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ABSTRACT

OBJECTIVE

The objective of this study was to determine whether cinnamon improves blood glucose, triglyceride, total cholesterol, HDL cholesterol, and LDL cholesterol levels in people with type 2 diabetes.

RESEARCH DESIGN AND METHODS

A total of 60 people with type 2 diabetes, 30 men and 30 women aged 52.2 ± 6.32 years, were divided randomly into six groups. Groups 1, 2, and 3 consumed 1, 3, or 6 g of cinnamon daily, respectively, and groups 4, 5, and 6 were given placebo capsules corresponding to the number of capsules consumed for the three levels of cinnamon. The cinnamon was consumed for 40 days followed by a 20-day washout period.

RESULTS

After 40 days, all three levels of cinnamon reduced the mean fasting serum glucose (18–29%), triglyceride (23–30%), LDL cholesterol (7–27%), and total cholesterol (12–26%) levels; no significant changes were noted in the placebo groups. Changes in HDL cholesterol were not significant.

CONCLUSIONS

The results of this study demonstrate that intake of 1, 3, or 6 g of cinnamon per day reduces serum glucose, triglyceride, LDL cholesterol, and total cholesterol in people with type 2 diabetes and suggest that the inclusion of cinnamon in the diet of people with type 2 diabetes will reduce risk factors associated with diabetes and cardiovascular diseases.

To review full text of these scientific studies please visit www.glycoprinclinicalstudies.com

Scientific Research Studies

PANCREAS TONIC



Glycoprin is the New Brand name of Pancreas Tonic

Metabolism; Vol. 53, Issue 9, Sept. 2004,
pages 1166-1173

Effect of Pancreas Tonic® (an ayurvedic herbal supplement) in type 2 diabetes mellitus*1

Stanley H. Hsia, a, b, Mohsen Bazargana, b and
Mayer B. Davidson

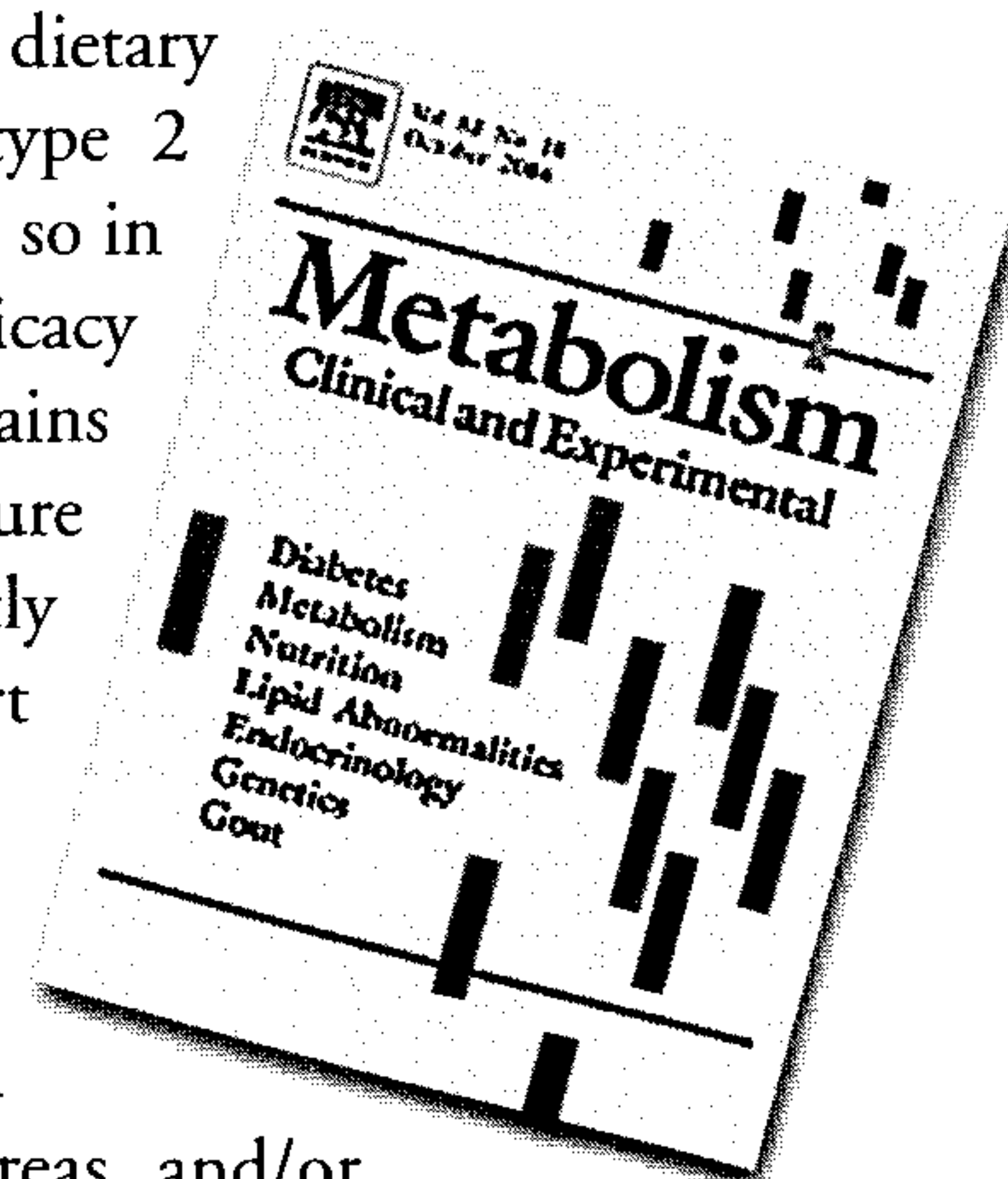
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Received 31 October 2003; accepted 21 April 2004.
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ABSTRACT:

Although there is widespread use of herbal dietary supplements that are believed to benefit type 2 diabetes mellitus, few have been proven to do so in properly designed randomized trials; their efficacy for intermediate-term glucose control remains unclear. Pancreas Tonic® is a botanical mixture of traditional Indian Ayurvedic herbs currently available as a dietary supplement. We report the results of a single-center, randomized, double-blind, placebo-controlled 3-month trial of Pancreas Tonic® in type 2 diabetic patients inadequately treated with diet/lifestyle or stable doses of sulfonylureas and/or metformin for at least 3 months. Patients with type 2 diabetes for 1 year were entered into 2 strata of hemoglobin A1c (HbA1c) levels (stratum



1: 8.0% to 9.9%; stratum 2: 10.0% to 12.0%). All subjects began a 1-month single-blind placebo run-in phase, followed by randomization in a 2:1 ratio of active treatment: placebo, to 3 months of double-blind treatment with either Pancreas Tonic® or matching placebo (2 capsules 3 times a day). Concurrent oral agents were continued unchanged throughout the study. The primary outcome was the change in HbA1c from randomization; results of each stratum were analyzed independently. The baseline characteristics of 36 subjects who completed the study were comparable between treatment groups. Nineteen subjects entered stratum 1 and 17 entered stratum 2. A statistically significant reduction of HbA1c from randomization to end-of-study was seen in the stratum 2 subjects (Pancreas Tonic®: 10.1% Å} 1.0% to 8.8% Å} 1.9%, P = .004; placebo: 10.8% Å} 1.4% to 11.2% Å} 1.8%, not significant [NS]). No significant HbA1c reductions were seen in the stratum 1 subjects. There were no significant treatment-related differences in the fasting plasma glucose (FPG), lipids, body mass index (BMI), body composition, blood pressure, insulin sensitivity estimates using the minimal model, glucose and insulin responses to a meal challenge, quality of life, adverse events, or other safety indices between treatment groups. Pancreas Tonic® was well tolerated. Treatment with Pancreas Tonic® (2 capsules 3 times per day) for 3 months significantly improved glucose control in type 2 diabetic patients with HbA1c levels between 10.0% to 12.0%. This study represents the first properly designed, prospective intervention trial of therapy with an Ayurvedic herbal supplement for intermediate-term glucose control in type 2 diabetes.

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Glycoprin is the new brand name of Pancreas Tonic

Journal of Investigative Medicine, Volume: 52 *

Issue: 01-S1 * 2004 * January * Page: S106

Western

WESTERN ABSTRACTS, WAFMR,

WSCI, WAP, and WSPR

Joint Plenary Session II, 1:45 PM Thursday,

January 29, 2004 159

Effectiveness of the Ayurvedic Herbal Supplement Pancreas Tonic® in Patients with Type 2 Diabetes Mellitus

S.H. Hsia, M. Bazargan, M.B. Davidson, Charles R. Drew University of Medicine and Science, Los Angeles, CA.



ABSTRACT:

Although there is a widespread use of herbal dietary supplements that are believed to benefit type 2 diabetes mellitus, few have been proven to do so in properly designed randomized trials; their efficacy for long-term glucose control remains unclear. Pancreas Tonic® is a botanical mixture of traditional Indian Ayurvedic herbs currently available as a dietary supplement. We report the results of a single-center, randomized, double blind, placebo-controlled 3-month trial of Pancreas Tonic® in type 2 diabetic patients inadequately treated with diet / lifestyle or stable doses of sulfonylureas and/or metformin for at least 3 months.

METHODS:

Patients with type 2 diabetes for > 1 year were entered into strata of hemoglobin A1c (HbA1c) levels (stratum 1: 8.0-9.9%; stratum 2: 10.0-

12.0%) All subjects entered a 1 month single-blind placebo run-in phase, followed by randomization in a 2:1 ratio of active treatment: placebo, to 3 months of double-blind treatment with either Pancreas Tonic® or matching placebo (2 capsules tid). Concurrent oral agents were continued unchanged throughout the study. Subjects were seen in follow-up at 2,4,8 and 12 weeks after randomization. The primary outcome was the change in HbA1c from randomization; results of each stratum were analyzed independently. Secondary outcomes included fasting plasma glucose (FPG), fasting lipid profiles, BMI, blood pressure (BP), body composition, insulin sensitivity estimates using the minimal model, glucose and insulin responses to a meal challenge, a quality-of-life questionnaire, and safety parameters (hematology and biochemistry, EKG, and adverse clinical events).

RESULTS:

The baseline characteristics of 36 subjects who completed the study were comparable between treatment groups. Nineteen subjects entered stratum 1 and 17 entered stratum 2. A statistically significant reduction of HbA1c from randomization to end-of-study was seen in the stratum 2 subjects (Pancreas Tonic®: 10.1 + 1.0 to 8.8 + 1.9%, $p = 0.004$; placebo: 10.8 + 1.4 to 11.2 + 1.8%, NS). A transient non-significant reduction of FPG compared to placebo was seen in stratum 2, 1 month into therapy ($p = 0.08$). There were no treatment-related differences in the other secondary outcome variables, adverse events or other safety indices between treatment groups. Pancreas Tonic® was well tolerated.

CONCLUSIONS:

Treatment with Pancreas Tonic® (2 capsules tid) for 3 months significantly improved glucose control in type 2 diabetic patients with HbA1c levels between 10.0-12.0%. This study represents the first properly designed, prospective intervention trial of therapy with an Ayurvedic herbal supplement for long-term glucose control in type 2 diabetics.

JIM-52-01-S1-12849

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JAMA India

Journal of the American Medical Association

REPRINT JAMA INDIA

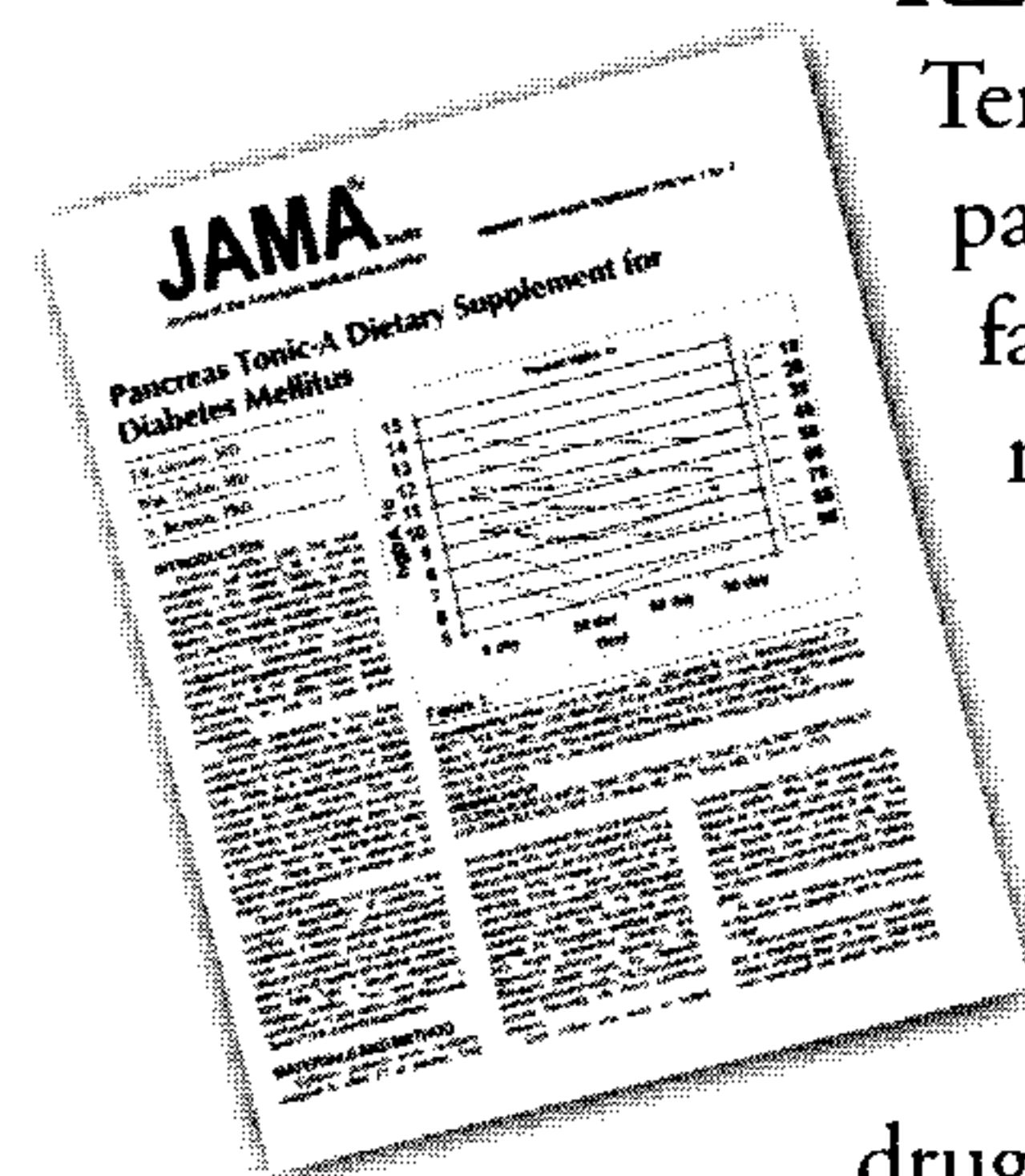
FEBRUARY 2002 Vol. 1 No. 2

Pancreas Tonic-A Dietary Supplement for Diabetes Mellitus

J.R. Gerson, MD, Wm. Taylor, MD, N. Berman, PhD

RESULT:

Ten patients completed the protocol. Eight other patients were dropped during the study period for failure to obtain laboratory exams or to present for medical follow-up at the scheduled time. Of the 10 patients who finished the protocol, 6 were in the group taking Pancreas Tonic® and 4 in the control group.



1. No patient experienced an allergic reaction, drug interaction, or reported side effects. Results of liver function tests revealed transient elevation of alkaline phosphatase in both the placebo group and the group taking Pancreas Tonic® at thirty days. Both groups returned to pre study levels at 60 days and remained unchanged for the duration of the study. The likely explanation for this was laboratory specimen handling error. Other liver function tests were within normal limits in both groups, as were results of CBC and urine analysis.

DISCUSSION

The data demonstrate a marked and consistent decrease in HgbA1c in all patients on Pancreas Tonic® (figure 1). No such decline was found in the control group (figure 2). This effect on HgbA1c began as early as 4 weeks and continued throughout the study period. The average decline in % HgbA1c in the study group was 1.96% for those who completed the protocol. The average HgbA1c for both groups is shown in (figure 3). A reduction in

HgbA1c was detected in all patients regardless of age, sex, or hypoglycemic medication. No patient in either group was advised to increase their medication during the study period.

These data indicate that, in this small group of subjects, Pancreas Tonic® was effective in reducing HgbA1c without serious side effects. This supports the need for further study of this herbal, dietary supplement in the larger group of patients.. It would be interesting to study the effect of Pancreas Tonic® on both insulin secretion, resistance, and beta cell mass as part of a larger proposed study.

Glycoprin is the New Brand name of Pancreas Tonic

Journal of Pediatric Endocrinology & Metabolism
Los Angeles, CA - October 31-November 3, 2000

Volume 13, Supplement 4 - 1242, 128

A DOUBLE BLIND CLINICAL TRIAL OF "PANCREAS TONIC®"

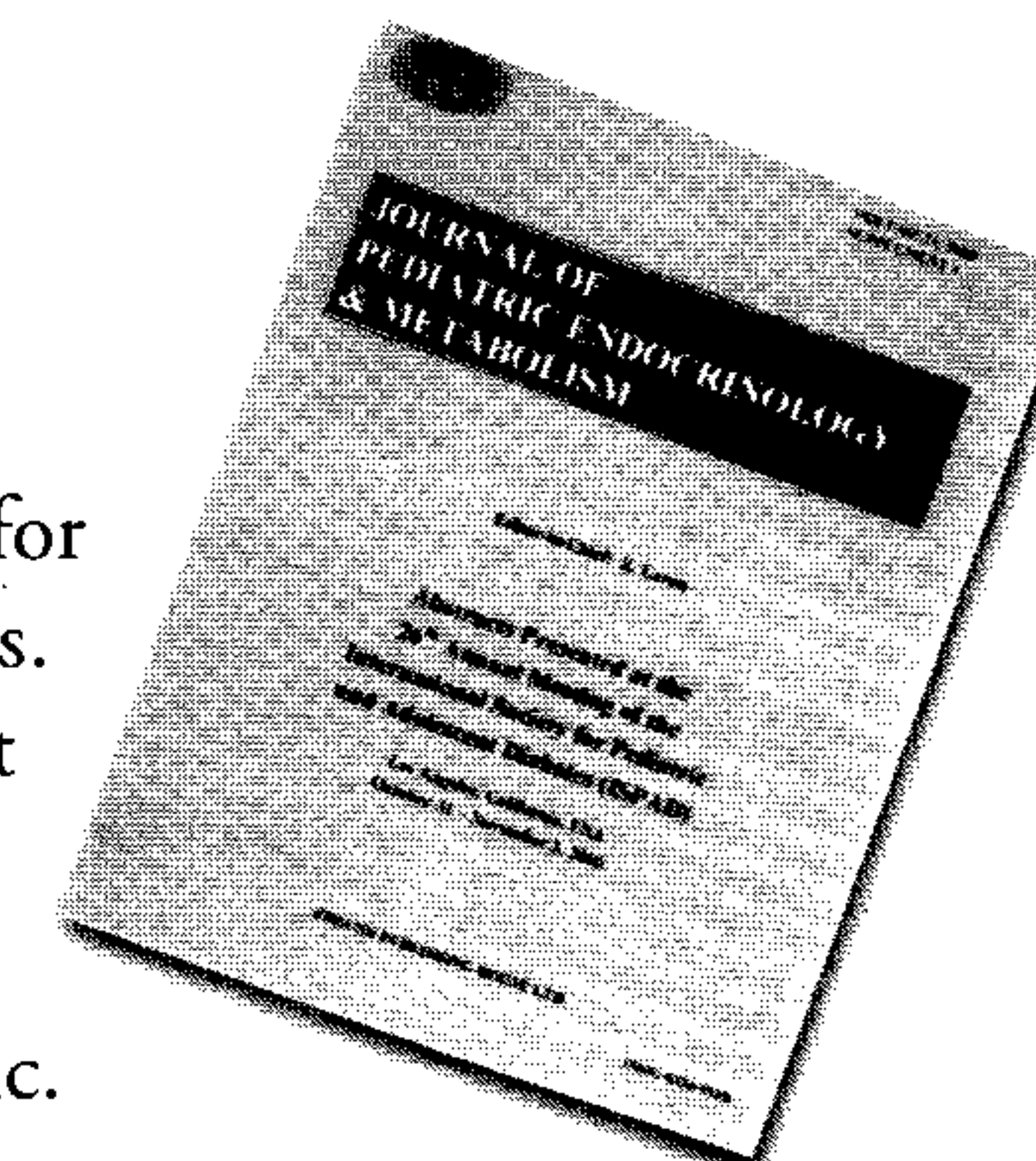
A DIETARY SUPPLEMENT FOR DIABETES MELLITUS

J. R. Gerson, MD*, Redondo Beach, CA, USA; Wm Taylor, MD,
Paramount CA, USA; N. Berman, PhD, Harbor-UCLA Medical
Center, Carson, CA, USA.

ABSTRACT

CONTEXT:

Herbal supplements have long been used for diabetes control in non-western countries. Alternative medicine is becoming more a part of the landscape in the United States. Recently, animal models have shown efficacy of certain herbal compounds to reduce HgbA1c.



OBJECTIVE:

To evaluate the safety and efficacy of an herbal compound "Pancreas Tonic[®]" used in Ayurvedic Medicine in India.

DESIGN:

A prospective, randomized, double blind, placebo-controlled study comparing Pancreas Tonic[®] to usual medications and diet.

SETTING AND PATIENTS:

The patients were the private patients of William Taylor, MD, a practicing Internist. Eighteen patients were entered into the study.

MAIN OUTCOME MEASURES: All patients were interviewed each month. They reported any adverse effects or allergic reactions. They were also queried regarding changes in diet or medications. Venous blood was obtained and tested for HgbA1c, blood sugar, liver function tests, CBC, BUN and creatinine, and urine analysis. Vital signs and weight were also recorded.

Results: There were no episodes of adverse effects, allergic reactions, drug interactions, or abnormal laboratory results in the study group when compared to the placebo group. HgbA1c values decreased by an average of 1.96% in the study group when compared to the placebo group ($p < 0.0001$) and the groups were significantly different on the change to the last available value ($p = 0.0004$).

CONCLUSION:

This combination of herbs used as a dietary supplement in addition to usual diet and medication significantly reduced HgbA1c in a small group of patients. There were no adverse effects noted. A larger group of patients should be studied with mechanism of action as an outcome measure.

Glycoprin is the New Brand name of Pancreas Tonic

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REPRINT OF MEDICINE AND SURGERY
MAY 2002

The Antiseptic' Vol.99 No. 1 P: 12-13

Effect of Pancreas Tonic[®] on diabetes mellitus with diabetes retinopathy:

A prospective and randomized study.

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Director Dr. Patnaiks Laser Eye Institute, New Delhi

INTRODUCTION:

There are at least 20 million diabetics in India, the highest ever reported number from anywhere in the world. In 1995, the estimated prevalence of diabetes among adults was 4% and it is expected to rise to 8.9% by 2025.¹ Diabetes currently listed as the seventh leading cause of death among the general population. Diabetes happened to be a major cause of visual impairment and blindness. It also contributes substantially to the end stage of renal disease, non traumatic lower extremity amputation, cardiovascular disease, stroke, peripherals vascular disease, disability and premature mortality etc.

Diabetic complications develop in relation to the duration and degree of hyperglycemia. Major risk factors for micro-vascular complications include duration of disease, poor glycemic control, anaemia and associated hypertension. Improved glycemic control may also be associated with weight gain which may be either intensive treatment or conventional treatment. It is known that patients assigned to insulin treatment had a greater gain in weight (4kg) than those assigned to chlorpropamide (2.6kg) or glibenclamide (1.1kg).^{2,3} Improved glycemic control may required more to intensive self care and substantial life style rhanages. Patients treated with insulin who had two or more hypoglycemic episodes during previous years reported more tention, more overall mood disturbances and less work satisfaction. There is no doubt that reduction of HbA1c value from 9% to 7% was estimated to decrease the life time risk of blindness by 2.3% (from 2.6% to 0.3%) and to lengthen life by 1.3 years. Of course, benefit depend strongly on Age and the base-line level of glycemic control.

The retina changes in diabetes mellitus is known as diabetic retinopathy. It is a microangiopathy effecting the retina pre-capillary, arterioles capillaries and venules. The factors thought to be responsible for microvascular occlusion include thickening of the capillary basement membrane, capillary endothelial cell damage and proliferation, changes in red blood cells leading to defective oxygen transport, and increase stickness and aggregation of

platelets. The consequence of retina capillary non-perfusion in retina ischaemia which in turn causes retina hypoxia. The two main effects of retinal hypoxia are arteriovenous shunts and neovascularisation. The neovascularisation is thought to be caused by vasoformative substances elaborated by hypoxic retinal tissues in an attempt to revascularize hypoxic area of the retina. The structural integrity of the vessel walls depend on the endothelial cells and pericytes around the capillaries. In normal healthy individuals, there is one pericyte to each endothelial cells, whereas, in diabetic patients, there is reduction in the number of pericytes. This reduction in pericytes is thought to be responsible for distension of capillary walls, the consequences are, increased vascular permeability, haemorrhage and retinal oedema which may be either diffuse or localised. Poor prognosis depends on poor glycemic control, extensive macular capillary non-perfusions, insulin quantity gradually reduces after taking Pancreas Tonic® over a period of time. There is also a possibility of becoming non-insulin dependent, which is seen more in children.

For type II diabetes Pancreas Tonic® is very effective. On evidence of patient history and clinical trials, there is even a greater possibility of permanent cure from diabetes. Pancreas Tonic® is advised along with allopathic medicine for upto a few months till the glucose level reaches an optimum point.

There is no side effect in such parallel therapy. After normal blood sugar level is achieved, Pancreas Tonic® should be continued for another few months for regeneration of beta cells.

DOSAGE:

Two capsules three times a day, 15 minutes before meals.

In hypoglycemia one capsule two times a day, 15 minutes before meals is advised.

In diabetic retinopathy Pancreas Tonic® is also very effective to cure. It reduces the incidence of microvascular complications. Pancreas Tonic® restrains proliferation after pan-retinal photocoagulation. So, blindness is also restrained through Pancreas Tonic®, Dr. N.K.Pattnaik has focused in his own trials.

Glucoprin is the New Brand name of Pancreas Tonic

Journal Of The National Medical Association,
1998, Vol.90, No. 10, page; 614-618

ANTI-DIABETIC EFFECTS OF A DIETARY SUPPLEMENT “PANCREAS TONIC”

Ramachandra M. Rao, PhD, Fathi A. Salem, MD, and Irene Gleason-
Jordan, MD - Los Angeles, California

ABSTRACT:

Pancreas Tonic, a dietary supplement, contains plant products shown to possess hypoglycemic activity. This study investigated the effect of Pancreas Tonic on serum glucose, glycosylated hemoglobin, and pancreatic islet cell regeneration of rats. Results showed that body weights of three groups of rats were not significantly different from each other before the study period, and after the 12 week study, weights increased with nonsignificant difference among the groups.

The diabetic group had significantly higher serum glucose levels compared with controls, and the diet-treated group had significantly lower serum glucose levels compared with the diabetic group. The diabetic group's glycosylated hemoglobin was significantly higher compared with the control group, and the diet-treated group had significantly lower glycosylated hemoglobin levels compared with the diabetic and control groups. Histological analysis of the pancreas showed a generalized reduction in size and number of islets in the diabetic group and regeneration of islet cells in the diet-treated group compared with the diabetic group. The diabetic group had a significant reduction in the number of cells compared with controls. The diet-treated group contained a significantly increased number of cells compared with the diabetic group. These data suggest that Pancreas Tonic® induced an antidiabetic effect through pancreatic islet cell regeneration in experimental rats.

(J Nat. Med Assoc. 1998; 90:61 4-618.)

Research Studies on Glycoprin Ingredients

Study 1

Journal of Ethnopharmacology 72 (2000)
331-336

Short communication

Effects of *Momordica charantia* powder on serum glucose levels and various lipid parameters in rats fed with cholesterol-free and cholesterol-enriched diets

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Received 19 October 1999; received in revised form 23 April 2000; accepted 1 May 2000

ABSTRACT

The effects of dietary bitter melon (*Momordica charantia*) freeze-dried powder on serum glucose level and lipid parameters of the serum and liver were studied in rats fed diets supplemented with and without cholesterol. Rats were fed the diets for 14 days containing bitter melon freeze-dried powder at the level of 0.5, 1 and 3% without an added dietary cholesterol (experiment I) and those containing bitter melon at the level of 1% with or without 0.5% cholesterol and 0.15% bile acid (experiment II). No adverse effect of dietary bitter melon powder on growth parameters and relative liver weight were noted. Dietary bitter melon resulted in a consistent decrease in serum glucose levels in rats fed cholesterol-free diets, but not in those fed

cholesterol-enriched diets, although no dose-response was noted. Addition of cholesterol to the diets as compared to those without added cholesterol caused hypercholesterolemia and fatty liver. Bitter melon had little effect on serum lipid parameters, except for high density lipoprotein (HDL)-cholesterol; HDL-cholesterol levels tended to decrease by dietary cholesterol, while they were consistently elevated by dietary bitter melon both in the presence and absence of dietary cholesterol, indicating an antiatherogenic activity of bitter melon. In addition, bitter melon exhibited a marked reduction in the hepatic total cholesterol and triglyceride levels both in the presence and absence of dietary cholesterol; the reduction of triglyceride levels in the absence of dietary cholesterol was in a dose-dependent manner. These results suggest that bitter melon can be used as a health food.

Study 2

Diabetes Research and Clinical Practice 40 (1998)
145-151

Effects of *Momordica charantia* fruit juice on islet morphology in the pancreas of the streptozotocin-diabetic rat

I. Ahmed a, E. Adeghate a.*, A.K. Sharma a D.J. Pallot a, J. Singh b

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b Department of Applied Biology, University of Central Lancashire, Preston PR1 2HE, UK

Accepted 11 February 1998

ABSTRACT

An investigation was made of the effect of *Momordica charantia* fruit juice on the distribution and number of α and β cells in the pancreas of streptozotocin (STZ)-induced diabetic rats using immunohistochemical methods. The results indicated that there was a significant (Student's *t*-test, $P < 0.004$) increase in the number of α cells in *M. charantia*-treated animals when compared with untreated diabetics, however, their number was still

significantly less than that obtained for normal rats. There was also a significant ($P < 0.006$) increase in the number of β cells in STZ-diabetic rats compared to non-diabetic rats. This increase in the number of β cells was not affected by *M. charantia* treatment. The number of cells did not change significantly in *M. charantia*-treated rats when compared with untreated diabetic rats. Our results suggest that oral feeding of *M. charantia* fruit juice may have a role in the renewal of α cells in STZ-diabetic rats or alternately may permit the recovery of partially destroyed α cells.

Study 3

Toxicology Letters 94 (1998) 37—46

Momordica charantia (Bitter Gourd) peel, pulp, seed and whole fruit extract inhibits mouse skin papillomagenesis

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University, New Delhi-I 10067, India.

Received 28 August 1997; received in revised form 20 October 1997;
accepted 21 October 1997

ABSTRACT

The present study was designed to elucidate the inhibitory potential of *Momordica charantia* (Bitter Gourd) peel, pulp, seed and whole fruit extract on mouse skin papillomagenesis with the modulatory influence of biotransformation system enzymes. Topical application of *Momordica* whole fruit extract (100 μ l/animal per day) during the peri-initiation stage (1 week before and 2 weeks after initiation) by 7,12-dimethylbenz(a) anthracene (DMBA) and/or during the tumor promotion stage reduced the (i) tumor burden to 4.26, 3.72 and 3.11 (positive control value: 5.42); (ii) cumulative number of papillomas to 81, 67 and 53 (positive control value: 103); and (iii) percent incidence of mice bearing papillomas to 100, 94 and 94, respectively (positive control value: 100). In a comparison of the anticarcinogenic efficacy of *Momordica* peel, pulp, seed and whole fruit extract (100 MI/animal per

day), after topical treatment during the pre-initiation and during the tumor promotion stage, revealed the modulation of the (i) tumor burden (tumors/mouse) to 3.06, 3.61, 3.17 and 3.11; (ii) cumulative number of papillomas to 49, 65, 54 and 53; and (iii) percent incidence of mice bearing papillomas to 84, 100, 94 and 94, respectively. Significant elevation in the sulfhydryl ($-SH$) level was observed in the liver and skin tissues by the topical treatment of *Momordica* peel, pulp, seed and whole fruit extract. Elevation in the hepatic levels of cytosolic glutathione S-transferase (GST) and microsomal cytochrome b5 was also observed by the topical treatment of *Momordica* peel, seed and whole fruit extract. The results suggest the maximum chemopreventive potential is in the *Momordica* peel. Equivocal efficacy is in the *Momordica* seed and whole fruit extract. Biotransformation system enzymes may be the cause of this reduced papillomagenesis

Study 4

Pharmacol Res. 1996 Jan;33(1):1-4

DEMONSTRATION OF THE HYPOGLYCEMIC ACTION OF MOMORDICA CHARANTIA IN A VALIDATED ANIMAL MODEL OF DIABETES

SHUBHASHISH SARKAR, MADDALI PRANAVA and ROSALIND MARITA, A.

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Development Centre, Sarkhej Gandhinagar Highway, Thaltej, Ahmedabad-
380 054, India

Accepted 21 October 1995

ABSTRACT

In an effort to establish and document the hypoglycaemic activity of *Momordica charantia* in validated models of diabetes, the alcoholic extract of

the pulp was studied. In the normal glucose primed rat model, *M. charantia* fruit extract, 500 mg/kg, depressed the plasma glucose levels by 10—15% at 1 h. Under similar conditions, tolbutamide (100 mg/kg) caused approximately 40% reductions in plasma glucose both at 1 and 2 h. At 500 mg/kg, the efficacy of *M. charantia* was 25—30% of tolbutamide. The reduction in plasma glucose in normal glucose primed rat was not accompanied by increased insulin secretion. There was no evidence of tachyphylaxis to the effect of *M. charantia* extract on repeated dosing. In streptozotocin diabetes rats, it improved the oral glucose tolerance causing significant ($P < 0.002$) reduction in plasma glucose of 26% at 3.5 h while metformin caused 40—50% reduction at 1, 2 and 3.5 h. *M. charantia* extract (500 mg/kg) caused a 4—5-fold increase in the rate of glycogen synthesis from U-¹⁴C-glucose in the liver of normally fed rats. These data suggest that the mechanism of action of *M. charantia* could be partly attributed to increased glucose utilization in the liver rather than an insulin secretion effect. This is the first report on the effect of *M. charantia* in characterized and validated animal model systems known to respond to oral hypoglycaemic drugs.

Study 5

PHARMACOLOGY OF A HYPOGLYCAEMIC PRINCIPLE ISOLATED FROM THE FRUITS OF MOMORDICA CHARANTIA LINN

(Mrs.) M. M. Lollikara and M.R. Rajarama Rao

(Department of Chemical Technology, University of Bombay, Bombay 19)

Received 3 February 1966

Charantin, a non-nitrogenous, neutral principle giving positive color tests for phytoesterolins is isolated in a pure state from the fruits of *Momordica charantia*. Charantin lowers blood sugar in fasting rabbits, the fall being gradual from the 1st to 4th hour, and recovering slowly to initial level. Charantin (50 mg/kg) administered orally lowers blood sugar 42 per cent at the 4th hour, the mean fall during 5 hours being 28 per cent. The cumulative hypoglycaemic potency curve is not linear, but tends to flatten out as the dose is increased. Charantin is more potent than tolbutamide in

hypoglycaemic activity but the pattern of blood sugar changes is similar to tolbutamide. The hypoglycaemic activity of charantin in depancreatized cats is less, but not abolished, indicating a pancreatic as well as extra-pancreatic action. It exerts non-specific antispasmodic and mild cholinergic-blocking activity.

Study 6

SHORT COMMUNICATION

Effect of Bitter Melon (*Momordica Charantia*) Fruit Juice on the Hepatic Cytochrome P450-Dependent Monooxygenases and Glutathione S-Transferases in Streptozotocin-Induced Diabetic Rats*

Haider Raza, Ijaz Ahmed, Mohammad S. Lakhani,
Ashutosh K. Sharma, David Pallot and William Montague

DEPARTMENTS OF BIOCHEMISTRY AND ANATOMY, FACULTY
OF MEDICINE AND HEALTH SCIENCES,
UAE UNIVERSITY, AL AIN, UNITED ARAB EMIRATES

ABSTRACT

Bitter melon (*Momordica charantia*), commonly known as karela, has been reported to have hypoglycaemic, antiviral, antidiabetic, and antitumor activities. In the present study, we have investigated the effects of oral feeding of karela fruit juice on the hepatic cytochrome P450 (CYP) and glutathione S-transferase (GST) drug-metabolizing enzymes in the streptozotocin (STZ)-induced diabetic rat. Hepatic CYP contents, ethoxycoumarin-O-deethylase (ECOD), ethoxyresorufin-O-deethylase (EROD), aniline hydroxylase (AH), and aminopyrene N-demethylase (APD) activities were measured in control, diabetic, and karela juice fed animals. Diabetic rats exhibited a 50—100% increase in AH and EROD activities that was reversed by karela juice feeding. In addition, a decrease (17—20%) in the activities of APD and ECOD was observed in diabetic rat liver. Feeding of karela juice to

the diabetic animals brought the level of APD close to that of control animals, while ECOD was further reduced to 60% of the control value. The cytosolic glutathione concentration was decreased in diabetic rats, and karela juice feeding normalized the effect. However, an increase (of 20—30%) in the OST activity was observed in both diabetic and karela juice fed rats. Western immunoblot analysis of CYP and GST isozymes exhibited a differential response during diabetes. The expression of CYP1A1, 2B1, 2E1, 3A4, and 4A2 was apparently increased in the diabetic rat liver. The expression of OST alpha and p1 appeared to be increased in diabetes, while a decrease in OST mu was observed. Our results suggest that the changes in hepatic phase I and phase II drug-metabolizing enzyme activities in the STZ-induced diabetic animals may be associated with the altered expression of different CYP and OST isozymes. In addition, we have also observed that karela does not always reverse the effects on drug-metabolizing enzymes in STZ-induced diabetes. *BIOCHEM PHARMACOL* 52;10:1639—1642, 1996.

Study 7

Indian J. Nat. Prod., 1990, 6 (1)1

Hypoglycemic Principle of *Momordica Charantia* Seeds

G. Handa, J. Singh*, M. L. Sharna, A. Kaul, Neerja** and R. Zafar*
Regional Research Laboratory, Iammu Tawi - 180 001

ABSTRACT

The glyco-alkaloid vicine obtained from *Momordica charantia* seeds has been identified as 2, 6-diaminopyrimidinol-5-D glucopyranoside on the basis of chemical and spectral evidence. It has been found to possess 32.6% hypoglycemic activity when tested in fasting albino rats and is nonhaemolytic.

To review full text of these scientific studies please visit www.glycoprinclinicalstudies.com

Study 8

Indian J. Physiol. Pharmacol. 1995; 39(2): 173.174

Short Communication - Effects of *Trigonella Foenum Graecum* (Fenugreek) on Blood Glucose in Normal and Diabetic Rats

P. KHOSLA*, D. D. GUPTA AND R. K. NAGPAL*

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Medical College, Rahtak - 124 001

ABSTRACT:

Trigonella foenum Graecum (Fenugreek) was administered at 2 and 8 g/kg dose orally to normal and alloxan induced diabetic rats. It produced a significant fall ($P < 0.05$) in blood glucose both in the normal as well as diabetic rats and the hypoglycemic effect was dose related.

Study 9

Journal of Ethnopharmacology. 35 (1991) 71-75
Elsevier Scientific Publishers Ireland Ltd.

Hypoglycemic activity of *Pterocarpus marsupium* wood*

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(Accepted May 14, 1991)

ABSTRACT:

Feeding of the ethyl acetate-soluble fraction of an absolute ethanol extract of *Pterocarpus marsupium* wood for 5 days significantly lowered blood sugar levels with a corresponding increase in the blood insulin level in alloxan-diabetic rats.

To review full text of these scientific studies please visit www.glycoprinclinicalstudies.com

Study 10

J. Nat. Prod. 1997, 60, 609-610

609

Anti-hyperglycemic Activity of Phenolics from *Pterocarpus marsupium*

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Received October 25, 1996

ABSTRACT:

Glucose levels in rats with hyperglycemia induced by streptozotocin were determined after ip administration of marsupsin (1), pterosupin (2), and pterostilbene (3), three important phenolic constituents of the heartwood of *Pterocarpus marsupium*. Marsupsin and pterostilbene significantly lowered the blood glucose level of hyperglycemic rats, and the effect was comparable to that of 1,1 -dimethylbiguanide (metformin).

Study 11

Can. J. Physiol.Pharmacol.76: 1017-1023 (1998)

Inhibitory effect of gymnemic acid on intestinal absorption of oleic acid in rats

L.F. Wang, H. Luo, M Miyoshi, T. Imoto, V. Hiji, and T. Sasaki

ABSTRACT:

Gymnemic acid, a mixture of triterpene glycosides extracted from the leaves of *Gymnema sylvestre*, is known to inhibit the intestinal absorption of glucose in human and rats. This work examined the effect of gymnemic acid on oleic acid absorption by the method of intestinal perfusion in rats. The results showed the following.

(i) Gymnemic acid potently inhibited the absorption of oleic acid in intestine. (ii) This inhibition was dose dependent and reversible. (iii) The extent of inhibition and the recovery progress were extremely similar to that of glucose absorption. (iv) Taurocholate did not affect the inhibitory effect of

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gymnemic acid on oleic acid absorption, but lowering its concentration facilitated the recovery from the inhibition. (v) The absorption of oleic acid was not affected by other glycosides such as phloridzin, stevioside, and glycyrrhizin. These new findings are important for understanding the roles of gymnemic acid in therapy of diabetes mellitus and obesity.

Study 12

Journal of Ethnopharmacology, 30 (1990)

281-294 281

Elsevier Scientific Publishers Ireland Ltd.

USE OF GYMNEMA SYLVESTRE LEAF EXTRACT IN THE CONTROL OF BLOOD GLUCOSE IN INSULIN- DEPENDENT DIABETES MELLITUS

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(Accepted June 25, 1990)

SUMMARY

GS4, a water-soluble extract of the leaves of *Gymnema sylvestre*, was administered (400 mg/day) to 27 patients with insulin-dependent diabetes mellitus (IDDM) on insulin therapy. Insulin requirements came down together with fasting blood glucose and glycosylated haemoglobin (HbA_{1c}) and glycosylated plasma protein levels, While serum lipids returned to near normal levels with GS4 therapy, glycosylated haemoglobin and glycosylated plasma protein levels remained higher than controls. IDDM patients on insulin therapy only, showed no significant reduction in serum lipids, HbA_{1c} or glycosylated plasma proteins when followed up after 10—12 months. GS4 therapy appears to enhance endogenous insulin, possibly by regeneration/revitalisation of the residual beta cells in insulin-dependent diabetes mellitus.

To review full text of these scientific studies please visit www.glycoprinclinicalstudies.com

Study 13

Physiology & Behavior, Vol. 30, pp. 1-9. Pergarnon Press, 1983. Printed in the U.S.A.

Effects of Sweetness Perception and Caloric Value of a Preload on Short Term Intake

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Received 20 June 1979

ABSTRACT:

Effects of sweetness perception and caloric value preload on short term intake. *PHYSIOL BEHAV* 30(1) 1—9, 1983.—To determine the effects of calories and sweetness perception on intake, fasted normal weight subjects drank a preload sweetened with sucrose (1.1 g/kg) or L-asparthyl-L-phenylalanyl-methyl ester (Aspartame, 0.011 g/kg). or with no added sweetener. Sweetness perception of the load was reduced in half of the subjects by oral application of *Gymnema sylvestre* extracts. One hour after the preload, a meal of snack foods was presented and amounts of nutrients eaten were calculated. Subjects whose perception of sweetness had been decreased for the preload ate less total and sweet calories than did those with normal perception. Calories did not affect intake. The effect of calories and perception of the load was also assessed on variables presumed to correlate with satiety. Sucrose pleasantness ratings were not related to calories, perception or intake. Subjects' estimates of the amount of milk shake that they would drink if given the opportunity to do so and hunger ratings were related to overall intake and carbohydrate intake, respectively. The findings indicate that hedonistic aspects of taste are of greater importance than calories in determining short term intake.

Study 14

European Journal of Biochemistry, Vol. 138, pp.9-37.

Role of Hydrophobic Amino Acids in Gurmarin, a Sweetness-Suppressing Polypeptide

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Received 21 July 1997; accepted 14 October 1997

ABSTRACT:

The sweetness-suppressing polypeptide gurmarin isolated from *Gymnema sylvestre* consists of 35 amino acid residues and contains three intramolecular disulfide bonds. Nuclear magnetic resonance analysis showed that the hydrophobic side chains of Tyr-13, Tyr-14, Trp-28, and Trp-29 in gurmarin are oriented outwardly. Together with the hydrophobic side chains of Leu-9, Ile-11, and Pro-12, they form a hydrophobic cluster, and therefore these hydrophobic groups are assumed to act as the site for interaction with the receptor protein. To examine the roles of these hydrophobic amino acids, they were replaced by Gly. The resulting [Gly13,14,28,29]gurmarin and [Gly9,11,13,14,28,29] - gurmarin did not suppress the responses to sucrose, glucose, fructose, or Gly. This result strongly suggests that these hydrophobic amino acids are involved in the interaction with the receptor protein

Study 15

Journal of Ethnopharmacology. 30 (1990)
295-305 295

Elsevier Scientific Publishers Ireland Ltd.

ANTIDIABETIC EFFECT OF A LEAF EXTRACT FROM GYMNEMA SYLVESTRE IN NON-INSULIN- DEPENDENT DIABETES MELLITUS PATIENTS

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(Accepted June 26, 1990)

SUMMARY

The effectiveness of GS4, an extract from the leaves of *Gymnema sylvestre*, in controlling hyperglycaemia was investigated in 22 Type 2 diabetic patients on conventional oral anti-hyperglycaemic agents. GS4 (400 mg/day) was administered for 18—20 months as a supplement to the conventional oral drugs. During GS4 supplementation, the patients showed a significant reduction in blood glucose, glycosylated haemoglobin and glycosylated plasma proteins, and conventional drug dosage could be decreased. Five of the 22 diabetic patients were able to discontinue their conventional drug and maintain their blood glucose homeostasis with GS4 alone. These data suggest that the beta cells may be regenerated/repared in Type 2 diabetic patients on GS4 supplementation. This is supported by the appearance of raised insulin levels in the serum of patients after GS4 supplementation.

Study 16

Journal of Ethnopharmacology, 30 (1990)
265-279

Elsevier Scientific Publishers Ireland Ltd.

POSSIBLE REGENERATION OF THE ISLETS OF LANGERHANS IN STREPTOZOTOCIN-DIABETIC RATS GIVEN GYMNEMA SYLVESTRE LEAF EXTRACTS

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(Accepted June 25, 1990)

SUMMARY

Two water soluble extracts, GS3 and GS4, obtained from the leaves of *Gymnema sylvestre*, were tested in streptozotocin treated rats for their effects on blood glucose homeostasis and pancreatic endocrine tissue. In the diabetic rats, fasting blood glucose levels returned to normal after 60 days of GS3 and after 20 days of GS4 oral administration. Blood collected during the conduct of oral glucose tolerance tests was used to assay for serum insulin. GS3 and GS4 therapy led to a rise in serum insulin to levels closer to normal fasting levels. In diabetic rat pancreas, both GS3 and GS4 were able to double the islet number and beta cell number. This herbal therapy appears to bring about blood glucose homeostasis through increased serum insulin levels provided by repair/regeneration of the endocrine pancreas.

Study 17

Journal of Ethnopharmacology, 22 (1988)
45-49 45

Elsevier Scientific Publishers Ireland Ltd.

EFFECT OF TRIGONELLA FOENUM GRACEUM ON BLOOD GLUCOSE LEVELS IN NORMAL AND ALLOXAN-DIABETIC MICE.

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(Accepted September 4, 1987)

SUMMARY

The hypoglycemic effects of a decoction and an ethanol extract of *Trigonella foenum graecum* seeds on the serum glucose levels of normal and alloxan diabetic mice were studied. A single 0.5 ml oral dose of 40–80% decoctions to normal as well as alloxanized mice was followed by hypoglycemia developed over a 6 h period. Reduction in blood glucose concentration was highly significant, was maximum at 6 h and was dose-dependent. The hypoglycemia caused by the ethanol extract (200–400 mg/kg) in alloxanized mice was also dose-dependent and 200 mg/kg was comparable in effect to 200 mg/kg tolbutamide.

Study 18

Prostaglandins. Leukotrienes and Essential Fatty
Acids (1997) 56(5). 379–384

Pearson Professional Ltd 1997

Effect of ginger (*Zingiber officinale* Rosc) and fenugreek (*Trigonella foenum graecum* L) on blood lipids, blood sugar and platelet aggregation in patients with coronary artery disease

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SUMMARY:

In a placebo-controlled study the effect of ginger and fenugreek was examined on blood lipids, blood sugar, platelet aggregation, fibrinogen and fibrinolytic activity. The subjects included in this study were healthy individuals, patients with coronary artery disease (CAD), and patients with non-insulin-dependent diabetes mellitus (NIDDM) who either had CAD or were without CAD. In patients with CAD powdered ginger administered in a dose of 4 g daily for 3 months did not affect ADP- and epinephrine-induced platelet aggregation. Also, no change in the fibrinolytic activity and fibrinogen level was observed. However, a single dose of 10 g powdered ginger administered to CAD patients produced a significant reduction in platelet aggregation induced by the two agonists. Ginger did not affect the blood lipids and blood sugar. Fenugreek given in a dose of 2.5 g twice daily for 3 months to healthy individuals did not affect the blood lipids and blood sugar (fasting and post prandial). However, administered in the same daily dose for the same duration to CAD patients also with NIDDM, fenugreek decreased significantly the blood lipids (total cholesterol and triglycerides) without affecting the HDL-c. When administered in the same daily dose to NIDDM (non-CAD) patients (mild cases), fenugreek reduced significantly the blood sugar (fasting and post prandial). In severe NIDDM cases, blood sugar (both fasting and post prandial) was only slightly reduced. The changes were not significant. Fenugreek administration did not affect platelet aggregation, fibrinolytic activity and fibrinogen.

Study 19

Journal of Ethnopharmacology 70 (2000) 9-15
**Hypoglycaemic and other related actions of
Tinospora cordifolia roots in
alloxan-induced diabetic rats**

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Received 24 August 1998; received in revised form 14 July 1999;
accepted 28 July 1999.

ABSTRACT

Tinospora cordifolia is widely used in Indian Ayurvedic medicine for treating diabetes mellitus. Oral administration an aqueous *T. cordifolia* root extract (TCREt) to alloxan diabetic rats caused a significant reduction in blood glucose and brain lipids. The extract caused an increase in body weight, total haemoglobin and hepatic hexokinase. The root extract also lowers hepatic glucose-6-phosphatase and serum acid phosphatase, alkaline phosphatase, and lactate dehydrogenase in diabetic rats. Thus TCREt has hypoglycaemic and hypolipidaemic effect

Study 20

Indian Journal of Experimental Biology Vol.34,
June 1996, PP. 600-602
**Kinetic studies of purified malate
dehydrogenase in liver of
streptozotocin-diabetic rats and the effect
of leaf extract of *Aegle marmelose* (L.)
*Correa ex Roxb.***

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Received 16 June 1995; revised 18 September 1995

ABSTRACT

The functional basis of diabetes-mellitus to a certain extent, can be elucidated by studying diabetes-induced changes in metabolic enzymes. Malate dehydrogenase (MDH). is an enzyme directly involved in glucose metabolism. The kinetic parameters of MDH-I and its purified cytosolic isozyme, S-MDH-I, have been studied in the liver of streptozotocin-diabetic rats; also the potential of the leaf extract of *A. marmelose* as an anti-diabetic agent was investigated. The K_m of the liver enzyme increased significantly, in both crude and purified preparations in the diabetic state when compared to the respective controls. Insulin as well as leaf extract treatment of the diabetic rats brought about a reversal of K_m values to near normal. V_{max} of purified S-MDH was significantly higher in the diabetic state when compared to the control. Insulin and leaf extract treatment did not reverse this change. Since MDH is an important enzyme in glucose metabolism, the variation in its quantitative and qualitative nature may contribute to the pathological status of diabetes. The fact that leaf extract of *A. marmelose* was found to be as effective as insulin in restoration of blood glucose and body weight to normal levels, the use of *A. marmelose* as potential hypoglycemic agent is suggested.

Diabetes mellitus is a metabolic disorder associated with altered glucose metabolism as well as with the changes in protein and lipid metabolism'. Malate dehydrogenase (MDH) (EC 1.1:37) is an important enzyme in glucose metabolism. The cytosolic isozyme of MDH, S-MDH plays an important role in gluconeogenesis. In diabetes, gluconeogenesis is accelerated. Experimentally induced diabetes has been shown to cause changes in metabolic enzymes in various tissues 2- 4 Enzymes of glucose metabolism have also been studied in diabetic subjects.

Study 21

Journal of Ethnopharmacology 73 (2000)
461-470

www.elsevier.com/locate/jethpharm

Anti-hyperglycemic effect of *Eugenia jambolana* and *Tinospora cordifolia* in experimental diabetes and their effects on key metabolic enzymes involved in carbohydrate metabolism

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Received 15 December 1999; received in revised form 10 July 2000;
accepted 29 July 2000

ABSTRACT

In India, the decoction of kernels of *Eugenia jambolana* (EJ) and extracts of *Tinospora cordifolia* (TC) are used as a household remedy for diabetes. These also form constituents of many herbal formulations for diabetes that are marketed in this country. The anti-hyperglycemic effect of aqueous and alcoholic extracts as well as lyophilized powder of these two plants was evaluated in diabetic animals using different doses of diabetogenic agents for varying duration (21—120 days) so as to assess their effect in mild (plasma sugar > 180 mg/dl, duration 21 days), moderate (plasma sugar > 280 mg/dl, duration 120 days) and severe (plasma sugar > 400 mg/dl, duration 60 days) diabetes mellitus. In the pilot study (mild diabetes), maximum reduction of 73.51 and 70.37% in glucose levels was seen in animals receiving 200 mg/kg per day of lyophilized powder of EJ and 400 mg/kg per day of aqueous extract of TC after 3 and 15 weeks of treatment, respectively. There percent reduction in glucose decreased significantly in the moderate and severe diabetes; 55.62 and 17.72% for EJ and 48.81 and 0% for TC at the similar time intervals. The alteration in hepatic and skeletal muscle glycogen content and hepatic glucokinase, hexokinase, glucose-6-phosphate and phosphofructokinase levels in diabetic mice were partially restored by EJ but not by TC.

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Study 23

Indian J Physiol Pharmacol 2000; 44 (1): 69—74

A STUDY OF HYPOGLYCAMIC EFFECTS OF AZADIRACHTA INDICA (NEEM) IN NORMAL AND ALLOXAN DIABETIC RABBITS

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Departments of Pharmacology and Biochemistry, Pt. B.D. Sharma
P.G.I.M.S., Rohtak — 124 001 (Received on May 20, 1999)

ABSTRACT

Hypoglycaemic effect was observed with *Azadirachta indica* when given as a leaf extract and seed oil, in normal as well as diabetic rabbits. The effect, however, was more pronounced in diabetic animals in which administration for 4 weeks after alloxan induced diabetes, significantly reduced blood glucose levels. Hypoglycaemic effect was comparable to that of glibenclamide. Pretreatment with *A. indica* leaf extract or seed oil administration, started 2 weeks prior to alloxan, partially prevented the rise in blood glucose levels as compared to control diabetic animals. The data suggests that *A. indica* could be of benefit in diabetes mellitus in controlling the blood sugar or may also be helpful in preventing or delaying the onset of the disease.

Study 24

Diabetes Care 26:3215-3218, 2003

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Clinical Care/Education/Nutrition
Original Article

Cinnamon Improves Glucose and Lipids of People With Type 2 Diabetes

To review full text of these scientific studies please visit www.glycoprinclinicalstudies.com