Hypoglycemic Activity of *Bidens pilosa* and Chrome Picolinate as Coadjutant

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Abstract

The objective of this work is to evaluate hypoglycemic activity of *Bidens pilosa*extract used in traditional medicine, and with addition of chromium as an coadjutant. Healthy rats and rats with induced diabetes with Streptozotocin (STZ) were used; 45 mg/kg *B. pilosa* extract, chromium picolinate and the mixture of both were given. The concentration of 100 mg/kg of extract with 200 mg of picolinate showed higher hypoglycemic effect. *B. pilosa*has hypoglycemic activity but the addition of chromium as adjuvant increased this effect, which supports the use of this plant in traditional medicine

Keywords: Diabetes mellitus, *bidens pilosa*, chrome, hypoglycemic

1. Introduction

Diabetes Mellitus, (D.M.), is a serious problem ofpublic health[1], with high ranges of incidence and mortality, this disease is caused by insufficient insulin production, resistance to the insulin or both conditions. There are more than 220 million peoplewith DM in the world. In Mexico, diabetes has become the leading cause of death by contributing 12% of total deaths. More than 80% of deaths by diabetes are recorded in countries of low and mediumincome. Nearly, the half of those deaths correspond to people of less than 70 years, and 55% to women[2]**.** According to the guides of ALAD 2006, the control, diagnosis and treatment of the DM is based on these causes: feeding habits, physical activity[3,4], and healthy way of life[5]. In traditional medicine, diabetes (DM) is treated with the use of medicinal plants[6].

Onepossible effect of plants extracts is to simulate the fast effect of insulin, another possibility is that they have a residual effect, promoting a better use of the insulin, thereby, regulating processes of generation of energy in the aerobic cycle. Or it is relate with the decrease of the absorption of the carbohydrates in the digestive tract throughdifferent mechanisms (7). There are very few plants whose hypoglycemic effects have been investigatedand identified their active principles responsible for these effects. However, some plants possesslow hypoglycemic activity, which can be used as adjutants of the insulin therapy: using burdock, pods of beans, eucalyptus, Sage, Copalchi, Pau d ' Arco, Juniper, Thistle Holy, walnut, nettle, blueberry, corn, carrot. *Bidens pilosa* is a medicinalplant, that has been used in the traditional medicine, in several drugs and aspopular ingredient in herbal teas., being useful all their parts to treat different ailments[8]. In Mexico the cooking of the stem of *B. pilosa*, as antidiabetic, leaves orallyas antiemetic, antipyretic, soothing, etc. The aqueous extract of the whole plant presented hypoglycemic effect in mice with hyperglycemia induced by alloxan[9], in Florida, the infusion is used for treat arthritis, as diuretic and antidiabetic. In Colombia, the decoction is used for liver diseases, indigestion, diarrhea, expectorant and hypoglycemic[10]. Thenatural products have been used for a long time in traditional systems as adjuvants for the control of the diabetes, one of these products is the chrome[11], an ore present in plants, also in the environment in different forms. Cr (III) is an essentialnutritious element that apparently plays a role important in the metabolism of plants and animals[12]. It is necessary for the metabolism of the glucose, proteins and the fats in mammals[13]. In first studies on the chrome, it is obtained an extract starting from beeryeast that improved the tolerance to the glucose in rats with deficiency of the ore[14], the signals of deficiency in the human being include the loss of weight, interferes in the metabolism of the sugar[15], also can cause unfavorable conditions for the heart, metabolic disorders, etc. It is estimated that an ingestion of between 50 and 200 mg/day is sufficient and presents not risk[11].

2. Methodology

2.1. Plant

2.1.1. Collection and identification of Bidens pilosa

The plant specimen of *Bidens pilosa* was collected from road side of Allende-El Fraile, Paso Hondo town, and was dried under room temperature, subsequently the plant is taken to the Dept. of Botany of the Faculty of Biological Sciences, UANL, for identification with no. 024777. Then it is collected abundantly, randomly, choosing only those specimens that look healthy, without damage, leaving it to dry in thecited conditions.

2.1.2. Bidens pilosa methanolic extract

The leaves are ground in an electric mill, then 50 g. of crushed powder of the leaves, placed in a flask 300 ml of methanol and then stirred with an electric stirrer with sweeps for 48 hours, and subsequently filtered into flask kitasatto with vacuum pump, as extracting solvent, then it is left to dry obtaining *B. pilosa* methanolic extract, and weighed for further use.

2.1.3. Determination of the chromium

It was performed in anabsorption atomicspectrophotometer (Perkin-Elmer 5100). The AA is a technical of quantitative analysis that allows determine the content of metal present in a sample, in this case, the chrome content in dried and groundleaves of *B. pilosa*[16].

2.1.4. Phytochemical qualitative analysis

To methanolic extract of *B. pilosa* were tested colorful compounds and functional groups: Dragendorff (alkaloids), Shinoda (flavonoids), Lieberman-Burchard (triterpenes and steroidal compounds), Molish (sugars), Baljet (sesquiterpenlactones), NaOH (lactones), potassium permanganate (double links) [17].

2.2. Animal model

2.2.1. Determination of the streptozotocin dose (SZT) to induce diabetes

SZT reagent was administered intraperitoneally in three doses: 35 mg/dL, 45 mg/dL and 55 mg/dL to induce diabetes in Sprague Dawley male rats healthy, 8 weeks, with an average weight of 300 g after prolonged lack of food [18], were monitored to determine basal glycemia every 7 d to obtain values of 170 to 300 mg/dL.

3. Experimental Approach

Trials were made with groups of five healthy rats and groups of five experimentally-induced diabetic rats which were randomly distributed. Glycemia was monitored In fasting every 7 d, from a drop of blood from the tail with the Onetouch Basic Plus meter. Dissolved 100, 200 and 400 mg/kg of the weight of the extract in distilled water in a volume of 0.5 ml and administered intragastrically at a single intake at the same hour, during 21 (DM) and 28 (healthy) uninterrupted days, as well as to all the treatments. Received food and water Ad libitum.

3.1. Experimental induction of diabetes

To induce the DM in rats was applied EZT 45 mg/kg in a 0.5 ml volume of water via the intraperitoneal route. Glycemia in fasting, was determined every week to confirm glucose levels. The bioassay with diabetic rats induced with EZT, continued in the following way:

Group I: diabetic rats receiving water by intragastric tube (positive control)
Group II: Diabetic rats receiving 100 mg/kg of the extract.
Group III: Diabetic rats receiving 200 mg/kg of extract.
Group IV: Diabetic rats who received 400 mg/kg of extract.
Group V: healthy rats receiving water (negative control)

The second bioassay with induced diabetic rats, was performed in the same conditions of the first test with the following doses:

Group IA: diabetic rats receiving 200 mg/kg of chromium picolinate.
Group IIB: Diabetic rats receiving 200 mg/kg of chromium picolinate and extract 100 mg/dL. Group IIIC: Diabetic rats receiving water by intragastric tube (positive control)

3.2. Artemia salinaLethality essay

Lethality test is performed in triplicate with 4 replications each, with A. salina larvae, µg/mL, 750 µg/mL, 500 µg/mL and 250 µg/mL19 were exposed for 24 h to 4 concentrations of the methanol extract *B. pilosa* with hypoglycemic effect at concentrations of 1000 µg/mL, 750 µg/mL, 500 µg/mL and 250 µg/mL[19].

4. Results and Conclusions

It was obtained a yield of 3.03% w/w of the leaves of methanolic extract of *B. pilosa* and was soluble in methanol and ethanol, with a content of chromium of 28.87 µg/L.

The qualitative tests for partial identification of functional groups in the extract of *B. pilosa* tested was positive for: flavonoids, alkaloids, triterpenes, steroidal, lactones and sesquiterpenlactones compounds. These functional groups within the secondary metabolites in the extract and the addition of chrome are postulated to be the active ingredients that favors the hypoglycemia in diabetic rats. Results for blood sugar levels in the study groups (II, III and IV) and controls (I & V) are shown in Figure 1, the three doses administered showed a decrease in blood sugar levels up to 3 weeks; in the fourth week only increased blood sugar levels to doses of 200 and 400 mg/dL, being the most effective dose of 100 mg/kg by keeping blood sugar levels close to the levels of the control. Given these results, this dose was chosen to assess the hypoglycemic effect using adjuvant chromium picolinate. The decrease of glycemia is present after 2 weeks under the treatments (Figure 2). The combination of chromiumpicolinate and *B. pilosa* extract had the expected in Group IIB during the three weeks of the trial; to the IA group which was administered only chromium picolinate showed resistance to keep glucose levels in decline (as it was demonstrated in the fourth week). The feasibility displayed on *A. salina* at

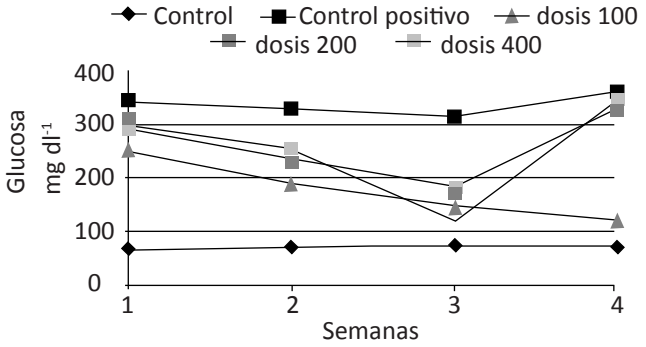

Figure 1: Hypoglycemic effect of *B. pilosa* extract at different concentrations on diabetic rats

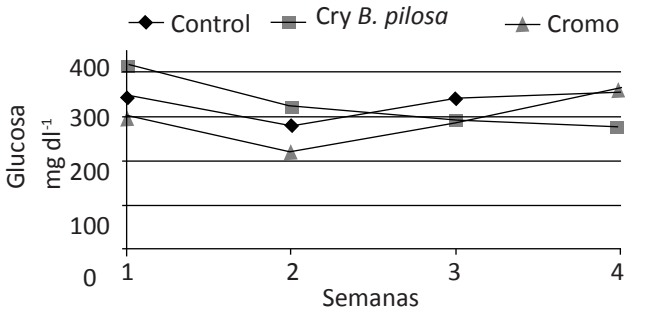

Figure 2. Hypoglycemic effect of chromium (200 mg kg^{-1}), extract *B. pilosa* picolinate (100 mg kg^{-1}) with chromium picolinate (200 mg kg^{-1})

various concentrations as shown in Table 1, *B. pilosa* is not toxic according to the criteria of Deciga C M[19].

The National Academy of Sciences of the United States recommends a safe and adequate doses of trivalent chromium in the diet that range from 50 to 200 µg day^{-1} in humans, and the average intake in our diet is only between 50 and 80 µg

Table 1: Viability of *Artemia salina* with different concentrations of the extract of *B. pilosa*

	Extract concentration (µg ml^{-1})				Control	
B. pilosa	1000	750	500	250	Positive	Negative
% Viability	6.4	6.4	8.0	6.9	100	3.9

per day, which is insufficient. Some studies in animals, and clinical in humans have shown that supplementation with Cr in the form of chromium picolinate is safe and that there is a significant decrease in glycosilated hemoglobin [15], [20].

Secondary metabolites identified in *B. pilosa* , used empirically for its hypoglycemic effect, match research reported in other plants also employed by this action and have given remarkable results on the glicemia[4].

The great diversity of pharmacological actions attributed to *B. pilosa* Linné is due to the variety of chemical compounds in it, can be of significant importance in action empirical use as hypoglycemic.[12] Hypoglycemic activity has been demonstrated with all parts of the plant, but mainly with the fruits. Seems to be due to saponins steroids (charantines, mainly 3-glucosyl-beta-sitosterol and 3-glucosil-5, 25-stigmastadienol), to (similar to insulin) peptides and alkaloids, but it is unknown if the activity is mainly due to one of the groups or to the whole. Regarding the mechanism of action of the drug, is still not known too well; some authors indicate that it increases the number of beta cells in the pancreas, while others have demonstrated similar to insulin or increase of their release activity. Therefore, the hypoglycemic action may occur by pancreatic and extrapancreatic mechanisms.[21]

B. pilosa has hypoglycemic activity and the addition of adjuvant chromium picolinate increases this effect, which supports the use of this plant in traditional medicine.

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