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Acute and chronic [hypoglycemic](#page1) effect of [*Ibervillea*](#page1) sonorae root extracts-II

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**Abstract**

*Ibervillea sonorae*’s root, or “wareque” (Cucurbitaceae), is widely used in Mexican traditional medicine for the control of diabetes mellitus.

In the present study, the hypoglycemic effects produced by the acute and chronic administration of various extracts of *Ibervillea sonorae* were investigated. Both the traditional preparation (aqueous decoction) and the raw extract (juice) from the root resulted in significant reductions of glycemia in healthy mice after intraperitoneal administration at a dose of 600 mg/kg. Additionally, ground dried root was used to obtain a dichloromethane (DCM) extract and a methanol (MeOH) extract. The DCM extract induced a clear reduction of glycemia in healthy (*P* < 0.05) and in alloxan-diabetic mice. The intraperitoneally administered DCM extract caused a severe hypoglycemia that produced lethality in all the treated animals when doses of 300 and 600 mg/kg body weight were used. Since the DCM extract showed a marked hypoglycemic activity, it was administered daily per os to alloxan diabetic rats, employing corn oil and tolbutamide as controls. After 41 days of DCM extract administration at a dose of 300 mg/kg/day, diabetic rats showed improvement in glycemia, body weight, triglycerides, and GPT in comparison with the diabetic control group. Total cholesterol, GOT, and uric acid blood levels were not affected. © 2005 Elsevier Ireland Ltd. All rights reserved.

*Keywords:* Hypoglycemic plants; Antidiabetic plants; Medicinal plants; *Ibervillea sonorae*; Cucurbitaceae

**1. Introduction**

Diabetes mellitus is the metabolic disorder with the high-est rates of prevalence and mortality world-wide (Harris et al., 1998; Barcelo and Rajpathak, 2001). In Mexican traditional

medicine, the root of *Ibervillea sonorae* Greene (syn. *Maxi-*

*mowiczia sonorae* S. Wats.; Cucurbitaceae), popularly known

as “wareque”, is one of the most widely used plant remedies for the treatment of this disease (Xolalpa-Molina, 1994). In previous acute studies, a single intraperitoneal administra-

tion of the traditional preparation of *Ibervillea sonorae* roots showed dose-dependent hypoglycemic activity in healthy and

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alloxan diabetic [mice and rats.](#page5) Moreover, when it was in-traperitoneally injected at doses as high as 850 mg/kg body weight, or orally administered at doses as high as 2000 mg/kg, no signs of toxicity were observed in healthy mice (Alarcon-Aguilar et al., 2002a). Nevertheless, there is no knowledge about the chemical nature of its active components or about the effects caused by its chronic administration that permit the establishment of a basis for its clinical use in the control of diabetes mellitus. Hence, many questions still remain unan-swered regarding this interesting medicinal resource. The aim of this research was to study the hypoglycemic effects pro-duced by the administration of various organic and aqueous

extracts of *Ibervillea sonorae* roots in healthy and alloxan diabetic mice and to determine the hypoglycemic effect pro-duced by the chronic administration of the active extract in alloxan diabetic rats.

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**2. Materials and methods**

*2.1. Plant material*

Fresh roots of *Ibervillea sonorae* were acquired from the

Sonora Herbal Market at Mexico City. This material was authenticated by experts in ethnobotany at the Medicinal Plant Herbarium from the Mexican Security Social Institute (IMSSM-Herbarium Voucher Specimen Num. 14,184).

*2.2. Traditional preparation*

Ground dried root of *Ibervillea sonorae* (100 g) was

steeped in boiling water (300 ml) for 30 min and then left to cool at room temperature. Next, this decoction was de-canted and centrifuged. The supernatant was then freeze-dried, yielding 10.62% (w/w). Doses of 300 and 600 mg/kg body weight of this preparation were administered to healthy mice by intraperitoneal (i.p.) injection, by dissolving the product in 4 ml/kg weight of Isotonic Saline Solution (ISS) (Pisa Laboratories).

*2.3. Raw extract*

The root of *Ibervillea sonorae* (1.176 kg) was cut in small

slices and its juice was obtained with a Turmix electric ex-tractor. The juice was filtered, obtaining a liquid (488 ml) which was freeze-dried, yielding 2.7% (w/w). This material was then administered to healthy mice in the same conditions and doses as in the traditional preparation.

*2.4. Preparation of Ibervillea sonorae root extracts*

Two samples of 100 g dried and powdered root were extracted by maceration (two times for 2 weeks) with dichloromethane (DCM, 600 ml) and methanol (MeOH, 600 ml). The extracts were concentrated under reduced pres-sure and pooled, yielding 1.87% and 14.09% (w/w) of DCM and MeOH extract, respectively. The DCM and MeOH ex-tracts were administered at doses of 300 and 600 mg/kg to experimental animals, dissolved in 4 ml/kg body weight of a suitable vehicle. The DCM extract was dissolved in corn oil and the MeOH extract in ISS.

*2.5. Phytochemical screening of the DCM Ibervillea sonorae root extract*

In order to determine the presence of [alkaloids, flavones,](#page5) coumarines, tannins, terpenes, sterols, saponins and sugars, a preliminary phytochemical study with the DCM extract was performed by coloring and precipitation assays follow-ing the Farnsworth’s method (Farnsworth, 1966). For the de-termination of phenols, flavones and alkaloids, an analysis by thin layer chromatography (Silica Gel 60F-254 Merck) using chloroform/ethyl acetate (1:1) mixtures as the mobile phase and spraying the plates with vanillin, AlCl3, and Dra-gendorff‘s reagents, respectively, as well as 2% Ce(SO 4)2 solution in 2N H2SO4, was also performed.

*2.6. Animals*

Male adult CD-1 mice (25–35 g) and male adult Wis-tar rats (250–350 g), with free access to water and [food,](#page6) were used. [The](#page6) handling of the laboratory animals was performed in agreement with the statutes of the CICUAL (Institutional Committee for the Care and Use of the An-imals) by the Official Mexican Rule (NOM-062-ZOO-1999, revised in 2001). The animals were kept in an air-conditioned animal room with a 12 h light–12 h dark cy-cle. Experimental diabetes in both groups was induced by two intravenous injections of alloxan (Alloxan monohydrate (2,4,5,6-(1H, 3H)-pyrimidinetetrone, Sigma–Aldrich) at in-tervals of 48 h (2 × 75 mg/kg). Blood glucose levels were determined seven days after the last administration. An-imals with glycemia values ≥200 mg/dl were considered diabetic.

*2.7. Biological assays*

*2.7.1. Hypoglycemic effect of the freeze-dried decoction and freeze-dried juice of Ibervillea sonorae root in healthy mice*

Healthy fasted mice (18 h) were allotted into six groups of six mice. Extracts and control substances were adminis-tered by i.p. injection. Group 1 received 4 ml/kg of ISS as control. Group 2 received 150 mg/kg of tolbutamide as pos-itive control (Artosin, tablets of 500 mg, Roche). Groups 3 and 4 received 300 and 600 mg/kg of the freeze-dried de-coction. Groups 5 and 6 received 300 and 600 mg/kg of the freeze-dried juice.

*2.7.2. Hypoglycemic effect of the organic extracts in healthy mice*

Healthy fasted mice (18 h) were allotted into six groups of six mice. Extracts and control substances were administered by i.p. injection. Groups 7 and 8, served as controls, receiving 4 ml/kg of ISS and corn oil, respectively. Groups 9 and 10 received 300 and 600 mg/kg body weight of the DCM extract. Groups 11 and 12 received 300 and 600 mg/kg of the MeOH extract.

*2.7.3. Hypoglycemic effect of the DCM extract in alloxan-diabetic mice*

Alloxan diabetic mice with free access to water and food were distributed into four groups of six mice. Groups 13 and 14 (controls) received 4 ml/kg by i.p. injection of corn oil and tolbutamide (150 mg/kg), respectively. Groups 15 and 16 received 300 and 600 mg/kg by i.p. administration of the DCM extract.

*2.7.4. Hypoglycemic activity produced by the daily administration of DCM extract to alloxan-diabetic rats*

The DCM extract of *Ibervillea sonorae* root (300 mg/kg body weight per day) was administered daily to 10 alloxan diabetic rats per os (p.o.) during 6 weeks. Two groups of

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10 diabetic rats were used as control and reference, re-ceiving ISS (4 ml/kg) and tolbutamide (150 mg/kg), respec-tively. Body weight, blood glucose levels, uric acid, as-partate aminotransferase (AST or GOT), alanine amino-transferase (ALT or GPT), total cholesterol and triglyc-erides levels in plasma were determined at days 1, 14, 27, and 41.

In all cases, DCM extract and tolbutamide were dissolved in 4 ml/kg body weight of corn oil and ISS, respectively.

*2.7.5. Biochemical parameters*

Blood samples in mice were obtained from the tail’s vein and glycemia levels were determined at the beginning of the experiment (0 min), and at 120, 240 and 360 min after the administration of substances. Blood samples in rats were ob-tained from the tail’s vein also at the beginning of the exper-iment in order to determine glycemia in all animals. Next, during each measurement interval, four rats were randomly chosen and anesthetized with ether to obtain 1 ml of blood in heparinized vials by cardiac puncture. Plasma was sepa-rated immediately by centrifugation at 756 × *g* for 10 min and uric acid, GOT, GPT, total cholesterol and triglycerides lev-els were quantified using reactive strips for Reflotron System (Roche Diagnostics). Glycemia was quantified in an Accu-Chek Sensor Comfort Glucose apparatus using reactive strips (Roche Diagnostics).

*2.8. Statistical analysis*

Results are expressed as mean ± S.E.M. The significance of the differences between the means of control and the means of the test studies was established by the Student’s *t*-test for independent samples (*P* < 0.05).

**3. Results**

Table 1 shows the acute hypoglycemic effect obtained in healthy and alloxan-diabetic mice after administration of

*Ibervillea sonorae’s* freeze-dried decoction, juice, DCM ex-tract and MeOH extract. Basal glycemia did not change sig-nificantly in the control groups, whereas tolbutamide reduced it at 120 and 360 min (*P* < 0.05) in healthy mice and also caused significant reductions at 120, 240 and 300 min in dia-betic mice. Freeze-dried decoction and freeze-dried juice sig-nificantly lowered the glycemia at doses of 600 mg/kg. The DCM extract presented a significant hypoglycemic effect at doses of 300 and 600 mg/kg after 360 min, inducing severe hypoglycemia. When the MeOH extract was injected at a dose of 600 mg/kg, it caused reduction of the basal glycemia at 360 min (*P* < 0.05)[. In](#page4) diabetic mice, the DCM extract caused significant reductions at doses of 300 and 600 mg/kg, reach-ing glycemic levels below 100 mg/dl at 240 min. However, after 240 min all the animals died for both doses.

Table 2 shows the changes in body weight and biochemical parameters after the chronic administration of DCM extract to alloxan-diabetic rats. The data presented were compiled from animals that survived the entire experimental proce-dure (some animals died during the experimental procedure due to the effects of ether anesthesia and/or cardiac punc-ture). In the control group the body weight was progres-sively reducing and the glycemia was significantly increased at day 41 (*P* < 0.05). In addition, an important increase in the triglycerides levels (*P* < 0.05) was noticed, as well as a mod-erate, but not significant increase in GPT (*P* > 0.05). Signif-icant changes in uric acid, GOT, or cholesterol levels were not present in the control animals. The tolbutamide-treated group did not show important changes in body weight and,

Table 1

Hypoglycemic effects produced by the intraperitoneal administration of freeze-dried juice and decoction of *Ibervillea sonorae* root, dichloromethane (DCM)

and methanol (MeOH) extracts in healthy and alloxan diabetic mice (*n* = 6)

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study | Treatment | Dose | Blood glucose (mean ± S.E.M.) (mg/dl) | | | | | | |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  | In fasting | | | 120 min | |  |  | 240 min | |  |  |  | 360 min | |  |  |  |  |  |
|  |  |  |  |  | |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |
| 1. Healthy mice | Control (ISS) | 4 ml/kg | 69.9 | ± 3.3 | | 69.0 | ± | 4.6 \* |  | 72.1 | ± | 2.9 |  |  | 63.7 | ± 3.4 | | \* |  |  |  |
|  | Tolbutamide | 150 mg/kg | 61.6 | ± 2.7 | | 54.3 | ± | 2.9 |  | 56.8 | ± | 3.0 |  |  | 52.4 | ± 2.4 | |  |  |  |  |
|  | Freeze-dried juice | 300 mg/kg | 66.4 | ± 9.3 | | 75.0 | ± | 5.0 |  | 65.0 | ± | 6.2 |  |  | 57.0 | ± 5.4 | | \* |  |  |  |
|  |  | 600 mg/kg | 56.3 | ± 4.9 | | 59.2 | ± | 3.4 |  | 47.8 | ± | 2.7 |  |  | 43.0 | ± 2.6 | |  |  |  |  |
|  | Freeze-dried decoction | 300 mg/kg | 60.3 | ± 4.2 | | 53.3 | ± | 5.1 |  | 54.0 | ± | 2.8 | \* |  | 53.8 | ± 4.2 | | \* |  |  |  |
|  |  | 600 mg/kg | 63.5 | ± 1.2 | | 67.0 | ± | 1.5 |  | 48.4 | ± | 3.0 |  |  | 38.2 | ± 3.2 | |  |  |  |  |
| 2. Healthy mice | Control (ISS) | 4 ml/kg | 64.6 | ± 5.8 | | 68.3 | ± | 7.8 |  | 63.6 | ± | 7.2 |  |  | 57.3 | ± 3.3 | |  |  |  |  |
|  | Control (corn oil) | 4 ml/kg | 56.2 | ± 4.9 | | 61.3 | ± | 4.8 |  | 67.8 | ± | 5.5 |  |  | 56.0 | ± 3.8 | | \* |  |  |  |
|  | DCM extract (corn oil) | 300 mg/kg | 66.6 | ± 3.9 | | 68.2 | ± | 6.1 |  | 71.3 | ± | 4.0 | \* |  | 46.0 | ± 4.6 | | \* |  |  |  |
|  |  | 600 mg/kg | 68.8 | ± 6.6 | | 60.2 | ± | 7.7 |  | 35.2 | ± | 5.4 |  |  | 20.0 | ± 1.1 | |  |  |  |  |
|  | MeOH (ISS) | 300 mg/kg | 59.0 | ± 6.4 | | 60.4 | ± | 3.9 |  | 58.0 | ± | 2.2 |  |  | 54.6 | ± 3.5 | | \* |  |  |  |
|  |  | 600 mg/kg | 53.6 | ± 1.2 | | 65.8 | ± | 3.2 |  | 49.8 | ± | 2.7 |  |  | 41.6 | ± 4.4 | |  |  |  |  |
| 3. Alloxan diabetic mice | Control (corn oil) | 4 ml/kg | 410.3 | ± 18.4 | | 422.0 | ± | 15.8 | \* | 396.2 | ± | 20.5 | | \* | 370.4 | ± 13.4 | | | \* | |  |
|  | Tolbutamide | 150 mg/kg | 403.0 | ± | 11.6 | 333.5 | ± | 23.0 | \* . | 330.8 | ± | 14.0 | |  | 315.6 | ± | 18.6 | |  |  |  |
|  | DCM extract (corn oil) | 300 mg/kg | 444.0 |  | 333.6 | 38.9 | 9.8 | \* |  | a |  |  |  |  |  |
|  | ± 25.0 | | ± | \* | 94.5 | ± |  | \* | a |  |  |  |  |  |  |
|  |  | 600 mg/kg | 400.7 | ± 18.4 | | 217.2 | ± | 36.5 |  | 95.6 | ± | 23.6 | |  |  |  |  |  |  |  |  |

1. Animals died before 360 min.

∗ Significantly different from pre-value in fasting: *P* < 0.05. ISS: isotonic saline solution.

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| extractof*Ibervillea* | a | (mg/dl) | ±377.8.48 | & | ±189.85.96 | & | ±88.21.13 | \* | ±375.3.2 | ±3154.61.8 | ±92.22.00 | ±970.0.87 | ±285.6.69 | ±89.1.220 |  |  |  |  |  |
| Triglycerides | ±262.76.74 | ±5261.69.8 | ±80.12.48 |  |  |  |  |  |
| adichloromethane |  |  |  |  |  |  |  |  |  |  |  | \* |  | \* |  |  |  |  |  |
| Totalcholesterol | (mg/dl) | ±101.51.1 | ±116.35.5 | ±103.32.4 | ±101.51.2 | <100 | <100 | <100 | <100 | <100 | <100 | <100 | <100 |  |  |  |  |  |
|  | a |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| tolbutamide,and | GPT |  | ±7106.56.8 | ±114.14.10 | ±120.59.50 | ±5149.53.5 | ±77.18.14 | ±53.12.28 | ±060.21.5 | ±565.3.30 | ±77.15.01 | ±558.6.35 | ±645.17.3 | ±54.0.245 |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  | \* |  |  |  |  |  |
|  | (I.U.) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| cornoil(control), | a |  | ±8136.40.1 | ±136.27.27 | ±71.26.01 | ±1122.40.0 | ±76.9.802 | ±67.15.03 | ±663.23.1 | ±365.17.0 | ±66.8.094 | ±4660.5.9 | ±959.8.54 | ±71.5.250 |  |  |  |  |  |
| GOT |  |  |  |  |  |  |
|  | (I.U.) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | a |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| of | (mg/dl) |  | ±722.0.46 | ±2.0.2418 | ±2.0.3366 | ±752.0.61 | ±2.0.2418 | ±2.0.1117 | \* | \* | ±2.0.2420 | ±072.0.08 | ±742.0.60 | \* , & |  |  |  |  |  |
| dailyadministration | Uricacid |  | ±002.0.11 | ±002.0.10 | ±3.0.4935 |  |  |  |  |  |
|  | a |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| plasmaafterperos | Glycemia(mg/dl) |  | ±3345.48.2 | ±413.49.28 | ±460.64.28 | ±9505.41.7 | ±310.27.14 | ±338.19.31 | ±0424.39.9 | ±34404.66. | ±355.37.95 | ±40324.38. | ±72386.50. | ±307.53.54 |  |  |  |  |  |
|  |  |  |  |  |  | & |  |  | & |  |  |  |  | \* |  |  |  |  |  |
| in | Weight(g) |  | ±3291.28.7 | ±308.30.81 | ±276.17.99 | ±5246.40.4 | ±258.27.12 | ±234.22.85 | ±5246.37.8 | ±3260.21.9 | ±285.35.42 | ±2328.27.9 | # | # |  |  |  |  |  |
| triglycerideslevels |  | ±3341.29.6 | ±335.27.38 |  |  |  |  |  |
| Table2Bodyweight,glycaemia,uricacid,GOT,GPT,totalcholesteroland±*sonorae*root(meanS.E.M.)toalloxandiabeticrats | StudyTime(days)*n* |  | Control(4ml/kg)010 |  |  |  | Tolbutamide(150mg/kg)010 | \* |  |  | Dichloromethaneextract(300mg/kg)010 | # | \*,&, | \*,&, | GOT:aspartateaminotransferase.GPT:alanineaminotransferase.a |  |  |  |  |
|  | 149 | 277 | 417 | 148 | 276 | 414 | 149 | 276 | 416 | ∗ | & | # |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | 0.05. | *t* = 0: *P* < 0.05. | *P* < 0.05. |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | ±Mean S.E.M. of four rats. | Significantly different from control: *P* < | Significantly different from pre-value at | Significantly different from tolbutamide: |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

although triglycerides levels were increased, the difference with respect to basal [values](#page4) was not significant. Glycemic levels were significantly increased at day 27 in this group. However, the other parameters (uric acid, GOT, GPT and cholesterol) [did not](#page4) change after 41 days of treatment with this drug (Table 2).

The DCM extract produced an important increase in the body weight and a moderate reduction of the glycemia (Table 2). Both parameters were appreciably different with respect to the values in the control group (*P* < 0.05). Uric acid showed a moderately significant change with respect to its previous value at the beginning of the experiment (*t* = 0). In this group, GOT, GPT, total cholesterol, and triglycerides levels did not show important variations after 41 days of treat-ment

The results obtained from the preliminary chemical anal-ysis showed only the presence of phenols and sterols, as in-dicated by the vanillin reagent and coloring sterols assay, respectively.

**4. Discussion**

An aqueous decoction of the root of *Ibervillea sonorae* is

the common form of administration used in Mexico for the treatment of type 2 diabetes. The traditional remedy is pre-pared with approximately 5 g of dried root steeped in 500 ml of boiling water for 15 min and then cooling at room tem-perature. This preparation’s yield is 30% (1.5 g in a volume of 300 ml) and it is orally administered to diabetic patients before every [meal three times a day (75 mg/kg/day). How-](#page6)ever, in order to start a drug discovery process from plant extracts with reputed biological activity, various researchers recommend doses that range between 10 and 1000 mg/kg (Saleem et al., 1999; Grover et al., 2000; Aderibigbe et al., 2001; Kanegusuku et al., 2002; Hui-Chen et al., 2004; Suba et al., 2004). Previous studies of the traditional [preparation of](#page5)

*Ibervillea sonorae* have shown that it reduces the glycemiaof experimental animals in a dose-dependent manner, having a different effect with each of the administered doses of 150, 300, 600 and 850 mg/kg (Alarcon-Aguilar et al., 2002a). Al-though the daily dose employed in diabetic patients is clearly smaller (75 mg/kg) than the one used in experimental ani-mals (300 and 600 mg/kg), in the present study we decided to use intermediate doses because our main objective was to detect the hypoglycemic activity caused by the extracts in the experimental models.

In the first experiment the results showed that both, a sample of root boiled in water and the root’s juice caused the same hypoglycemic effect in healthy mice. Therefore,

the hypoglycemic activity of *Ibervillea sonorae* is caused by substances that naturally exist in the root, and not due to transformations induced by heating. For this reason, the in-tact plant material was used to obtain the extracts. Due to the fact that the DCM extract caused a severe hypoglycemia in fasting healthy mice, it was chosen to study the acute and

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chronic hypoglycemic effects in alloxan diabetic mice and rats. The DCM extract markedly reduced blood glucose lev-els in alloxan diabetic mice when it was i.p. administered. Moreover, it also caused symptoms of severe hypoglycemia, including generalized convulsions and subsequent death of all studied animals between 240 and 360 min. Conversely, the p.o. chronic administration of DCM extract increased body weight and moderately reduced glycemia, thus showing an improvement in the diabetic status of these animals when compared to the control and tolbutamide-treated groups.

Triglycerides levels in the control and tolbutamide-treated groups were increased. However, in animals treated with DCM extract, triglycerides levels did not change during the 41 days of the experiment. These results, in combination with the observed body weight gain and reduction in glycemia of the DCM extract-treated group, suggest that the hypo-glycemic activity of the plant could be explained by an im-provement in the sensibility of the insulin and/or by the re-duction of insulin resistance. In previous studies we have determined that traditional preparation of *Ibervillea sono-*

*rae* reduced the glycemia in healthy and mild diabetic mice(with b-cells functioning), but not in severe diabetic animals (without b-cells functioning). Therefore, endogenous insulin is necessary to observe hypoglycemic activity with *Ibervillea* *sonorae*.

Values of GPT were also increased in the control [group,](#page6) but not in the tolbutamide and DCM extract-treated groups. Abnormal levels in plasma of GOT and GPT is of clinical and toxicological importance, being indicative of tissue damage by toxicants or disease conditions [(Singh et al., 2001). Ex-](#page6)perimental [diabetes](#page6) induced by alloxan in rats causes tissue damage in the pancreas, liver, kidneys and heart, which can be reflected on the increment of GOT and various hepatic en-zymes, such as GPT (Rerup, 1970; Stanely et al., 2000; Singh et al., 2001). DCM extract and tolbutamide did not changed GOT levels; however, the DCM extract significantly reduced GPT plasmatic levels with respect to the control group.

After 14 days of treatment with DCM extract, some an-imals showed diarrhea and decreased motor activity. The same symptoms were observed in both the control and the tolbutamide-treated groups at the end of the treatment. No macroscopic alterations in the liver or kidneys were ob-served in any group, but colon inflammation, mainly in the DCM extract-treated animals, was present. Literature reveals that various compounds isolated from Cucurbitaceae species, some of which have hypoglycemic effects, are also consid-ered toxic agents. In addition, [the presence of alkaloid gluco-](#page6)sides, flavones, steroidal [saponins (charantins),](#page5) sterols, [phe-](#page5)nolics, cucurbitacin triterpenes and other tetracyclic triter-penes, as well as insulin-like peptides, has been reported in this family (Marles and Farnsworth, 1995; Alarcon-Aguilar et al., 2002a; Alarcon-Aguilar et al., 2002b; Hernandez-Galicia et al., 2002). The chemical analysis showed that the DCM

extract of *Ibervillea sonorae* has compounds containing hy-droxyl groups, as suggested by the positive reaction for phe-nols, and sterols identified by the vanillin reagent. Work on

the isolation and the chemical characterization of the hypo-glycemic principles of the crude drug is in progress.

In conclusion, the i.p. administered DCM extract could contain compounds that elicit exceptionally significant hypo-glycemic activity in healthy and alloxan diabetic mice. Fur-thermore, the daily p.o. administration of this extract to rats produced reduction of the glycemia and triglycerides levels, without evident toxic effects.

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