Hypoglycemic activity of root water decoction, sesquiterpenoids, and one polysaccharide fraction from Psacalium decompositum in mice

ARTICLE *in* JOURNAL OF ETHNOPHARMACOLOGY · MARCH 2000

Impact Factor: 3 · DOI: 10.1016/S0378-8741(99)00039-2 · Source: PubMed

6 AUTHORS, INCLUDING:

Ricardo Reyes-Chilpa
Universidad Nacional Autónoma de…
92 PUBLICATIONS **1,065** CITATIONS

SEE PROFILE

Rubén Román-Ramos
Metropolitan Autonomous University
75 PUBLICATIONS **1,550** CITATIONS

SEE PROFILE

ELSEVIER

Journal of Ethnopharmacology 69 (2000) 207–215

Journal of ETHNO-PHARMACOLOGY

www.elsevier.com/locate/jethpharm

Hypoglycemic activity of root water decoction, sesquiterpenoids, and one polysaccharide fraction from *Psacalium decompositum* in mice

F.J. Alarcon-Aguilar [a,*], M. Jimenez-Estrada [b], R. Reyes-Chilpa [b], B. Gonzalez-Paredes [b], C.C. Contreras-Weber [a], R. Roman-Ramos [a]

[a] *Departamento de Ciencias de la Salud, Divisione Ciencias Biológicas y de la Salud, Universidad Autónoma Metropolitana, Unidad Iztapalapa, Apdo. Postal 55-535, 09340 México D.F., Mexico*

[b] *Instituto de Química, Universidad Nacional Autonoma de México, Ciudad Universitaria, 04510 México D.F., Mexico*

Received 1 November 1998; received in revised form 23 February 1999; accepted 1 March 1999

Abstract

The hypoglycemic activity of *Psacalium decompositum* (Asteraceae) was investigated in fasting healthy mice and alloxan-diabetic mice. The freeze-dried water decoction significantly reduced the blood glucose in normal mice (from 50.9 ± 4.7 to 32.5 ± 3.1 mg/dl) and in mild diabetic mice (from 208.5 ± 13.0 to 52.3 ± 7.0 mg/dl), 240 min after intraperitoneal administration ($P < 0.005$). This preparation also diminished fasting glycemia in severe diabetic mice, but the effects were minor (from 394.4 ± 9.4 to 289.3 ± 39.5 mg/dl). The main sesquiterpenoid constituents from *P. decompositum* roots, cacalol, cacalone and maturin, as well as the transformation product cacalol acetate, did not show a hypoglycemic effect on healthy mice. Nevertheless, two polysaccharide fractions (F1 and F3) obtained from the freeze-dried water extract significantly reduced the fasting glycemia in healthy mice. The best results were obtained with the F1 fraction.

Keywords: Hypoglycemic plants; Anti-diabetic plants; Medicinal plants; *Psacalium decompositum* (H.B.K.) Cass.; Sesquiterpenic compounds; Furoeremophylanes; Cacalol and related compounds

1. Introduction

Diabetes mellitus (DM) is one of the most important health problems worldwide, showing high indices of prevalence and mortality. DM can be defined as a group of metabolic diseases characterized by chronic hyperglycemia, resulting from defects in insulin secretion, insulin action, or both, giving rise to impaired function in the carbohydrate, lipid and protein metabolism (ADA, 1997; Committee Report, 1997).

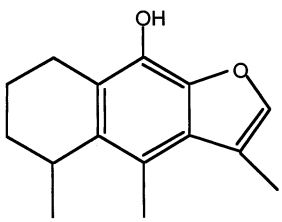
The pharmacological treatment of DM is based on oral hypoglycemic agents and insulin. However, DM is also treated in Mexican traditional medicine through anti-diabetic plants (Roman-Ramos et al., 1991, 1992a, 1995; Alarcon-Aguilar

* Corresponding author.

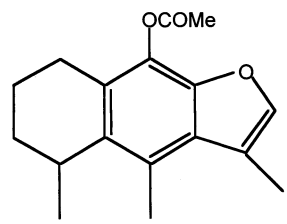
0378-8741/00/$ - see front matter
PII: S0378-8741(99)00039-2

et al., 1998). One of the most important is *Psacalium decompositum* (Gray) Rob. Et Brett. (Syn. *Cacalia decomposita* A. Gray), *Asteraceae*, popularly known as 'Matarique' (Bye, 1986; Aguilar et al., 1994). The decoction prepared from the roots of *P. decompositum* has been shown to diminish glycemic levels in temporally hyperglycemic rabbits, when it was orally administered, and it has exhibited intraperitoneal hypoglycemic effects in healthy mice (Alarcon-Aguilar et al., 1997). Nevertheless, hypoglycemic activity of the freeze-dried *P. decompositum* root water decoction in healthy mice and alloxan-diabetic animals has not been investigated.

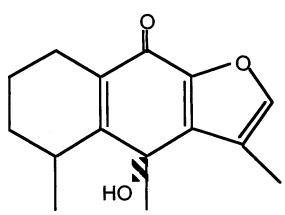
Phytochemical studies of *P. decompositum* roots have shown that sesquiterpenoid compounds, such as cacalol, cacalone, maturin, maturinone and maturone (Fig. 1), are the main constituents of the hexane extract. (Romo and Joseph-Nathan, 1964; Correa and Romo, 1966; Yuste et al., 1976; Romo de Vivar, 1985). Recent analysis by thin layer chromatography (TLC) has also shown the presence of cacalol, cacalone, and maturin in the traditional preparation (root water decoction) of *P. decompositum* (Alarcon-Aguilar et al., 1997). However, the hypoglycemic effects of these compounds and other root chemical constituents have not been studied.



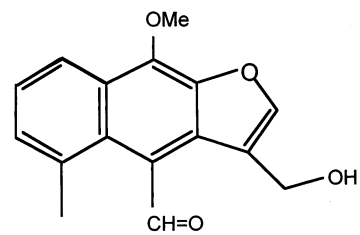
1: Cacalol



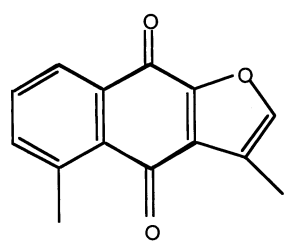
1a: Cacalol acetate



2: Cacalone



3: Maturin



4: Maturinone

Fig. 1. Natural (1–4) and transformed (1a) sesquiterpenoids from *Psacalium decompositum* roots.

This study had the following objectives: (a) to determine the hypoglycemic activity of the freeze dried *P. decompositum* root water decoction in healthy mice and alloxan-diabetic mice; (b) to evaluate the hypoglycemic effect of the sesquiterpenoids, cacalol, cacalol acetate, cacalone, and maturin, in healthy mice; and (c) to evaluate the hypoglycemic effect of polysaccharide fractions obtained from a water extract of *P. decompositum* roots in healthy mice.

2. Material and methods

2.1. Plant material

Roots of *P. decompositum* were acquired from the Sonora Herbal Market at Mexico City (Herbarium IMSSM-Voucher Specimen 11489). The dried roots (40 g) were put in boiling water (300 ml) for 10 min and then left to cool at room temperature. The decoction was filtered and then freeze-dried. The dry residue was dissolved in isotonic saline solution (ISS) and directly administered to the experimental animals (200 mg dry residue per kg body weight).

2.2. Isolation of compounds from the roots of *P. decompositum*

P. decompositum roots (950.5 g) were grounded and extracted four times at room temperature with hexane (3 l, 24 h). The extracts were concentrated under reduced pressure and pooled, obtaining 68.18 g (yield 7.17%). Part of the hexane extract (15 g) was subjected to column chromatography with alumina (390 g), eluting with hexane, ethyl acetate and mixtures of these solvents. Fractions eluted with hexane and ethyl acetate (9.99/0.01) afforded cacalol (yield 1.8%, 270 mg), cacalone (58 mg) and maturin (30 mg). Acetylation of cacalol to obtain cacalol acetate was carried out as described in Lotina et al. (1991). Identity of compounds was established by comparison of their spectroscopic (^{1}H nuclear magnetic resonance, infrared, electron microscopy and ultraviolet) and physical data with those previously published (Correa and Romo, 1966; Yuste et al., 1976; Bohlmann et al., 1977; Lotina et al., 1991).

Then, the plant residue was next extracted four times at room temperature with methanol (3 l, 24 h). The water was evaporated with high vacuum obtaining a residue (72.72 g, yield 7.65%). This material was macerated with methanol (200 ml, 24 h) obtaining a precipitate (WMP, 57 g, yield 78.4%) and a methanol soluble fraction (WMS, 15 g). The WMP fraction (soluble in water) was first analyzed by high performance TLC (HPTLC) (Silica Gel 60, F254; Merck). The plates were previously impregnated with a mixture of 0.1 M diethanolamine and 10 mM acetic acid in acetonitrile and activated at room temperature during 1 h. The elusion system was acetonitrile/water (8:2). After developing, the plates were sprayed with a reagent (8% alpha-naphthol in ethanol) suitable for detecting polysaccharides. Four main components, F1, F2, F3, and F4 with Rf 0.15, 0.29, 0.40 and 0.47, respectively, were detected. A preliminary comparison of F1–F4 fractions was also performed by HPTLC using sucrose (Rf 0.25), fructose (Rf 0.41), glucose (Rf 0.51), galactose, arabinose, xylose, rhamnose (all of which had Rf 0.50), maltoheptaose (M7) (Rf 0.15), maltohexaose (M6), maltopentaose (M5), maltotetraose (M4), from Sigma, and maltodextrines (Aldrich), with Rf 0.06, as standards. Finally, part of the WMP (460 mg) was subjected to preparative TLC (pTLC) using pretreated silica gel plates (Merck, 2 mm) and an elusion system as already described. Yields of the four main components F1, F2, F3, and F4 were 37.17 (171 mg), 21.73 (100 mg), 23.80 (109.5 mg), and 15.21% (70 mg), respectively.

Polysaccharide fractions F1–F4 could also be obtained directly from the freeze-dried water decoction following the procedure described. Percentage yields were similar to those previously mentioned.

2.3. Experimental animals

The experimental animals used were male adult mice (CD1-strain) weighing from 20 to 30 g, fed with Purina nutrition and water ad libitum. Prior to each study, the animals were subjected to fasting for 18 h.

2.4. Induction of experimental diabetes

Experimental diabetes in mice, submitted to fasting for 18 h, was induced by three subcutaneous injections of alloxan. The alloxan was administered at intervals of 48 h, in a dose of 150 mg/kg body weight each (total dose of 450 mg/kg weight). Seven days after the last administration, animals were fasted for 18 h and blood glucose levels determined. These animals were included in two experimental groups: (a) mild alloxan-diabetic mice, whose basal glycemia ranged between 150 and 350 mg/dl; and (b) severe alloxan-diabetic mice, whose basal glycemia was higher than 350 mg/dl.

2.5. Biological assays

2.5.1. Hypoglycemic activity of P. decompositum root dry residue in healthy and alloxan-diabetic mice

Healthy mice were divided into three groups of 10 animals each (Groups I–III). Group I served as control and received ISS; Group II received fast action insulin (Regular Insulin Lilly) as reference (0.1 IU/kg weight); and Group III received dry residue plant (200 mg/kg).

Mild alloxan-diabetic mice were divided into two groups of 14 animals each (Groups IV-V). Group IV served as control and received ISS; Group V received dry residue plant (200 mg/kg). Severe alloxan-diabetic mice also were divided into two groups: Group VI with 26 animals and Group VII with nine animals. Group VI served as control and received ISS; Group VII received dry residue plant (200 mg/kg).

2.5.2. Effects of the compounds isolated from P. decompositum roots on fasting-blood glucose levels in healthy mice

Healthy mice were divided into 13 groups of seven to ten animals each. Two groups served as control and received ISS or corn oil; the rest of the groups received 50 and 100 mg/kg body weight of the following substances: cacalol, cacalol acetate, cacalone, maturin (all of which were dissolved in corn oil) and WMP extract dissolved in ISS. The other nine groups with eight to 17 animals were used to study the hypoglycemic effect of the substances isolated from the WMP extract, all of which were dissolved in ISS before its administration at the experimental animals.

In all cases, the control substances, plant dry residue and isolated compounds were injected intraperitoneally (4 ml/kg wt.). Blood samples were obtained by amputation of the tail tip in fasting ($t = 0$), and 120 and 240 min after substance administration. Glycemia was determined by the glucose-oxidase peroxidase method with Haemo-Glukotest 20-800 reagent strips (Boehringer-Mannheim)and their valuation was made on a Reflolux-S lightmeter (Boehringer-Mannheim).

2.6. Statistical analysis

Results are expressed as mean $\pm$ SEM. The significance of the differences between the means of tests and control studies was established by Student's t-test for independent samples with one tail. P values less than 0.05 were considered significant.

3. Results

The freeze-dried *P. decompositum* root water decoction, administered at a dose of 200 mg/kg body weight, caused significant hypoglycemic effect in healthy (Table 1) and mild-alloxan diabetic mice (Table 2). In severe alloxan-diabetic mice, the decrease of the blood glucose level was minor (Table 3), with an important reduction 240 min after administration ($P < 0.01$).

Concerning the main compounds of *P. decompositum* roots, the sesquiterpenoids, cacalol, cacalone and maturin, failed to produce any significant hypoglycemic effect in normal mice ($P > 0.01$). Only the precipitate obtained from the freeze dried water extract after treatment with methanol (WMP) caused a significant decrease ($P < 0.01$) in fasting glycemia (Table 4) administered at different doses (50, 100, and 200 mg/kg).

The four polysaccharide fractions isolated by pTLC from the WMP were tested, but only F1 and F3 fractions showed a hypoglycemic effect in

Table 1
Effect of freeze-dried *P. decompositum* root water decoction on blood glucose levels in healthy fasting mice

Group	Study	Blood glucose (mg/dl) (mean ± SEM)		
		In fasting	120 min	240 min
I	Control (ISS) ($n = 10$)	51.8 ± 5.6	49.1 ± 3.9	48.4 ± 4.0
II	Regular insulin ($n = 10$)	51.3 ± 3.8	35.1 ± 2.2**	34.1 ± 3.1**
III	*P. decompositum* ($n = 10$)	50.9 ± 4.7	31.2 ± 2.0**	32.5 ± 3.1**

** Significantly different from its pre-value in fasting, $P < 0.005$.

Table 2
Effect of freeze-dried *P. decompositum* root water decoction on fasting blood glucose levels in mild alloxan-diabetic mice

Group	Study	Blood glucose (mg/dl) (mean ± SEM)		
		In fasting	120 min	240 min
IV	Control (ISS) ($n = 14$)	276.8 ± 17.3	232.0 ± 24.3	206.1 ± 32.1
V	*P. decompositum* ($n = 14$)	208.5 ± 13.0	89.9 ± 8.9**	52.3 ± 7.0**

** Significantly different from its pre-value in fasting, $P < 0.005$.

Table 3
Effect of freeze-dried *P. decompositum* root water decoction on fasting blood glucose levels in severe alloxan-diabetic mice.

Group	Study	Blood glucose (mg/dl) (mean ± SEM)		
		In fasting	120 min	240 min
VI	Control (water) ($n = 26$)	421.2 ± 7.4	405.6 ± 11.7	369.6 ± 24.7
VII	*P. decompositum* ($n = 9$)	394.4 ± 9.4	376.7 ± 32.2	289.3 ± 39.5**

** Significantly different from its pre-value in fasting, $P < 0.005$.

healthy mice (Table 5). In the first case, significant decreases in fasting glycemia ($P < 0.01$) were observed 120 and 240 min after administration. F3 only caused a reduction on fasting glycemia with the highest dose, 240 min after administration.

The F1 fraction from the WMP showed, on HPTLC, a chromatographic behavior similar to a maltoheptaose, M-7 (Sigma). The four main fractions, F1–F4, showed chromatographic behavior distinct from that shown by the monosaccharides and the disaccharide studied. The chemical identity of F1 fraction is currently under study.

4. Discussion

The results of this investigation confirm the previously observed oral and intraperitoneal hypoglycemic effect of *P. decompositum* in temporally hyperglycemic rabbits and in healthy mice, respectively (Alarcon-Aguilar et al., 1997), and show that the freeze-drying process maintains its pharmacological properties. In addition, the freeze-dried water decoction exhibits the biggest hypoglycemic activity in mild alloxan-diabetic mice, and the minor hypoglycemic effect was observed in severe alloxan-diabetic mice.

Table 4
Effect of the compounds and WMP fraction obtained from the roots of *P. decompositum* on fasting blood glucose levels in healthy mice ($n = 10$)

Study	*n*	Dose (mg/dl)	Blood glucose (mg/dl) (mean ± SEM)		
			In fasting	120 min	240 min
Control (ISS)	10	–	54.6 ± 2.8	52.5 ± 4.2	50.6 ± 3.2
Control (Corn oil)	10	–	58.1 ± 3.0	54.2 ± 3.3	54.1 ± 4.1
Cacalol	8	50	54.5 ± 5.5	47.4 ± 4.4	46.8 ± 6.0
	7	100	58.1 ± 4.6	59.4 ± 4.3	58.7 ± 3.2
Cacalol acetate	8	50	52.7 ± 4.3	60.7 ± 5.7	46.1 ± 2.3
	9	100	53.1 ± 2.8	50.3 ± 3.3	44.9 ± 2.8
Cacalone	8	50	56.9 ± 3.9	59.6 ± 3.9	52.5 ± 4.3
	9	100	57.9 ± 4.5	58.0 ± 3.1	50.4 ± 3.6
Maturin	10	50	61.1 ± 3.9	60.3 ± 3.1	52.5 ± 3.5
	10	100	64.7 ± 2.2	64.3 ± 2.0	62.2 ± 3.7
WMP+[a]	8	50	61.6 ± 4.0	54.1 ± 2.4	44.6 ± 3.1**
	9	100	52.8 ± 3.5	43.7 ± 1.9*	31.2 ± 3.5**
	10	200	57.8 ± 4.2	34.8 ± 3.5**	29.9 ± 3.0**

* Significantly different from its pre-value in fasting, $P < 0.01$.
** Significantly different from its pre-value in fasting; $P < 0.005$.
[a] WMP+, methanol insoluble precipitate from water extract.

The hypoglycemic activity reported in *P. decompositum* herein agrees with the results obtained by Roman-Ramos et al. (1992b) with other anti-diabetic plants, such as *Psacalium peltatum* (H.B.K.) Cass. (Syn. *Senecio peltiferus* Hemsl.), a taxonomically related species (Bye et al., 1995). P. *peltatum* caused a hypoglycemic effect in mild alloxan-diabetic rabbits but had no effect in

Table 5
Effect of the polysaccharide fractions isolated from the WMP of *P. decompositum* on fasting blood glucose levels in healthy mice ($n = 10$)

Study	*n*	Dose (mg/dl)	Blood glucose (mg/dl) (mean ± SEM)		
			In fasting	120 min	240 min
Control (SSI)	17	-	62.2 ± 4.3	62.8 ± 4.3	59.7 ± 3.4
F1	10	100	67.9 ± 4.3	61.9 ± 3.7	50.9 ± 2.0**
	10	200	57.6 ± 3.0	45.6 ± 2.3**	37.6 ± 2.6**
F2	8	100	63.6 ± 4.4	62.5 ± 4.9	59.9 ± 3.0
	10	200	55.5 ± 3.6	50.2 ± 4.0	54.7 ± 4.7
F3	10	100	73.5 ± 3.9	71.6 ± 2.9	63.2 ± 2.4
	9	200	57.6 ± 2.3	51.7 ± 3.3	40.3 ± 3.6**
F4	9	100	50.9 ± 4.6	51.1 ± 5.8	55.1 ± 4.1
	10	200	52.9 ± 4.2	51.4 ± 3.6	51.7 ± 3.2

** Significantly different from its pre-value in fasting, $P < 0.005$.

severe alloxan diabetic rabbits (Roman-Ramos et al., 1992b).

The results with *P. decompositum* show some activity in severe-diabetic mice. This last effect could be explained because the diabetes induced in the rabbits resulted be more severe (fasting glycemia >400 mg%) than in the mice (fasting glycemia from >350 mg%). Thus, the alloxan administered to the experimental mice could cause a minor damage in the pancreatic beta cells. These results suggest that the hypoglycemic activity of *P. decompositum* roots requires the presence of functioning beta cells. At present, we are starting experiments trying to measure plasma insulin of mice.

On the other hand, some studies indicate that the traditional preparations obtained from medicinal plants in some cases contain both beneficial and toxic substances. Pharmacological and chemical studies, performed to isolate and to characterize chemically beneficial therapeutic substances, are very important because in this way, it is possible to separate both active principles. These studies, therefore, could reduce the health hazard associated with the use of complex mixtures of unknown substances (Atherton, 1994).

In fact, Sullivan (1981) detected, in a qualitative analysis by TLC, at least seven pyrrolizidine-type alkaloids in a water decoction of *P. decompositum*. Pyrrolizidine alkaloids are hepatotoxic chemicals and have shown carcinogenic and mutagenic activities in experimental models (Kapadia et al., 1990; Plaa, 1991). According to this, *P. decompositum* water decoction represents a health hazard when it is used by the population in the diabetes mellitus control (Sullivan, 1981). Therefore, it was considered highly important to begin the detection and isolation of the substance(s) with hypoglycemic activity in *P. decompositum* roots. It would start with the sesquiterpenoid compounds previously identified in this plant, cacalol, cacalone, and maturin, as well as the transformation product, cacalol acetate.

These sesquiterpenoids are the major components obtained from the hexane extract of *P. decompositum* roots. They are also very common in the water decoction and are known to exhibit anti-microbial and allelo-chemical properties (Lotina et al., 1991; Jimenez-Estrada et al., 1992; Alarcon-Aguilar et al., 1997). The major relative concentration of these compounds in 950.5 g dried plant was for cacalol (1.17 g). Cacalone and maturin showed minor relative concentrations: 0.190 and 0.096 g/950.5 g dried plant, respectively. The results of the pharmacological screening with these four compounds showed that none of them is responsible for the hypoglycemic effect of the water decoction when tested in healthy mice at doses of 100 and 200 mg/kg body weight. Therefore, it was necessary to direct the attention to other non-yet identified chemical components from this source.

WMP produced an important hypoglycemic effect when it was administered at 50, 100 and 200 mg/kg. The HPTLC analysis suggested the presence of four main components. The relative concentrations of these compounds in 950.5 g dried plant were 21.19 (F1), 12.39 (F2), 13.57 (F3), and 8.70 g (F4). Two of them (F1 and F3) showed a hypoglycemic effect in healthy mice. The polar fraction, F1, was the most active and showed a chromatographic behavior similar to a maltohepataose (M7). Although F3 also showed a hypoglycemic effect, it was only evident at a dose of 200 mg/kg ($t=240$ min). Since F1–F4 showed different Rf values compared with mono- and disaccharides, we can conclude that these fractions contain polysaccharides. These final results suggest some synergistic activity between both compounds. There are some cases where the pharmacological activity reported in a plant can be explained just by the existence of a synergistic complex of principles, isolated from the same, whose actions are particularly difficult to reproduce with pure substances. In these cases, the principles are different in their relative activities (Capasso-Francesco, 1985). Studies will be carried out to evaluate synergistic actions between both compounds.

It is interesting to note that many plant polysaccharides have been reported to exhibit hypoglycemic effects (Ivorra et al., 1989; Ling-Hua and Pei-Gen, 1993). Some hypoglycemic polysaccharides were isolated from the roots of *Panox ginseng* (Oshima et al., 1985), *Dioscorea japonica* (Hikino et al., 1986), *Lithospermum erythrorhizon*

(Konno et al., 1985), *Anemarrhena asphodeloides* (Takahashi et al., 1985), *Trichosanthes kirilowii* (Ling-Hua and Pei-Gen, 1993), etc. The majority of these substances have shown hypoglycemic activity in normal mice and alloxan-induced hyperglycemic mice.

In conclusion, the freeze-dried water decoctions obtained from *P. decompositum* roots exhibit hypoglycemic activity, in both normo-glycemic mice and alloxan-diabetic mice. Chemical and pharmacological investigations carried out to evaluate the hypoglycemic effects of the components isolated from this medicinal root showed that cacalol and related sesquiterpenoid compounds have no hypoglycemic effect. Compound F1, isolated from the active WMP, reduces significantly the fasting glycemia in mice. Chemical studies are now being undertaken to characterize this final compound.

References

ADA (1997) Clinical practice recommendations 1997. Screening for Diabetes. Diabetes Care 20(1), 22-24.

Aguilar, A., Camacho, J.R., Chino, S., Jacques, P., Lopez, M.E., 1994. Herbario Medicinal del Instituto Mexicano del Seguro Social. IMSS, Mexico, p. 55.

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

Alarcon-Aguilar, F.J., Roman-Ramos, R., Perez-Gutierrez, M.S., Aguilar-Contreras, A., Contreras-Weber, C.C., Flores-Saenz, J.L., 1998. Study of the Anti-hyperglycemic effect of medicinal plants used as anti-diabetics. J. Ethnopharmacol. 61, 101–110.

Atherton, D.J., 1994. Towards the safer use of traditional remedies. Br. Med. J. 308, 673–674.

Bohlmann, F., Zdero, C., Grenz, M., 1977. Naturlich vorkommende Terpen-Derivative, 78. Weitere Inhaltsstoffe aus sudafrikanischen Senecio-Arten. Chem. Ber. 110, 474–486.

Bye, R.A. Jr., 1986. Medicinal plants of the Sierra Madre: comparative study of TaraLumara and Mexican market plants. Econ. Bot. 40, 103–124.

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. Plenum Press, New York, p. 65 Chapter 4.

Capasso, F., 1985. Medicinal plants: an approach to the study of naturally occurring drugs. J. Ethnopharmacol. 13, 111–114.

Committee Report, 1997. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 20, 1183–1197.

Correa, J., Romo, J., 1966. The constituents of Cacalia decomposita A. Gray. Structure of maturin, maturing, matron, and saturnine. Tetrahedron 22, 685–691.

Hikino, H., Konno, C., Takahashi, M., Murakami, M., Kato, Y., Karikura, M., Hayashi, T., 1986. Isolation and hypoglycemic activity of dioscorans A, B, C, D, E, and F; glycans of *Dioscorea japonica* rhizophores. Planta Med. 52, 168–171.

Ivorra, M.D., Paya, M., Villar, A., 1989. A review of natural products and plants as potential anti-diabetic drugs. J. Ethnopharmacol. 27, 243–275.

Jimenez-Estrada, M., Cruz, R., Valdez, J., Leon, J., Alarcon, G., Svestarova, B., 1992. Actividad antimicrobiana del cacalol y sus derivados. Rev. Latinoamericana Quim. 22, 14–17.

Kapadia, G., Ramdass, A., Bada, F., 1990. Pyrrolizidine alkaloids of Senecio glabellus. Int. J. Crude Drug Res. 28, 67–71.

Konno, C.h., Mizuno, T., Hikino, H., 1985. Isolation and hypoglycemic activity of lithospermans A, B, and C, glycans of *Lithospermum erythrorhizon* roots. Planta Med. 51, 168–171.

Ling-Hua, Z., Pei-Gen, X., 1993. Recent advances in studies of antihyperlipaemic and antihyperglycaemic compounds from Chinese traditional and herbal medicines. Phytother. Res. 7, 217–226.

Lotina, B., Roque, J.L., Jimenez-Estrada, M., Aguilar, M., 1991. Inhibition on oxigen evolution by cacalol and its derivatives. Z. Naturforsch. 46, 777–780.

Oshima, Y., Konno, C.h., Hikino, H., 1985. Isolation and hypoglycemic activity of panaxans I, J, K and L; glycans of *Panox ginseng* roots. Planta Med. 52, 168–171.

Plaa, G., 1991. Toxic responses of the liver. In: Amdur, M., Doull, J., Kaassen, C. (Eds.), Casarett and Doull's Toxicology: The Basic Science of Poisons. Pergamon Press, New York, p. 345.

Roman-Ramos, R., Flores-Saenz, J.L., Partida-Hernandez, G., Lara-Lemus, A., Alarcon-Aguilar, F., 1991. Experimental study of the hypoglycemic effect of some antidiabetic plants. Arch. Investigacion Med. 22, 87–93.

Roman-Ramos, R., Alarcon-Aguilar, F., Lara-Lemus, A., Flores-Saenz, J.L., 1992a. Hypoglycemic effect of plants used in Mexico as antidiabetics. Arch. Med. Res. 23, 59–64.

Roman-Ramos, R., Lara, A., Alarcon- Aguilar, F., Flores, J.L., 1992b. Hypoglycemic activity of some antidiabetic plants. Arch. Med. Res. 23, 105–109.

Roman-Ramos, R., Flores-Saenz, J.L., Alarcon-Aguilar, F.,

1995. Anti-hyperglycemic effect of some edible plants. J. Ethnopharmacol. 48, 25–32.

Romo, J., Joseph-Nathan, P., 1964. The constituents of *Ca*calia decomposita A. Gray. Structures of Cacalol and Cacalone. Tetrahedron 20, 2331–2337.

Romo de Vivar, A., 1985. Productos Naturales de Laflora Mexicana. Limusa, Mexico, p. 69.

Sullivan, G., 1981. Detection of pyrrolizidine-type alkaloids in matarique (*Cacalia decomposita*). Vet. Human Toxicol. 23, 6–7.

Takahashi, M., Konno, C.h., Hikino, H., 1985. Isolation and hypoglycemic activity of anemarans A, B, C, and D; glycans of *Anemarrhena asphodeloides* rhizomes. Planta Med. 51, 168–171.

Yuste, F., Diaz, E., Walls, F., 1976. The structure of Cacalone. J. Org. Chem. 41, 4103–4106.