

Journal of Ethnopharmacology 61 (1998) 101 ± 110

Study of the anti-hyperglycemic effect of plants used as antidiabetics

F.J. Alarcon-Aguilara a,\*, R. Roman-Ramos a, S. Perez-Gutierrez b, A. Aguilar-Contreras c, C.C. Contreras-Weber a, J.L. Flores-Saenz a

1. *Departamento de Ciencias de la Salud*, *Uni*6*ersidad AutoÂnoma Metropolitana Iztapalapa*, *A*6. *MichoacaÂn y La PurõÂsima*, *Col*. *Vicentina*, *09340*, *Apartado Postal 55*-*535*, *MeÂxico*, *D*.*F*., *MeÂxico*
2. *Departamento de Sistemas BioloÂgicos*, *Uni*6*ersidad AutoÂnoma Metropolitana Xochimilco*, *Apartado Postal 23*-*181*,

*MeÂxico D*.*F*., *MeÂxico*

1. *Herbarium*-*IMSSM*, *Centro MeÂdico Nacional Siglo XXI*, *Subjefatura de In*6*estigacioÂn*, *IMSS*, *MeÂxico*, *D*.*F*., *MeÂxico* Received 23 July 1997; received in revised form 16 January 1998; accepted 26 January 1998

**Abstract**

The purpose of this research was to study the anti-hyperglycemic effect of 28 medicinal plants used in thetreatment of diabetes mellitus. Each plant was processed in the traditional way and intragastrically administered to temporarily hyperglycemic rabbits. The results showed that eight out of the 28 studied plants signi®cantly decrease the hyperglycemic peak and:or the area under the glucose tolerance curve. These plants were: *Guazuma ulmifolia*, *Tournefortia hirsutissima*, *Lepechinia caulescens*, *Rhizophora mangle*, *Musa sapientum*, *Trigonella foenum graceum*, *Turnera diffusa*, and *Euphorbia prostrata*. The results suggest the validity of their clinical use in diabetes mellituscontrol, after their toxicological investigation. © 1998 Published by Elsevier Science Ireland Ltd. All rights reserved.

*Keywords:* Anti-diabetic plants; Hypoglycemic plants; Medicinal plants; Diabetes mellitus control

**1. Introduction**

Diabetes mellitus is considered to be a serious endocrine syndrome. The prevalence of diabetes mellitus in the general population is greater than 6% (ADA, 1997). Commonly practiced pharma-cological treatments of diabetes mellitus includes

\* Corresponding author.

oral hypoglycemic agents and:or insulin injections (Lebovitz and Pasmantier, 1990; Bailey, 1992; White, 1996). However, for many years people in Mexico have used plants to empirically treat dia-betes. World ethnobotanical information about medicinal plants reports almost 800 plants used in the control of diabetes mellitus. Aproximately 150 of these exist in Mexico (Alarcon-Aguilar et al., 1993). However, only a small number of them

0378-8741:98:$19.00 © 1998 Published by Elsevier Science Ireland Ltd. All rights reserved.

*PII* S0378-8741(98)00020-8

102 *F*.*J*. *Alarcon*-*Aguilara et al*. *: Journal of Ethnopharmacology 61 (1998) 101 ± 110*

have been studied. The plants more extensively studied in Mexico are the `nopal' *Opuntia strepta*-*cantha* (IbanÄ ez-Camacho and Roman-Ramos,1979, IbanÄ ez-Camacho et al., 1983; Meckes-Lozya and Roman-Ramos, 1986; Frati-Munari et al., 1991) and the `tronadora' *Tecoma stans* (Youssef-Hammouda et al., 1964; Meckes-Lozoya and IbanÄ ez-Camacho, 1985; Lozoya-Meckes and Mel-lado-Campos, 1985), although the hypoglycemic effect of other 33 antidiabetic Mexican plants have been proven (Roman-Ramos et al., 1991, 1992a, 1995; Alarcon-Aguilar et al., 1997).

The purpose of this research was to experimen-tally assess the anti-hyperglycemic effect of 28 plants used in diabetes mellitus control. In addi-tion, an analysis on the results obtained from the study of the hypoglycemic activity of anti-diabetic plants already studied in Mexico was also conducted.

**2. Material and methods**

*2.1. Plant materials*

Based on the ethnobotanical information on the antidiabetic plants, 28 of them were selected, collected, and botanically identi®ed (Table 1). From various states throughout the Mexican Re-public 14 plants were gathered, while a ®rther 14 plants were purchased from the Sonora Medicinal Herbal Market in Mexico City. A voucher speci-men of each plant was deposited at the Medicinal Plants Herbarium of the Mexican Institute of Social Security (IMSSM-Herbarium), with regis-tration numbers 11461 ± 11492. All the plants were prepared as previously described by Roman-Ramos et al. (1991). The decoctions were pro-cessed and 40 g of the dried plant was slowly boiled in 300 ml of water and heated for 10 min. The liquid phases from the decoctions were then ®ltered and directly administered to the animals (4 ml:kg body weight). The juices were obtained with the help of an electric extractor and they also were administered to the experimental animals (4 ml:kg body weight). The Table 1 show the yield in mg freeze-dried plant:4 ml of the each decoction of the plant.

*2.2. Experimental animals*

The experimental animals used were 63 New Zealand adult male rabbits weighing between 2.5 and 3.5 kg, fed with Purina feed and water ad libitum. The animals were submitted to a fasting period of 18 h prior to the study.

*2.3. Biological assays*

The rabbits were divided into seven experimen-tal groups consisting of nine animals each (63 rabbits in total). Eight glucose tolerance tests (GTTs) were practiced in each group. A 50% glucose solution was twice applied subcutaneously (2 g glucose:kg per turn) in each GTT, at time 0 and 60 min. Blood samples were obtained from the marginal vein of the left ear during the fasting period, and at intervals of 60 min for 5 h after injecting the ®rst glucose load. The animals in each group received (using a gastric tube): water as control in the ®rst GTT; tolbutamide as refer-ence (40 mg:kg weight) in the second; traditional preparation of the ®rst plant in the third; tradi-tional preparation of the second plant in the fourth; water (control) in the ®fth; tolbutamide in the sixth; traditional preparation of the third plant in the seventh; and traditional preparation of the fourth plant in the eighth GTT. The admin-istered volume of water, tolbutamide, and tradi-tional plant preparations was 4 ml:kg weight. Each GTT was performed at intervals of 7 days (1 week) for all groups.

*2.4. Blood glucose determination*

Glycemia was determined using the glucose oxi-dase peroxidase enzymatic method with Haemo-Glukotest 20-800 reagent strips and their assessment was made using a Re¯olux S light-meter (Boehringer Mannheim).

*2.5. Statistical analysis*

Results were expressed as mean S.E.M. The area under the glucose tolerance curve (AUGTC) and the mean glycemia value during the whole GTT were calculated using the rectangles method.

Table 1

Studied plants

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Scienti®c name | Family | Popular name in | Herbarium Ð IMSSM | Used parts | Preparation | Volume adminis- | Yield (mg:4 ml) |
|  |  | Mexico | Vaucher number |  |  | tered (ml:kg) |  |
|  |  |  |  |  |  |  |  |
| *A*. *mexicana* Willd | Leguminosae | Esta®ate | 11461 | Complete plant | Decoction | 4 | 214 |
| *A*.6*iminalis* HBK | Bignoniaceae | Azuchil | 11480 | Leaves | Decoction | 4 | 70 |
| *B*. *pilosa* L | Compositae | Aceitilla | 11473 | Complete plant | Decoction | 4 | 63 |
| *C*. *aurantium* L | Rutaceae | Naranja agria | 11462 | Fresh fruit | Juice | 4 | 450 |
| *C*. *multilobus* (Lex.) L.M | Euphorbiaceae | Chaya | 11483 | Leaves | Decoction | 4 | 146 |
| *E*. *preslii* | Euphorbiaceae | Golondrina | 11475 | Complete plant | Decoction | 4 | 65 |
| *E*. *prostrata* Ait | Euphorbiaceae | Golondrina | 11476 | Complete plant | Decoction | 4 | 70 |
| *E*. *caribaeum* (Jacq.) Roem. | Rubiaceae | Quina | 11478 | Bark | Decoction | 4 | 226 |
| & Schult |  |  |  |  |  |  |  |
| *E*. *polystachia* (Ort.) S | Leguminosae | Palo dulce | 11463 | Stem | Decoction | 4 | 53 |
| *G*. *ulmifolia* Lam. | Sterculiaceae | Guacima | 11488 | leaves | Decoction | 4 | 46 |
| *J*. *dioica* SesseÂ ex Cerv | Euphorbiaceae | Sangre grado | 11464 | Roots | Decoction | 4 | 34 |
| *L*. *caulescens* (Ort.) Epl | Labiatae | Salvia | 11477 | Flowers | Decoction | 4 | 102 |
| *M*. *indica* L. | Anacardiceae | Mango | 11465 | Leaves | Decoction | 4 | 120 |
| *M*. *piperita* L. | Labiatae | Hierbabuena | 11479 | Complete plant | Decoction | 4 | 166 |
| *M*. *sapientum*. L. | Musaceae | Platano | 11492 | Fresh ¯owers | Decoction | 4 | 259 |
| *O*. *europaea* L. | Oleaceae | Olivo | 11474 | Leaves | Decoction | 4 | 143 |
| *O*. *®cus*-*indica* L. | Cactaceae | Nopal | 11481 | Fresh stem | Juice | 4 | 184 |
| *P*. *edulis* D.C. | Bignoniaceae | Chote | 11482 | Fresh fruit | Juice | 4 | 627 |
| *P*. *americana* (L.) Mill. | Lauraceae | Aguacate | 11466 | Seeds | Decoction | 4 | 155 |
| *R*. *echinocarpa* Moc. Et | Rubiaceae | Granjel | 11467 | Fruit | Decoction | 4 | 54 |
| Sess |  |  |  |  |  |  |  |
| *R*. *tetraphylla* L. | Apocynaceae | Paulillo | 11485 | Leaves | Decoction | 4 | 117 |
| *R*. *mangle* L. | Rizophoraceae | Mangle rojo | 11468 | Stem | Decoction | 4 | 48 |
| *S*. *macrodonthus*Stand. | Nyctaginaceae | Apatzicua | 11487 | Roots | Decoction | 4 | 47 |
| *S*. *skinneri* Benth. | Leguminosae | Paracata | 11469 | Leaves | Decoction | 4 | 161 |
| *S*. *triquetra* Radlk. | Sapindaceae | Palo de 3 costil- | 11470 | Stem | Decoction | 4 | 47 |
|  |  | las |  |  |  |  |  |
| *T*. *foenum*-*graceum* L. | Leguminosae | Fenogreco | 11484 | Seeds | Decoction | 4 | 107 |
| *T*. *hirsutissima* L. | Boraginaceae | Lagrimas San | 11471 | Stem | Decoction | 4 | 45 |
|  |  | Pedro |  |  |  |  |  |
| *T*. *diffusa* Willd. | Turneraceae | Damiana | 11486 | Leaves | Decoction | 4 | 257 |
|  |  |  |  |  |  |  |  |

|  |
| --- |
| *F*.*J*. *Alarcon*-*Aguilara et al*. *: Journal of Ethnopharmacology 61 (1998) 101±110* |

|  |
| --- |
| 103 |

104 *F*.*J*. *Alarcon*-*Aguilara et al*. *: Journal of Ethnopharmacology 61 (1998) 101 ± 110*

Table 2

Glucose tolerance test in healthy rabbits with gastric administration of water (control), tolbutamide or plant preparation (group I)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study:prepara- | *t* 0 | Glycemia in mg:dl (mean9S.E.M) | | | |  |  |  |  |  |  |  |  |
| tion |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  | |  | |  | |  | |  |
|  |  |  | 60 min | 120 min | 180 min | | 240 min | | 300 min | | Mean glycemia | |  |
|  |  |  |  |  |  |  |  |  |  |  | during the GTT | |  |
|  |  |  | |  |  |  |  |  |  |  |  |  |  |
| Control (*n* 18) | 80.491.7 | 197.999.1 | | 221.096.5 | 200.8 | 94.3 | 171.59 | 5.3 | 153.39 | 6.4 | 181.69 | 5.8 |  |
| Tolbutamide | 80.591.9 | 171.895.3 | | 188.594.0\* | 185.9 | 95.2 | 151.89 | 5.2 | 133.19 | 6.2 | 160.99 | 4.7\* |  |
| (*n* 18) |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *P*. *americana* | 78.692.5 | 160.799.5 | | 195.397.1 | 173.9 | 914.1 | 147.69 | 9.9 | 134.69 | 10.2 | 156.89 | 9.4 |  |
| (*n* 9) |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *R*. *echynocarpa* | 80.191.2 | 190.299.4 | | 209.3910.7 | 179.4 | 97.0 | 153.59 | 11.2 | 126.89 | 7.5 | 167.29 | 8.6 |  |
| (*n* 9) |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *S*. *skinneri* (*n* | 85.393.6 | 209.9911.8 | | 237.79.9.4 | 213.9 | 97.9 | 168.69 | 6.0 | 135.79 | 6.2 | 188.19 | 8.0 |  |
| 9) |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *T*. *hirsutissima* | 78.192.2 | 164.697.7 | | 173.099.2\* | 164.5 | 97.3 | 138.39 | 7.3 | 129.99 | 5.1 | 148.99 | 7.0\* |  |
| (*n* 9) |  |  |  |  |  |  |  |  |  |  |  |  |  |

Signi®cantly different from control: \**P*B0.05.

The percentage of the decrease of the glycemia, caused on the hyperglycemic peak and on the area under the curve during GTT with respect to con-trol studies was estimated. The signi®cance of the differences between the means of tests and control studies were established by an analysis of variance using Duncan's Multiple New Range Test and by Student's *t*-test (Steel and Torrie, 1989). *P* values lower than 0.05 were considered as signi®cant.

**3. Results**

The results of the present study are summarized in Tables 2 ± 8. In the control studies, the highest glycemic levels were seen at 120 min (hyper-glycemic peak). After this moment, glycemia de-creased gradually without returning to its baseline values. There was no statistical difference among control-GTT in the different groups of rabbits.

Table 3

Glucose tolerance test in healthy rabbits with gastric administration of water (control), tolbutamide or plant preparation (group II)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study:prepara- | *t* 0 | Glycemia in mg:dl (mean9S.E.M) | | | | |  |  |  |  |  |  |  |  |
| tion |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  | |  | |  | |  | |  |
|  |  | 60 min | |  | 120 min | 180 min | | 240 min | | 300 min | | Mean glycemia | |  |
|  |  |  |  |  |  |  |  |  |  |  |  | during the GTT | |  |
|  |  |  | |  |  |  | |  |  |  |  |  |  |  |
| Control (*n* 18) | 78.691.9 | 181.09 | | 8.7 | 248.099.3 | 209911.2 | | 154.09 | 11.3 | 121.79 | 9.5 | 178.69 | 9.2 |  |
| Tolbutamide | 74.492.1 | 149.49 | | 6.9 | 218.398.7\* | 179.796.7 | | 124.69 | 9.7 | 97.797.6 | | 151.69 | 7.4 |  |
| (*n* 18) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *A*.6*iminalis* | 73.392.1 | 186.09 | | 13.7 | 265.8915.1 | 212.49 | 15.0 | 173.59 | 18.9 | 153.09 | 17.6 | 190.29 | 10.2 |  |
| (*n* 9) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *R*. *tetraphylla* | 72.692.2 | 187.49 | | 7.7 | 256.7912.2 | 207.19 | 12.9 | 153.09 | 11.6 | 112.19 | 8.6 | 179.39 | 9.9 |  |
| (*n* 9) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *S*. *macrodontus* | 73.692.1 | 192.296.6 | | | 227.0910.4 | 188.49 | 12.5 | 128.59 | 6.7 | 119.39 | 12.1 | 166.59 | 8.7 |  |
| (*n* 9) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *T*. *diffusa* (*n* | 79.691.8 | 149.997.8 | | | 208.6910.5\* | 181.09 | 6.1 | 140.39 | 7.3 | 97.89 | 6.3 | 153.797.1 | |  |
| 9) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

Signi®cantly different from control: \**P*B0.05.

|  |  |
| --- | --- |
| *F*.*J*. *Alarcon*-*Aguilara et al*. *: Journal of Ethnopharmacology 61 (1998) 101 ± 110* | 105 |

Table 4

Glucose tolerance test in healthy rabbits with gastric administration of water (control), tolbutamide or plant preparation (group III)

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study:prepara- | *t* 0 |  | Glycemia in mg:dl (mean9S.E.M.) | | | |  |  |  |  |  |  |
| tion |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  | |  |  | |  |
|  |  |  | 60 min | | 120 min | 180 min | 240 min | | 300 min | Mean glycemia | |  |
|  |  |  |  |  |  |  |  |  |  | during the GTT | |  |
|  |  |  |  | |  |  |  |  |  |  |  |  |
| Control (*n* 18) | 83.39 | 1.7 | 195.794.9 | | 231.995.8 | 196.394.3 | 175.79 | 4.4 | 137.795.4 | 182.09 | 4.6 |  |
| Tolbutamide | 83.49 | 1.9 | 152.895.9 | | 201.896.3\* | 178.098.0 | 161.29 | 4.5 | 120.894.6 | 159.29 | 5.6\* |  |
| (*n* 18) |  |  |  |  |  |  |  |  |  |  |  |  |
| *A*. *mexicana* | 85.09 | 2.8 | 148.899.2 | | 219.7915.0 | 183.9913.7 | 162.99 | 32.2 | 138.0911.4 | 165.89 | 11.1 |  |
| (*n* 9) |  |  |  |  |  |  |  |  |  |  |  |  |
| *E*. *polystachia* | 78.39 | 2.71 | 52.4912.3 | | 209.898.2 | 190.1914.6 | 174.09 | 12.6 | 147.9911.2 | 167.99 | 10.9 |  |
| (*n* 9) |  |  |  |  |  |  |  |  |  |  |  |  |
| *M*. *sapien*- | 78.992.2 | | 134.092.4 | | 192.495.4\* | 182.693.9 | 141.79 | 2.7 | 112.791.6 | 149.39 | 3.3\* |  |
| *tum*(*n* 9) |  |  |  |  |  |  |  |  |  |  |  |  |
| *S*. *triquetra*(*n* | 83.992.1 | | 160.296.5 | | 233.9915.0 | 243.1913.6 | 211.59 | 8.9 | 165.2912.4 | 194.79 | 10.2 |  |
| 9) |  |  |  |  |  |  |  |  |  |  |  |  |

Signi®cantly different from control: \**P*B0.05.

All the GTTs receiving tolbutamide resulted in lower glycemic values than those from the con-trol-GTTs (*P*B0.05).

The results obtained from the variance analysis showed that seven of the 28 studied plants signi®-cantly decreased the hyperglycemic peak (*P*B 0.05). These plants were: *Guazuma ulmifolia* (22.2%), *Tournefortia hirsutissima* (21.7%), *Lepe*-*chinia caulescens* (20.9%), *Trigonella foenum*-

*graceum* (17.7%), *Musa sapientum* (17.0%), *Rhizophora mangle* (16.1%), and *Turnera diffusa* (15.9%). Tolbutamide also caused a signi®cant reduction of the hyperglycemic peak (15.7%). Of the plants 13 showed reductions of the hyper-glycemic peak: *Euphorbia prostrata* (13.9%), *Jat*-*ropha dioica* (13.7%), *Persea americana* and *Euphorbia preslii* (11.6%), *Eysenhardtia polystachia* (9.5%), *Salpianthus macrodonthus*

Table 5

Glucose tolerance test in healthy rabbits with gastric administration of water (control), tolbutamide or plant preparation (group IV)

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study:prepara- | *t* 0 | Glycemia in mg:dl (mean9S.E.M.) | | | | |  |  |  |  |  |  |
| tion |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  | |  | |  |  |  | |  |
|  |  | 60 min |  | 120 min | | 180 min | | 240 min | 300 min | Mean glycemia during | |  |
|  |  |  |  |  |  |  |  |  |  | the GTT | |  |
|  |  |  | |  | |  |  |  |  |  |  |  |
| Control (*n* 18) | 84.991.4 | 198.595.8 | | 215.998.1 | | 181.19 | 8.0 | 170.497.0 | 129.695.0 | 174.69 | 6.4 |  |
| Tolbutamide | 82.190.9 | 155.897.0 | | 180.197.8\* | | 164.89 | 4.8 | 147.095.4 | 115.195.0 | 149.39 | 5.6\* |  |
| (*n* 18) |  |  |  |  |  |  |  |  |  |  |  |  |
| *E*. *caribaeum* | 87.593.3 | 189.89 | 7.1 | 208.09 | 6.5 | 181.99 | 6.0 | 176.195.2 | 131.795.2 | 173.19 | 5.8 |  |
| (*n* 9) |  |  |  |  |  |  |  |  |  |  |  |  |
| *M*. *indican* (*n* | 83.292.0 | 174.39 | 10.4 | 200.79 | 13.0 | 166.09 | 8.9 | 127.996.8 | 101.194.0 | 152.29 | 8.4 |  |
| 9) |  |  |  |  |  |  |  |  |  |  |  |  |
| *O*. *europaea* | 78.191.4 | 215.49 | 10.2 | 246.59 | 12.1 | 237.79 | 10.4 | 208.598.0 | 197.398.0 | 209.29 | 11.0 |  |
| (*n* 9) |  |  |  |  |  |  |  |  |  |  |  |  |
| *R*. *mangle* (*n* | 83.792.9 | 159.99 | 9.7 | 181.19 | 12.6\* | 159.19 | 9.1 | 138.695.0 | 100.496.3 | 146.298.0\* | |  |
| 9) |  |  |  |  |  |  |  |  |  |  |  |  |

Signi®cantly different from control: \**P*B0.05.

106 *F*.*J*. *Alarcon*-*Aguilara et al*. *: Journal of Ethnopharmacology 61 (1998) 101 ± 110*

Table 6

Glucose tolerance test in healthy rabbits with gastric administration of water (control), tolbutamide or plant preparation (group V)

Study:preparation *t* 0 Glycemia in mg:dl (mean9S.E.M.)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | 60 min | 120 min | | 180 min | | 240 min | | 300 min | | Mean glycemia | | |
|  |  |  |  |  |  |  |  |  |  |  | during the GTT | | |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Control (n 18) | 73.092.1 | 189.597.9 | 245.9 | 95.3 | 219.99 | 9.2 | 180.29 | 10.2 | 152.39 | 5.3 | 189.5 | 9 | 7.3 |
| Tolbutamide | 75.092.0 | 152.595.6 | 217.5 | 95.8\* | 178.49 | 3.3 | 145.89 | 8.7 | 107.49 | 9.3 | 157.1 | 9 | 5.8\* |
| (*n* 18) |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *B*. *pilosa* (*n* 9) | 74.491.9 | 153.495.2 | 235.9 | 96.8 | 242.79 | 14.1 | 229.99 | 13.3 | 156.49 | 17.4 | 195.5 | 9 | 9.8 |
| *C*. *aurantium* | 73.891.6 | 206.797.9 | 247.1 | 99.8 | 255.29 | 5.9 | 237.49 | 8.6 | 156.29 | 9.5 | 212.3 | 9 | 7.5 |
| (*n* 9) |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *C*. *multilobus* | 71.891.8 | 155.493.5 | 251.9 | 94.9 | 265.79 | 9.1 | 235.29 | 13.3 | 156.39 | 14.7 | 204.5 | 9 | 7.8 |
| (*n* 9) |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *J*. *dioica* (n 9) | 70.591.9 | 177.096.0 | 211.5 | 911.8 | 190.79 | 12.3 | 171.89 | 8.3 | 140.29 | 7.8 | 171.3 | 9 | 8.7 |

Signi®cantly different from control: \**P*B0.05.

(8.5%), *Mangifera indica* (7.0%), *Randia echi*-*nocarpa* and *Artemisia mexicana* (5.3%), *Exostema caribaeum* and *Bidens pilosa* (3.7%), *Opuntia ®cus*-*indica* (3.2%), and *Parmentiera edulis* (1.3%); nev-ertheless their differences with respect to their control were not signi®cant (*P*\0.05). The other eight plants: *Mentha piperita*, *Olea europaea*, *Cit*-*rus aurantium*, *Cnidoscolus multilobus*, *Serjania triquetra*, *Astianthus* 6*iminalis*, *Ra*6*ol®a tetra*-*phylla*, and *Sena skinneri* did not show anyglycemia reduction in the hyperglycemic peak.

Regarding the area under the curve during the GTT, variance analysis showed that six of the

studied plants caused a signi®cant decrease in relation with their control (*P*B0.05). *G*. *ulmifolia* had the strongest effect (21.3%), followed by *L*. *caulescens* (18.2%), *M*. *sapientum* (18.0%), *T*. *hir*-*sutissima* (18.0%), *R*. *mangle* (16.3%), and *E*. *pros*-*trata* (15.9%). Tolbutamide caused a reduction ofthe area under the curve of 16.6%.

The next 11 plants caused non-statistically sig-ni®cant reductions of the area under the curve during the GTT: *T*. *diffusa* (13.9%), *P*. *americana* (13.7%), *M*. *indica* (12.8%), *E*. *preslii* (11.4%), *T*. *foenum*-*graceum* (10.4%), *J*. *dioica* (9.6%), *A*. *mexicana* (8.9%), *R*. *echinocarpa* (7.9%), *E*.

Table 7

Glucose tolerance test in healthy rabbits with gastric administration of water (control), tolbutamide or plant preparation (group VI)

Study:preparation *t* 0 Glycemia in mg:dl (mean9S.E.M.)

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | 60 min | 120 min | | 180 min | | 240 min | | 300 min | Mean glycemia | |
|  |  |  |  |  |  |  |  |  |  | during the GTT | |
|  | | | | |  |  |  |  |  |  |  |
| Control (*n* 18) 82.891.3 191.197.2 219.894.5 | | | | | 183.89 | 8.1 | 151.49 | 5.6 | 125.995.0 | 170.19 | 5.7 |
| Tolbutamide | 85.991.5 | 162.694.9 | 185.296.0\* | | 147.99 | 5.7 | 119.49 | 4.3 | 92.992.7 | 140.99 | 4.6 |
| (*n* 18) |  |  |  |  |  |  |  |  |  |  |  |
| *G*. *ulmifolia*(*n* | 90.793.5 | 150.896.5 | 171.09 | 8.7\* | 146.29 | 7.6 | 109.09 | 7.1 | 93.391.3 | 133.89 | 6.5 |
| 9) |  |  |  |  |  |  |  |  |  |  |  |
| *L*. *caulescens* | 86.193.1 | 141.097.0 | 173.89 | 14.9\* | 151.89 | 15.8 | 126.89 | 11.8 | 118.3910.4 | 139.19 | 11.3 |
| (*n* 9) |  |  |  |  |  |  |  |  |  |  |  |
| *P*. *edulis*(*n* 9) | 83.491.3 | 182.397.0 | 217.09 | 9.5 | 211.29 | 11.1 | 166.39 | 12.7 | 133.396.3 | 177.098.8 | |
| *T*. *foenum*-*g* (*n*87.893.5 | | 178.397.7 | 181.09 | 8.3\* | 168.69 | 9.2 | 140.39 | 6.2 | 99.395.4 | 152.497.1 | |
| 9) |  |  |  |  |  |  |  |  |  |  |  |

Signi®cantly different from control: \**P*B0.05.

|  |  |
| --- | --- |
| *F*.*J*. *Alarcon*-*Aguilara et al*. *: Journal of Ethnopharmacology 61 (1998) 101 ± 110* | 107 |

Table 8

Glucose tolerance test in healthy rabbits with gastric administration of water (control), tolbutamide or plant preparation (group VII)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study:prepara- | *t* 0 | Glycemia in mg:dl (mean9S.E.M.) | | | |  |  |  |  |  |  |  |  |  |
| tion |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  | |  |  | |  | |  | |  | | |  |
|  |  | 60 min | | 120 min | 180 min | | 240 min | | 300 min | | Mean glycemia | | |  |
|  |  |  |  |  |  |  |  |  |  |  | during the GTT | | |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Control (*n* 18) | 70.092.2 | 181.1 | 99.1 | 227.7910.1 | 199.49 | 10.8 | 163.09 | 9.7 | 124.99 | 8.1 | 173.7 | 9 | 9.0 |  |
| Tolbutamide | 74.192.8 | 146.7 | 95.0 | 183.498.2\* | 157.29 | 5.7 | 123.69 | 5.8 | 99.495.9 | | 139.5 | 9 | 5.8\* |  |
| (*n* 18) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *E*. *preslii* (*n* 9) | 68.892.1 | 157.5 | 914.6 | 201.3915.5 | 172.09 | 13.2 | 156.69 | 19.1 | 95.7910.1 | | 153.9 | 9 | 13.7 |  |
| *E*. *prostrata*(*n* | 68.392.2 | 141.1 | 95.1 | 196.0914.4 | 179.79 | 13.5 | 131.69 | 9.7 | 86.797.0 | | 146.1 | 9 | 9.1\* |  |
| 9) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *M*. *piperita* (*n* | 82.491.9 | 199.6 | 94.8 | 250.4912.6 | 226.09 | 12.9 | 198.09 | 12.0 | 151.09 | 3.3 | 196.1 | 9 | 8.9 |  |
| 9) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *O*. *®cus*-*indica* | 75.592.3 | 177.8 | 97.3 | 220.396.8 | 210.09 | 3.8 | 185.09 | 9.3 | 176.49 | 12.3 | 183.8 | 9 | 6.9 |  |
| (*n* 9) |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

Signi®cantly different from control: \**P*B0.05.

*polystachia* (7.7%), *S*. *macrodonthus* (6.8%), and *E*. *caribaeum* (0.9%). The other studied plants: *P*. *edulis*, *R*. *tetraphylla*, *O*. *®cus*-*indica*, *S*. *skinneri*, *A*.6*iminalis*, *S*. *triquetra*, *B*. *pilosa*, *M*. *piperita*, *C*. *multilobus*, *O*. *europaea*, and *C*. *aurantium* showedno reduction in the area under the glucose toler-ance curve.

**4. Discussion**

The aim of this study was to asses the anti-hy-perglycemic effect of 28 antidiabetic plants on transiently hyperglycemic healthy rabbits and is also a summary of the results previously obtained in Mexico with other antidiabetic plants studied under the same experimental conditions. The doses, expressed in mg:kg, administered from each plant were different because the traditional way of preparation and the volume:kg of admin-istration was used.

The results of this investigation revealed that eight out of the 28 studied plants (28.6%) have an anti-hyperglycemic effect. These plants caused a signi®cant decrease in the hyperglycemic peak and:or in the area under the curve during the GTT. However, if the statistical analysis of the results of the present investigation is made using Student's *t*-test, such as was reported by Perez et

al. (1984), the number of plants with anti-hyper-glycemic effect increases from 8 to 11 (40%, ap-proximately). The plants that could be added are: *P*. *americana*, *E*. *polystachia*, and *J*. *dioica*. Theresults suggest the validity of their clinical use in the diabetes mellitus control, after properly being toxicologically studied.

Based on this last analysis, 17 plants did not show signi®cant hypoglycemic effect, whether on the hyperglycemic peak or on the area under the curve during the GTT. However, we can not af®rm that this plants do not really have hypo-glycemic activity because the experimental model used by us does not detect hypoglycemic effect neither by reduction in glucose intestinal absorp-tion (`®ber effect') nor by storage of active sub-stance in the organism. In addition, some anti-diabetic plants only show hypoglycemic ac-tivity when they are surveyed in chronic studies, probably because the hypoglycemic substance has to reach a higher concentration in the body.

The studies carried out by Mohammed-Ali-Ajabnoor (1990) and Roman-Ramos et al. (1991) with *Aloe barbadensis* Miller in healthy and dia-betic mice, and in temporally hyperglycemic rab-bits, respectively, are a good example of this. *A*. *barbadensis* showed to have some effect in thechronic studies carried out by Mohammed-Ali, just three days after the beginning of the treat-

108 *F*.*J*. *Alarcon*-*Aguilara et al*. *: Journal of Ethnopharmacology 61 (1998) 101 ± 110*

ment. These results validate the hypoglycemic ac-tivity reported by the population and also allows for for emphasizing the necessity to carry out chronic studies.

On the other hand, it may be that some plants used as anti-diabetics, do not really have a hypo-glycemic effect. In this case the glycemia reduc-tion could be explained by low carbohydrate diet administered to the diabetic patients, and also by increased physical activity (Roman-Ramos et al., 1991). In some cases several plants are adminis-tered together, as complex mixtures, and all them are known as `anti-diabetic' plants.

This study on reports ten plants that already were experimentally and:or clinically studied: *T*. *diffusa*, *E*. *polystachia*, *P*. *edulis*, *B*. *pilosa*, *E*. *prostrata*, *L*. *caulescens*, *S*. *macrodonthus*, *T*. *foenum*-*graceum*, *O*. *®cus*-*indica*, and *O*. *europaea* (Akhtar et al., 1984; Perez et al., 1984; Roman-Ramos et al., 1991, 1992b; Raghuram et al., 1994; Frati-Munari et al., 1989; Gonzalez et al., 1992). The herein reported hypoglycemic activity in seven of them agrees with the results obtained by other researchers.

Perez et al. (1984) reported the hypoglycemic effect of *T*. *diffusa*, *E*. *polistachya*, *P*. *edulis*, and *B*. *pilosa*. The effects previously obtained from the®rst, agrees with ours results; nevertheless the results of the last three plants are contradictory. This may be due to the use of different plants species. In Mexico there are many examples of different plant species with identical popular names (Bye et al., 1995). There are also examples in which the same species has a wide variety of popular names (Aguilar et al., 1994). In this inves-tigation on medicinal plants these two cases re¯ect the predominant role a correct botanical identi®-cation of the studied plant material plays, and the need for using with voucher specimens that allow for the assurance in the study of a single plant species.

Other plants previously studied are *E*. *prostrata* (Akhtar et al., 1984) and *L*. *caulescens* (Roman-Ramos et al., 1992b), both having an effect in healthy rabbits, but not showing any activity in the diabetic model. These results suggest that some pancreatic function, or the presence of in-sulin, is required for the hypoglycemic activity of

these anti-diabetic plants.

Our results also reveal that the roots of *S*. *macrodonthus* decrease both the hyperglycemicpeak as well as the area under the curve during the GTT, however the differences in relation to the control study were not signi®cant. Although the hypoglycemic effect of *S*. *macrodonthus* was previously assessed by Roman-Ramos et al. (1991), they surveyed the decoction obtained from the leaves and stems.

The hypoglycemic effect of fenugreek seeds (*T*. *foenum*-*graceum*) has been demonstrated in exper-imentally induced diabetic rats, dogs, mice, and healthy volunteers, insulin-dependent diabetics and non-insulin-dependent diabetic patients (Ribes et al., 1984; Mohammad-Ali-Ajabnoor and Abdul-Karim-Tilmisany, 1988; Raghuram et al., 1994). This plant is one of the most extensively studied to date; however, it is the ®rst report that deals with the hyperglycemic effect of *T*. *foenum*-*graceum* in transiently hyperglycemic rabbits.

Frati-Munari et al. (1989), studyng the in¯u-ence of a dehydrated extract of *O*. *®cus*-*indica* on the glycemia of healthy volunteers and non insulin dependent diabetic patients, found that only in healthy subjects *O*. *®cus*-*indica* has there been hyperglycemic activity probably due to the plant's high ®ber content. Although we used healthy rabbits and hypoglycemic activity was not de-tected, our results agree with Frati-Munari's ex-planation because the experimental model employed by us discards the ®ber effect.

The hypoglycemic activity of the *O*. *europaea* leaves gathered throughout their annual cycle in Spain was studied by Gonzalez et al. (1992). They detected activity only in the leaves collected be-tween October and June. In the present investiga-tion *O*. *europaea* gathered during May and collec-ted in Mexico did not cause an hypoglycemic effect.

A general analysis of the results obtained at present with all the anti-diabetic Mexican plants whose hypoglycemic effect has been assessed in temporary hyperglycemic rabbits, including the plants studied in the present work, showed that 33 out of 62 plants studied have hypoglycemic activ-ity. The plants with the highest hypoglycemic effect, denoting a signi®cant decrease of over 15%

|  |  |
| --- | --- |
| *F*.*J*. *Alarcon*-*Aguilara et al*. *: Journal of Ethnopharmacology 61 (1998) 101 ± 110* | 109 |

of the area under the curve during the GTT are: *Guaiacum coulteri* (31.4%), *Cucurbita ®cifolia* (30.7%), *Psacalium peltatum* (27.9%), *Marrubium* 6*ulgare* (25.8%), *Opuntia streptacantha* (21.4%), *G*. *ulmifolia* (21.3%), *Solanum* 6*erbascifolium* (21.1%), *Phaseolus* 6*ulgaris* (20.8%), *Teucrium cubense* (19.4%), *Cecropia obtusifolia* (18.9%), *L*. *caules*-*cens* (26.0%), *M*. *sapientum* and *T*. *hirsutissima* (18.0%), *Tecoma stans* (17.5%), *Eriobotrya japon*-*ica* (17.2%), *Calea zacatechichi* (17.0%), *R*. *mangle* (16.3%), *E*. *prostrata* (15.9%), *Psacalium decom*-*positum* (15.6%), *Crataegus pubescens* and *S*. *macrodonthus* (15%) (Roman-Ramos et al., 1991,1992a, 1995; Alarcon-Aguilar et al., 1997).

We believe that these plants must be considered as excellent candidates for future studies on deter-mining the mechanisms of their hypoglycemic ac-tivity, as well as for the isolation and identi®cation of active hypoglycemic substances. In addition, further comprehensive pharmacologi-cal investigations, including experimental chronic studies, will be carried out to assess the likely toxicological effects of these antidiabetic plants.

**References**

ADA, 1997. Clinical practice recommendations 1997: Screen-ing for diabetes. Diabetes Care 20(1), 22 ± 24.

Aguilar, A., Camacho, J.R., Chino, S., JaÂcquez, P., LoÂ pez, M.E., 1994. Herbario Medicinal del Instituto Mexicano del Seguro Social. InformacioÂ n etnobotaÂnica, IMSS. Mexico, p. 253.

Akhtar, M.S., Khan, Q.M., Khaliq, T., 1984. Effects of *Eu*-*phorbia prostrata* and *Fumaria par*6*i¯ora* in normogly-caemic and alloxan-treated hyperglycaemic rabbits. Planta Medica 50, 138 ± 142.

AlarcoÂ n-Aguilar, F.J., RomaÂn-Ramos, R., Flores-SaÂenz, J.L., 1993. Plantas medicinales usadas en el control de la dia-betes mellitus. Ciencia 44, 363 ± 381.

Alarcon-Aguilar, F.J., Roman-Ramos, R., Flores-Saenz, J.L., Jimenez-Estrada, M., Reyes-Chilpa, R., Gonzalez-Paredes, B., 1997. Effects of three Mexican medicinal plants (Aster-aceae) on blood glucose levels in healthy mice and rabbits. Journal of Ethnopharmacology 55, 171 ± 177.

Bailey, C.J., 1992. Biguanides and NIDDM. Diabetes Care 15, 755 ± 772.

Bye, R., Linares. E., Estrada, E., 1995. Biological diversity of medicinal plants in Mexico. In: Arnason, J.T. et al. (Eds.), Phytochemistry of Medicinal Plants, ch. 4. Plenum Press, New York, p. 65.

Frati-Munari A., Clodoveo de Leon, Ariza-Andraca R., Ba-nÄ ales-Ham M., Lopez-Ledezma R., Lozoya., X., 1989. In¯uence of a dehydrated extract of the nopal (*Opuntia®*-*cus indica* Mill.) on glycemia. Archivos de InvestigacioÂ nMeÂdica 20, 211 ± 216.

Frati-Munari, A., Gordillo, B., Altamirano, P., Ariza, R., Cortes-Franco, R., Chavez-Negrete, A., Islas-Andrade, S., 1991. In¯uence of nopal intake upon fasting glycemia in type II and healthy subjects. Archivos de InvestigacioÂ n MeÂdica 22, 51 ± 56.

Gonzalez, M., Zarzuelo, A., Gamez, M.J., Utrilla, M.P., Jimenez, J., Osuna, Y., 1992. Hypoglycemic activity of olive leaf. Planta Medica 58, 513 ± 515.

IbanÄ ez-Camacho, R., RomaÂn-Ramos, R., 1979. Efecto hipoglucemiante del nopal. Archivos de InvestigacioÂ n MeÂdica 10, 223 ± 230.

Ibanez-CamanÄ cho, R., Meckes-Lozoya, M., Mellado-Campos, V., 1983. The hypoglycemic effect of *Opuntia streptacantha* studied in different animal experimental models. Journal of Ethnopharmacology 7, 175 ± 181.

Lebovitz, H.E., Pasmantier, R., 1990. Combination insulin-sulfonylurea therapy. Diabetes Care 13, 667 ± 675.

Lozoya-Meckes, M., Mellado-Campos, V., 1985. Is the *Tecoma stans* infusion an antidiabetic remedy? Journal ofEthnopharmacology 14, 1 ± 9.

Meckes-Lozoya, M., IbanÄ ez-Camacho, R., 1985. Hepatic glycogenolysis produced by intraperitoneal administration of total extract of *Tecoma stans* in rats. Archivos de InvestigacioÂ n MeÂdica 16, 387 ± 393.

Meckes-Lozya, M., Roman-Ramos, R., 1986. *Opuntia strepta*-*cantha*: a coadjutor in the treatment of diabetes mellitus.American Journal of Chinese Medicine 14, 116 ± 118.

Mohammad-Ali-Ajabnoor and Abdul-Karim-Tilmisany., 1988. Effect of *Trigonella foenum graceum* on blood glu-cose levels in normal and alloxan-diabetic mice. Journal of Ethnopharmacology 22, 45 ± 49.

Mohammed-Ali-Ajabnoor, 1990. Effect of aloes on blood glucose levels in normal and alloxan diabetic mice. Journal of Ethnopharmacology 28, 215 ± 220.

Perez, R.M., Ocegueda, A., MunÄ oz, L., Avila, J., Morrow, W., 1984. A study of the hypoglycemic effect of some Mexican plants. Journal of Ethnopharmacology 12, 253 ± 262.

Raghuram, T.C., Sharma, R.D., Sivakumar, B., Sahay, B.K., 1994. Effect of fenugreek seeds on intravenous glucose disposition in Non-insulin dependent diabetic patients. Phytotherapy Research 8, 83 ± 86.

Ribes, G, Sauvaire, Y., Baccou, J.C., Valette, G., Chenon, D., Trimble, E., LoubatieÁres-Mariani, M., 1984. Effects of fenugreek seeds on endocrine pancreatic secretions in dogs. Annals of Nutrition and Metabolism 28, 37 ± 43.

Roman-Ramos, R., Flores-Saenz, J.L., Partida-Hernandez, G., Lara-Lemus, A., Alarcon-Aguilar, F., 1991. Experi-mental study of the hypoglycemic effect of some antidia-betic plants. Archivos de InvestigacioÂ n MeÂdica 22, 87 ± 93.

Roman-Ramos, R., Alarcon-Aguilar, F.J., Lara-Lemus, A., Flores-Saenz, J.L., 1992a. Hypoglycemic effect of plants used in Mexico as antidiabetics. Archives of Medical Re-search 23, 59 ± 64.

110 *F*.*J*. *Alarcon*-*Aguilara et al*. *: Journal of Ethnopharmacology 61 (1998) 101 ± 110*

Roman-Ramos, R., Lara-Lemus, A., Alarcon-Aguilar, F., Flores-Saenz, J.L., 1992b. Hypoglycemic activity of some antidiabetic plants. Archives of Medical Research 23, 105 ± 109.

Roman-Ramos, R, Flores-Saenz, J.L., Alarcon-Aguilar, F.J., 1995. Anti-hyperglycemic effect of some edible plants. Journal of Ethnopharmacology 48, 25 ± 32.

Steel, R., Torrie, J., 1989. BioestadõÂstica, principios y proced-

imientos. McGraw-Hill, MeÂxico. p. 622. Youssef-Hammouda, Abdel-Kader Rashid and M. Samir

Amer., 1964. Hypoglycaemic properties of Tecomine and Tecostanine. Journal of Pharmacy and Pharmacology. 16, 833 ± 834.

White, J.R., 1996. The pharmacologic management of patients with tie II diabetes mellitus in the era of new oral agents and insulin analogs. Diabetes Spectrum 9, 227 ± 234.

. .