of the *Chuquiraga* genus has been demonstrated in a previous study using the aqueous extract of *Chuquiraga jussieui* in rats induced hyperglycemia in which it was found that the groups treated with the concentrations of 100 mg/kg, 200 mg/kg and 400 mg / kg showed a significant decrease in glucose levels at 10 days compared to Glibenclamide [13]. Other plants have been studied regarding the hypoglycemic effect such as *Psidium guajava* using aqueous extracts at a dose of 250 mg/dL and ethanolic extracts at a dose of 250 mg/kg and 500 mg/kg, with the aqueous extract at a dose of 250 mg/kg. kg, which gave better results 2 and 4 hours after its administration, these

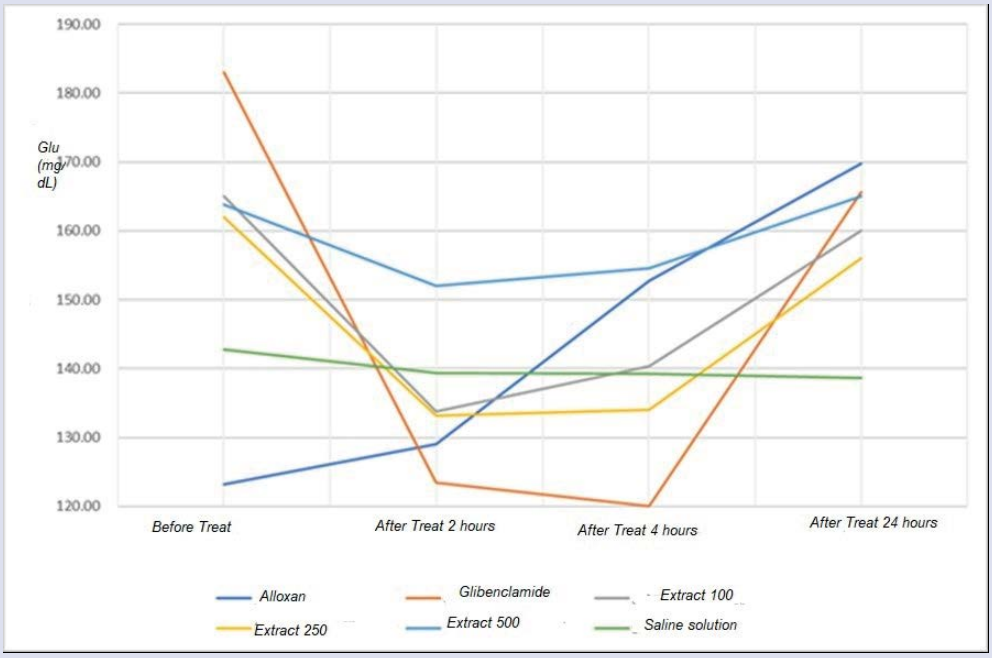

Figure 1. Glycemic levels (mg/dL) (line Y) between the pre and post treatment groups in mice (line X). BALB/c treated with ethanolic extract of *Chuquiraga weberbaueri*. A tendency to decrease glycemia compared to the blank control "saline solution" was demonstrated, in terms of the ethanolic extract of 100 mg/kg at 2 hours and the ethanolic extract of 250 mg/kg at 2 hours, and 4 hours.

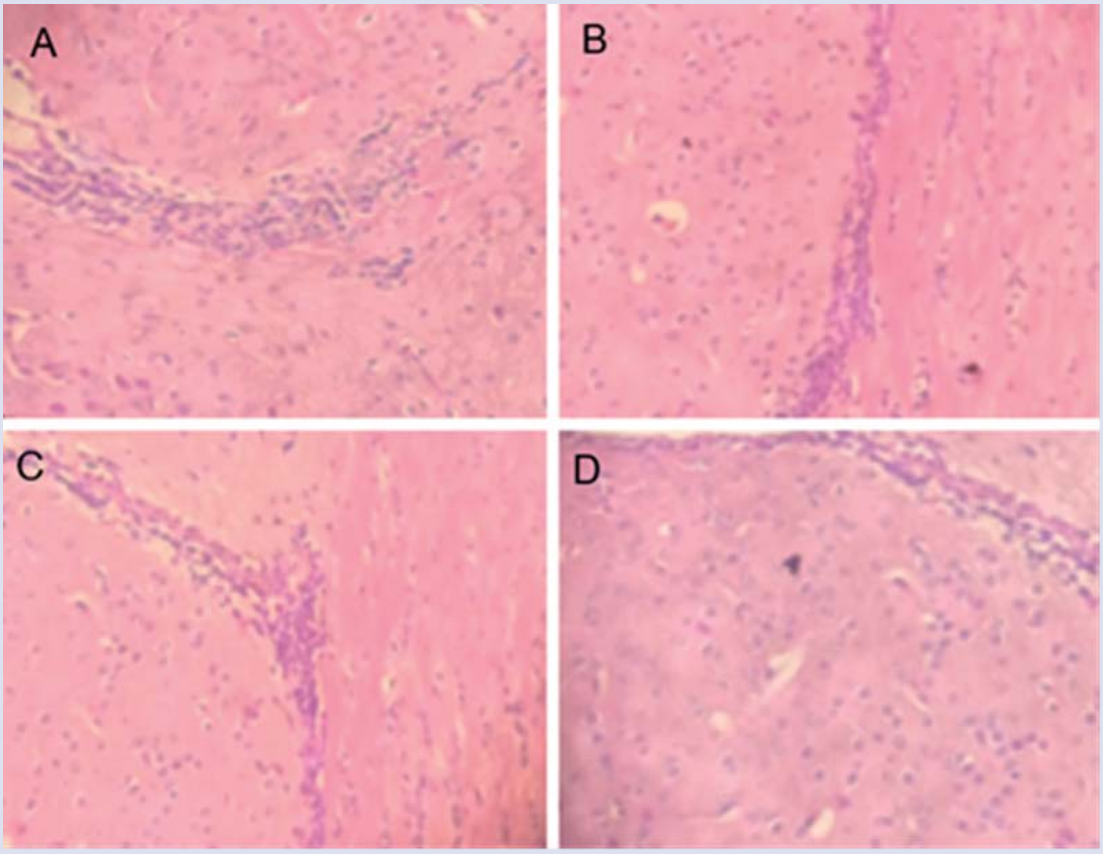

Figure 2. Brain slices. (A) Blank control group brain section. (B) Brain section with extract after 24 hours presents congestion although not conclusive. (C) Brain section with extract after 7 days without alterations. (D) Court of brain with extract after 14 days without alterations.

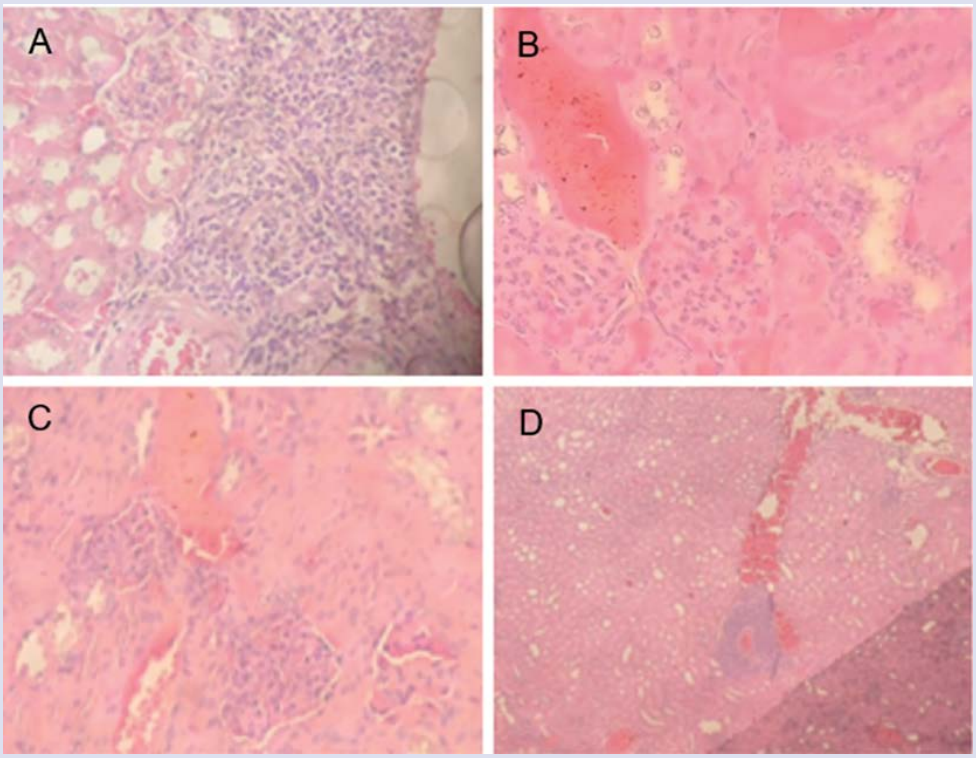

Figure 3. Kidney slides. (A) Blank control group section presents mild perivascular inflammatory infiltrate although not conclusive. (B) Cut with ethanolic extract after 24 hours without alterations. (C) Section with ethanolic extract after 7 days shows mild to moderate perivascular infiltrate although not conclusive. (D) Section with ethanolic extract after 14 days shows moderate perivascular and focal interstitial and mild perivascular inflammatory infiltrate although not conclusive.

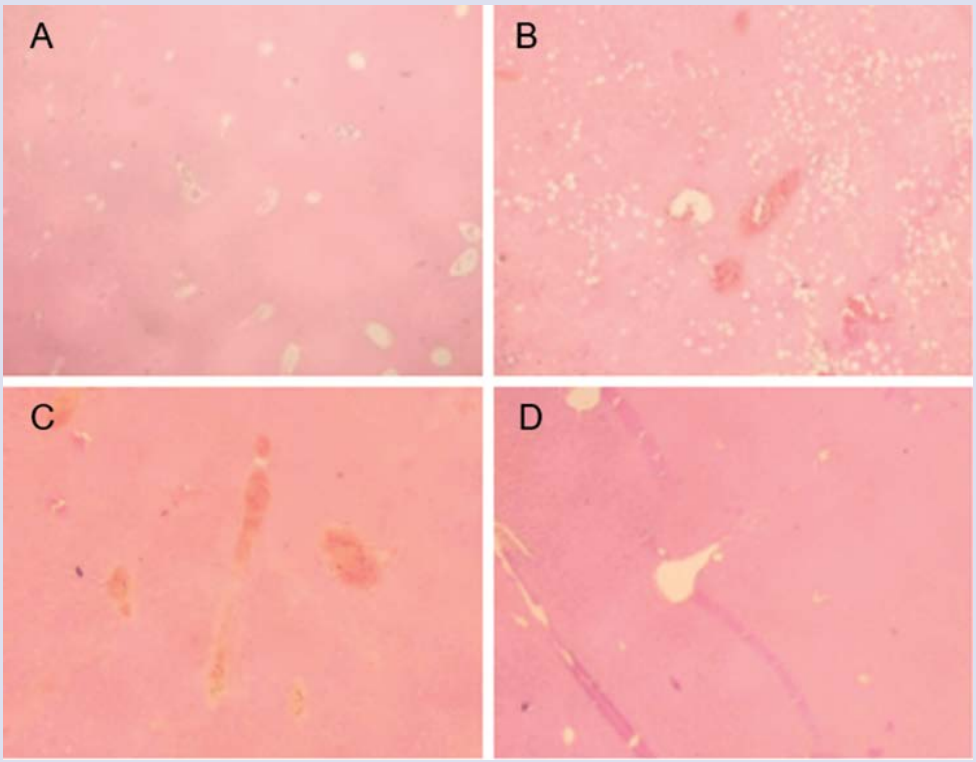

Figure 4. Liver slides. (A) Blank control group cut without alteration. (B) Section with ethanolic extract at 24 hours shows hepatic steatosis with perivascular inflammatory infiltrate although not conclusive. (C) Section with ethanolic extract after 7 days shows portal inflammatory infiltrate although not conclusive. (D) Cut with ethanolic extract after 14 days without alterations.

Table 2. Glycemic levels (mg/ dL) between the pre- and post-treatment groups in mice. BALB/ c treated with ethanolic extract of *Chuquiraga weberbaueri*.

GROUP	Dose (mg/kg)	Before treatment	Treatment 2 hours	Treatment 4 hours	Treatment 24 hours
Only Alloxan	100	123,20 ± 13,33 a, b, c (Before Alloxan)	129,00 ± 11,40 (2 hours Alloxan)	152,80 ± 19,01 (4 hours Alloxan)	169,80 ± 18,83 (24 hours Alloxan)
Glibenclamide	5	183,00 ± 21,27 a, d	123,40 ± 24,15	120,00 ± 19,30	165,60 ± 25,31
Ethanolic Extract (1)	100	165,00 ± 10,34 b	133,80 ± 13,1	140,40 ± 16,41	160,00 ± 25,13
Ethanolic Extract (2)	250	162,00 ± 4,52	133,20 ± 10,23	134,00 ± 25,61	156,00 ± 14,30
Ethanolic Extract (3)	500	163,80 ± 9,88 c	152,00 ± 9,69	154,60 ± 6,65	165,00 ± 18,48
Blank Control Only Saline Solution (0.9%)	2 ml	142,80 ± 8,46 d	139,40 ± 12,46	139,20 ± 8,16	138,60 ± 2,40

Table 3. Toxicity assay of the ethanolic extract of *Chuquiraga weberbaueri*.

Control / Extract	24h	7 days	14 days
Brain (Control)	Without modifications	Without modifications	Without modifications
Brain (extract)	Without modifications	Without modifications	Without modifications
Kidney (Control)	inconclusive	Without modifications	Inconclusive
Kidney (extract)	inconclusive	Inconclusive	Inconclusive
Liver (Control)	Without modifications	Without modifications	Without modifications
Liver (extract)	inconclusive	Inconclusive	Without modifications

results being statistically significant, compared to the ethanolic extract of 250 mg/kg and 500 mg/dl, which were not statistically significant [14]. Furthermore, it was observed that the administration of the ethanolic extracts of *Allium sativum* and *Capparis spinosa*, at a dose of 300 mg/kg administered for 12 days, produced discrete hypoglycemic effects in rats, with the ethanolic extract of *Allium sativum* having the best results, however, both extracts of *Allium sativum* and *Capparis spinosa* were statistically significant [36].

In our study regarding the decrease in glycemia, the treatment that gave the best result was 250 mg/kg, having a decrease in glycemia between 2 to 4 hours below the blank control, however, it was not statistically significant. In table 2, the effect of reducing glucose levels by the treatment at 2 hours at concentrations of 100 mg/kg and 250 mg/kg was observed, comparable in similarity to Glibenclamide and blank control (saline solution) as a control in which no statistical difference was evident between the treatments (*Chuquiraga weberbaueri*) and the controls (Glibenclamide and blank control). Therefore, the glycemia-reducing effect was observed after the administration of *Chuquiraga weberbaueri* (100 mg/kg and 250 mg/kg) treatments.

In comparison with aqueous extract of *Chuquiraga jussieui*, which had a greater effect with the dose of 400 mg/kg at 10 days where it was shown to be statistically significant [13]. As well as in the aqueous extract of *Psidium guajava* at a dose of 250 mg/kg, the best concentration at 4 hours was statistically significant [14]. In the study of *Allium sativum* and *Capparis spinosa*, it was observed that the best result was that of the alcoholic extract of *Allium sativum* at a dose of 300 mg/kg, this being statistically significant compared to the negative control [36].

In a phytochemical study of *Chuquiraga weberbaueri*, various secondary metabolites were found, including flavonoids, tannins, alkaloids and steroids in large quantities. In the case of flavonoids and saponins, they could be responsible for the decrease in blood glucose, as has been reported in previous studies. Additionally, in a study of *Psidium guajava* it was found that in the phytochemical analysis of the aqueous extract of leaves of *P. guajava*, which showed the best hypoglycemic effect, had a high content of flavonoids, tannins and saponins compared to the ethanolic extract in which these compounds were found, but in smaller quantities, so the amount and type of metabolites found in the aqueous extract would be related to the hypoglycemic effect according to the study [14]. Continuing with the studies of hypoglycemic plants, methanolic extract of *Momordica cimbalaria*, administered at a dose of 175 mg/kg for 30 days to diabetic mice, decreased blood glucose, and the proposed mechanism is the increase in insulin secretion by regeneration of β cells. pancreatic produced by the saponins found in the phytochemical analysis [37]. In the review of the effect of phenolic compounds on carbohydrate metabolism, it is concluded that flavonoids (flavones, flavonols, anthocyanins and proanthocyanidins), phenolic acids and tannins (elagitannins) inhibit the activity of the enzymes pancreatic β-amylase and β- intestinal glucosidase whose function is the release of glucose for the absorption of carbohydrates in the small intestine, resulting in a decrease in blood glucose [38].

Finally, in the toxicity test at a limit dose of 2000 mg/kg, no alterations were found that could be determinants related to the treatment with the extracts administered in the liver, kidney and brain tissues (figure 2, figure 3 and figure 4). These results are similar to an acute toxicity study. from the hydroalcoholic extract of the *Chuquiraga jussieui* plant where We reported that no signs or symptoms of toxicity were observed in the macroscopic analysis of the organs at a limit dose of 2000 mg/kg [39].

Among the limitations of this study was that it was developed in a murine model and therefore is a preclinical study.

With respect to the applicability in clinical practice and potential in clinical trials in humans, in our results it was possible to corroborate the decrease in serum glucose; however, the effect was less than that of glibenclamide and in addition, in the cytotoxicity test, no changes were observed. histological in the organs studied: brain, kidney, liver. Therefore, we consider that this plant could be used as an adjuvant treatment and for the prevention of type 2 diabetes mellitus. Regarding clinical trials in humans, a more in-depth study and follow-up over time is needed to study possible side effects [40].

CONCLUSION

The results of the study showed that *Chuquiraga weberbaueri* extract at doses of 100 mg/kg and 250 mg/kg had hypoglycemic effects in mice. Therefore, it is suggested to continue researching the promising effects of this plant in reducing hypoglycemia. In Peru, many people consume this plant empirically to reduce serum glucose levels, which is why this study is relevant because to date there are no studies that demonstrate its hypoglycemic activity.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The document was approved by the academic direction with academic resolution number 728.

CONSENT FOR PUBLICATION

"Not applicable".

AVAILABILITY OF DATA AND MATERIALS

The data sets used and/or analyzed during the present study are available from the corresponding author upon reasonable request.

CONFLICT OF INTERESTS

The authors declare that they have no competing interests.

FUNDING

Self-financed.

AUTHOR CONTRIBUTIONS

AAMR: was in charge of collecting and sending the sample for taxonomic analysis, participated in all the qualitative analysis processes of the plant, and execution of the project in murines (reception of murines, administration of drugs and dosing of serum levels in the established periods of the project), participated in the writing and publication of the project.

RIFC: participated in all the qualitative analysis processes of the plant, and execution of the project in murines (reception of murines, administration of drugs and dosing of serum levels in the established periods of the project) and participated in the writing and publication of the project.

JERJ: the main contributors in writing the manuscript and advice during the study.

JECF: Provided the environment and material for the execution of the project and participated in the preparation of the ethanolic extract.

JAG: performed the histological examination of the tissues

All authors read and approved the final manuscript.

ACKNOWLEDGEMENTS

Not applicable.

REFERENCES

1. Keays R. Diabetes. Curr Anaesth Crit Care. 2007;18(2):69–75. Available in: https://www.who.int/es/news-room/fact-sheets/detail/diabetes
2. Minsa: Cuatro de cada cien peruanos mayores de 15 años padecen diabetes en el Perú. Gob.pe. Disponible en: https://www.gob.pe/institucion/minsa/noticias/314367-minsa-cuatro-de-cada-cien-peruanos-mayores-de-15-anos-padecen-diabetes-en-el-peru
3. INEI. Instituto Nacional de Estadistica e Informatica. Gob.pe. Available in: https://m.inei.gob.pe/prensa/noticias/el-378-de-la-poblacion-de-15-y-mas-anos-de-edad-tiene-sobrepeso-en-el-ano-2019-12229/
4. Schmidt AM. Highlighting Diabetes Mellitus. Arterioscler Thromb Vasc Biol. Enero de 2018 ; 38(1). Available in:
5. https://doi.org/10.1161/atvbaha.117.310221
6. Diabetes management 2: long-term complications due to poor control. Nursing Times. 2017. Available in: https://www.nursingtimes.net/clinical-archive/diabetes-clinical-archive/diabetes-management-2-long-term-complications-due-to-poor-control-20-03-2017/
7. AVELLO L M, CISTERNAS F I. Fitoterapia, sus orígenes, características y situación en Chile. Rev Medica Chile.Octubre de 2010;138(10). Available in: https://doi.org/10.4067/s0034-98872010001100014
8. Mostacero León J. Características edafoclimáticas y fitogeográficas de las plantas medicinales del dominio andino noroccidental del Perú, durante 1976 al 2004. 2005;[298]-[298]. Available in:
9. https://pesquisa.bvsalud.org/portal/resource/pt/biblio-910778
10. The Plant List (2010). Version 1. Available in Internet; http://www.theplantlist.org/
11. Bussmann R, Sharon D. PLANTAS MEDICINALES DE LOS ANDES Y LA AMAZONIA - La Flora mágica y medicinal del Norte del Perú. 2015. Available in: https://pesquisa.bvsalud.org/portal/resource/pt/biblio-916684
12. Castillo-Vera H, Cochachin E, Albán J. Plantas comercializadas por herbolarios en el mercado del distrito de Cajabamba (Cajamarca, Perú). Bol Latinoam Caribe Plantas Med Aromáticas. 2017;16(3):303–18. Available in: https://www.redalyc.org/articulo.oa?id=85650470005
13. Beltrán H, Granda A, León B, Sagástegui A, Sánchez I, Zapata M. Asteraceae endémicas del Perú. Revista Peruana de Biología. 2006;13(2):64s-164s. Available in: https://www.redalyc.org/articulo.oa?id=195018608015
14. Palacios Lozada E. Economía y Plantas Medicinales. Pensamiento Crítico. 15 de julio de 2004; 3: 011-23. Available in: https://revistasinvestigacion.unmsm.edu.pe/index.php/econo/article/view/9048
15. Rivadeneira AAD. Efecto hipoglucémico del extracto acuoso de Chuquiraga jussieui J.F. Gmel, en ratas con diabetes inducida. Rev Cuba Plantas Med. 2019; 24(3). Available in: https://revplantasmedicinales.sld.cu/index.php/pla/article/view/781
16. Inocente-Camones MA, Guija-Poma E, Zarzosa-Norabuena E, Loja Herrera B, Ponce-Pardo JE. Efecto hipoglicemiante de los extractos acuoso y etanólico de Psidium guajava L. (Guayaba) en ratas diabéticas inducidas por aloxano. Horiz Méd Lima. abril de 2015;15(2):41–8. Available in: http://www.scielo.org.pe/scielo.php?script=sci_arttext&pid=S1727-558X2015000200007&lng=es.
17. Herrera-Calderon O, Chinchay-Salazar R, Palomino-Ormeño E, Arango-Valencia E, Arroyo J. Efecto hipoglucemiante del extracto etanólico de Geranium ruizii Hieron. (pasuchaca) en la hiperglucemia inducida por aloxano en ratas. An Fac Med. 2015;76(2):117–22. Available in: http://www.scielo.org.pe/scielo.php?script=sci_arttext&pid=S1025-55832015000300002&lng=es.
18. Nawel H, Berke B, Umar A, Cheze C, Gin H, Moore N. A review of Algerian medicinal plants used in the treatment of diabetes. J Ethnopharmacol. 2019; 238:111841. Available in;
19. https://www.sciencedirect.com/science/article/pii/S0378874118325017
20. Adetunji C, Palai S, Ekwuabu C, Egbuna C, Adetunji J, Ehis-Eriakha C, et al. General principle of primary and secondary plant metabolites: Biogenesis, metabolism, and extraction. 2020. p. 3–23. Available in: https://api.semanticscholar.org/CorpusID:229427147
21. Okoduwa SIR, Umar IA, James DB, Inuwa HM, Habila JD. Evaluation of extraction protocols for anti-diabetic phytochemical substances from medicinal plants. World J Diabetes. 2016;7(20):605–14. Available in:
22. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5155234/
23. Lock de Ugaz. Investigación Fitoquímica. 1994 . Available in: https://www.fondoeditorial.pucp.edu.pe/452__olga-lock-de-ugaz
24. Arias-Díaz J., Balibrea J. Modelos animales de intolerancia a la glucosa y diabetes tipo 2. Nutr. Hosp. 2007; 22(2): 160-168. Available in en: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S0212-16112007000200005&lng=es.

25. INSTITUTO NACIONAL DE SALUD, MINISTERIO DE SALUD. GUÍA DE MANEJO Y CUIDADO DE ANIMALES DE LABORATORIO: RATÓN]. 2008. Available in: http://bvs.minsa.gob.pe/local/INS/962_INS68.pdf
26. ALIMENTOS BALANCEADOS LA MOLINA. 2018. Available in: http://www.lamolina.edu.pe/facultad/Zootecnia/PIPS/Prog_Alimentos/ratones.htm
27. Alam F, Saqib QN us, Ashraf M. Zanthoxylum armatum DC extracts from fruit, bark and leaf induce hypolipidemic and hypoglycemic effects in mice- in vivo and in vitro study. BMC Complement Altern Med.2018;18(1):68.
28. Chen H, Feng R, Guo Y, Sun L, Jiang J. Hypoglycemic effects of aqueous extract of Rhizoma Polygonati Odorati in mice and rats. J Ethnopharmacol. 2001;74(3):225–9.
29. OpenEpi Menu. Available in:
30. https://www.openepi.com/Menu/OE_Menu.htm
31. Ighodaro OM, Adeosun AM, Akinloye OA. Alloxan-induced diabetes, a common model for evaluating the glycemic-control potential of therapeutic compounds and plants extracts in experimental studies. Med Kaunas Lith. 2017;53(6):365–74.
32. Accu-Chek® Instant Forward | Peru. Disponible en: https://www.accu-chek.com.pe/instant-fw
33. Parámetros fisiológicos ratón. Available in: https://www.humane-endpoints.info/es/raton/parametros-fisiologicos
34. BOE.es - DOUE-L-1996-81573 Directiva 96/54/CE de la Comisión, de 30 de julio de 1996, por la que se adapta, por vigesima segunda vez, al progreso técnico la Directiva 67/548/CEE del Consejo relativa a la aproximación de las disposiciones legales, reglamentarias y administrativas en materia de clasificación, embalaje y etiquetado de las sustancias peligrosas. [cited 27 of december - 2023]. Available in: https://www.boe.es/buscar/doc.php?id=DOUE-L-1996-81573
35. KIANI AK, PHEBY D, HENEHAN G, BROWN R, SIEVING P, SYKORA P, et al. Ethical considerations regarding animal experimentation. J Prev Med Hyg. 17 de octubre de 2022;63(2 Suppl 3):E255-66.
36. RJ_N_102-2012.pdf [Internet]. [cited 18 of february- 2024]. Available in :
37. https://cdn.www.gob.pe/uploads/document/file/1205675/RJ_N__102-2012.pdf?v=1596665558
38. 32.-Sivula CP, Suckow MA. Euthanasia. En: Weichbrod RH, Thompson GA (Heidbrink), Norton JN, editores. Management of Animal Care and Use Programs in Research, Education, and Testing [Internet]. 2nd ed. Boca Raton (FL): CRC Press/Taylor & Francis; 2018 [cited 18 of february of 2024]. Available in : http://www.ncbi.nlm.nih.gov/books/NBK500441/
39. 33.-962_INS68.pdf [Internet]. [cited 18 de february de 2024]. Available in: https://bvs.minsa.gob.pe/local/INS/962_INS68.pdf
40. 34.-Laferriere CA, Pang DS. Review of Intraperitoneal Injection of Sodium Pentobarbital as a Method of Euthanasia in Laboratory Rodents. J Am Assoc Lab Anim Sci JAALAS. 2020;59(3):254-63.
41. 35.-SPSS Statistics - Visión general [Internet]. 2022. Available in: https://www.ibm.com/es-es/products/spss-statistics
42. 36.- Hashemnia M. Blood glucose levels and pathology of organs in Alloxan-induced diabetic rats treated with hydro-ethanol extracts of Allium sativum and Capparis spinosa. Afr J Pharm Pharmacol. 2012;6 (21) 1559-1564.
43. 37.-Shubhapriya K, Koneri R, Sarvaraidu CH. Antidiabetic activity of saponins of Momordica cymbalaria in streptozotocin nicotinamide induced niddm mice. Ind J Pharmacol 2008; 40: 77.
44. 38.-Martín MD, Iriondo-DeHond A. Efecto de los compuestos fenólicos en el metabolismo de los carbohidratos. Rev Esp Nutr Comunitaria 2018; 24(1): 1-12
45. 39.-Dueñas Rivadeneira A, Cortés Rodríguez R, Marrero Chang O, Pérez Donato J, Olazábal Manso EE. Toxicidad aguda del extracto hidroalcohólico de la planta *Chuquiraga jussieui*, administrado vía oral en ratas. La Técnica. 2013;(10):12-7.
46. 40.-Kandi V, Vadakedath S. Clinical Trials and Clinical Research: A Comprehensive Review. Cureus.2023.15(2): e35077.

Cite this article: Raico AAM, Carrasco RIF, Jaimes JER, Flores JEC, Gamio JA. Effect of the Ethanolic Extract of *Chuquiraga weberbaueri* Tovar on Glycemia in BALB/c Mice. Pharmacogn J. 2025;17(1): 63-70.