



## *Costus spicatus* tea failed to improve diabetic progression in C57BLKS/J *db/db* mice, a model of type 2 diabetes mellitus

Amy C. Keller<sup>a</sup>, Ina Vandebroek<sup>b</sup>, Youping Liu<sup>c</sup>, Michael J. Balick<sup>b</sup>, Fredi Kronenberg<sup>d</sup>, Edward J. Kennelly<sup>a</sup>, Anne-Marie B. Brillantes<sup>c,\*</sup>

<sup>a</sup> Department of Biological Sciences, Lehman College and The Graduate Center, The City University of New York, Bronx, NY 10468, USA

<sup>b</sup> The New York Botanical Garden, Bronx, NY 10458, USA

<sup>c</sup> Department of Medicine, Division of Endocrinology and the Naomi Berrie Diabetes Center, Columbia University, 1150 St. Nicholas Avenue, New York, NY 10032, USA

<sup>d</sup> Rosenthal Center for Complementary and Alternative Medicine, Department of Rehabilitation Medicine, Columbia University, New York, NY 10032, USA

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### ABSTRACT

**Aim of the study:** *Costus spicatus* Sw. (Costaceae) is a prominent medicinal herb used by Dominicans in the Dominican Republic and the United States for the treatment of diabetes, a growing epidemic in the Hispanic community. An ethnobotanical survey of the Dominican community in New York City revealed the popular use of a tea from the *insulina* plant to treat hyperglycemia. *Insulina* was identified as *Costus spicatus*. We tested the ability of a tea made from the leaves of *Costus spicatus* to alter glucose homeostasis in C57BLKS/J (KS) *db/db* mice, a model of obesity-induced hyperglycemia with progressive beta cell depletion.

**Materials and methods:** From 6 to 16 weeks of age, Experimental and Control animals ( $n = 6/5$ ) were given *ad lib* access to *Costus spicatus* tea or water, respectively.

**Results:** Weight gain and progression of hyperglycemia and insulinopenia between the Experimental and Control groups were statistically indistinguishable. There was no difference between groups in average fed or fasting glucose and insulin concentrations. Intraperitoneal (IP) insulin tolerance testing after the 10-week study period showed that *Costus spicatus* tea consumption did not alter insulin sensitivity.

**Conclusions:** These data suggest that at the dose given, tea made from *Costus spicatus* leaves had no efficacy in the treatment of obesity-induced hyperglycemia. More investigation is needed to more fully explore dosages and the possible utility and biological activity of this common Dominican herbal remedy for the treatment of type 2 diabetes mellitus.

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### 1. Introduction

Diabetes is a leading cause of morbidity and mortality for a growing proportion of the world's population. The World Health Organization predicts a worldwide increase of 50% in diabetes-related deaths in the next 10 years, with a majority of deaths occurring in relatively wealthier nations (WHO, 2008).

Type 2 diabetes mellitus (T2DM) is a chronic and progressive illness that particularly targets the Hispanic population in the United States. According to the Center for Disease Control and Prevention

(CDCP) in 2005, Hispanic adults had diabetes prevalence rates 1.7 times that of non-Hispanic whites (CDCP, 2008). A recent study has shown a genetic predisposition to insulin resistance and T2DM in the Dominican Republic (Hamaguchi et al., 2004). In a recent meta-analysis, Hispanics had higher hemoglobin A<sub>1c</sub> values than non-Hispanics, indicating that glycemic control is poorer among the Hispanic population (Kirk et al., 2008). As Hispanics are the largest (12.5%) and fastest-growing minority group in the United States (Tucker et al., 2000), it is important to focus on their specific healthcare needs.

Currently available standard anti-diabetic medications have all been well-studied for their efficacies in lowering blood glucose (Inzucchi, 2002) and ultimately lowering rates of secondary complications of this disease. Nevertheless, several studies have documented the common use of traditional medicines for diabetes, such as herbal treatments, in the Hispanic immigrant population in the United States (Allen et al., 2000; Reiff et al., 2003; Hatcher and Whittemore, 2007; Johnson et al., 2006). Specifically, within

**Abbreviations:** T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; CDCP, Center for Disease Control and Prevention; IP-GIT, intraperitoneal glucose tolerance testing; IP-ITT, intraperitoneal insulin tolerance testing; ELISA, enzyme-linked immunosorbent assay; AOC, area over the curve.

\* Corresponding author. Tel.: +1 212 851 5305 fax: +1 212 851 5331.

E-mail address: [ab647@columbia.edu](mailto:ab647@columbia.edu) (A.-M.B. Brillantes).

the Dominican population, traditional medicine is often and consistently used as a source of health care (Ososki et al., 2002; Vandebroek et al., 2007). According to a study done on Dominican patients in an emergency room, 24% of those interviewed were using alternative medicine to treat their emergency room complaint (Allen et al., 2000). Also, Dominican herbal practitioners and their patients in New York City reported using conventional medicine in conjunction with traditional medicine (Reiff et al., 2003).

In the Dominican Republic, the herbal treatment called *insulina* is used as a treatment for hyperglycemia (Liogier, 2000). No research exists on its ethnobotanical importance among the Dominican community in New York City to treat diabetes. The Dominican community is the fastest growing Latino immigrant population in New York City, with a population of between 369,200 and 555,000 in 2000 (Vandebroek et al., 2007). Given the potentially wide application of *insulina* for the treatment of diabetes among the Dominican population, it is critical to define its efficacy. Therefore, the purpose of this study was to find out whether *insulina* is also known and used by Dominicans living in New York City to treat diabetes and to determine if any hypoglycemic effects can be brought about by consumption of *insulina* tea in a well-characterized mouse model of obesity-induced diabetes fed a standard chow diet. We studied the effects of 10 weeks of *insulina* tea consumption on weight gain, plasma glucose and serum insulin concentrations, and insulin sensitivity in male C57BLKSJ *db/db* mice consuming solely *insulina* tea as compared to control mice consuming water.

## 2. Methods and materials

### 2.1. Ethnobotany

As part of a larger, in-depth ethnobotanical survey that included 84 questions and addressed a variety of topics (including past and current use of medicinal plants, treatment modalities, provenance of herbal remedies, preference for using medicinal plants or pharmaceuticals, demographic information, acculturation, common health conditions and folk illnesses, harmful or toxic plants, and transmission of plant knowledge), we conducted individual interviews with 175 Dominican participants (166 laypeople who self-medicate with medicinal plants and nine plant specialists or traditional healers) about the nature of plant remedies used for 30 common health conditions, including diabetes. The City University of New York granted IRB approval for this survey (IRB #04-06-0599; PI: Dr. Michael Balick) and surveyors obtained oral informed consent from participants prior to interviewing. Convenience and snowball sampling were used to recruit participants of both sexes. We interviewed subjects in the waiting room of the Associates in Internal Medicine Clinic (Columbia University), in a community-based organization (Alianza Dominicana Inc.), at their homes, and a few interviews were also conducted at the Institute of Economic Botany of the New York Botanical Garden. Inclusion criteria were: been born in the Dominican Republic, currently living in New York City, 18 years or older, and some knowledge of medicinal plants. During the interview, which lasted between 1 and 2 h, each participant was asked whether they knew of any plants used to treat diabetes and whether they had ever been diagnosed with this disease. After affirmation, further questions were asked about the Dominican name(s) of the plant, plant part(s) used, and mode of administration. Dominican plant names recorded from the interviews were ranked according to their frequency of mention by participants. Those participants who reported information about *insulina* were subsequently contacted during a follow-up phone survey at a later date, and asked additional questions about the

exact amount of plant material needed, the amount of water, possible coadjuvants, the preparation time, and the dosage and duration of administration of this remedy. We were able to obtain in-depth information from 11 participants (55% of those who had initially mentioned *insulina* as a remedy for diabetes).

### 2.2. Ethnopharmacology

#### 2.2.1. Materials

Animal experimentation utilized a glucometer (Bayer), glucometer strips (Bayer), a mouse insulin ELISA kit (ALPCO), glucose (Sigma) and insulin solutions (Humulin R, Eli Lilly). Tea was filtered with 0.45  $\mu\text{m}$  nylon filter syringes (Phenomenex), and thin-layer chromatography used silica plates (Merck), vanillin (Sigma), sulfuric acid (Sigma), ethanol (J.T. Baker), and G.R. grade chloroform and methanol (J.T. Baker).

#### 2.2.2. Plant material

Dried plant material from *insulina*, (voucher AK004), was purchased at a *botánica*, a common source of traditional Dominican herbs, as well as other items of religious or healing value, in the Washington Heights neighborhood of Manhattan, New York. The botanical identity of this plant material was determined to be *Costus spicatus* Sw. (Costaceae) by Drs. Ina Vandebroek and Tom Zanoni at the New York Botanical Garden

A tea of *Costus spicatus* leaves was prepared according to a consensus of dosage and administration reported by Dominicans who self-medicate with this medicinal plant, and specifications given by the *botánica* staff. This preparation consisted of soaking for 10 min and boiling for 5 min an average of 17.31 g of the dried leaves in 1.890 L of distilled, deionized water. The resulting water extract was strained and stored at 4 °C for no longer than 48 h. An aliquot of 5–10 ml of tea was re-filtered through a 0.45  $\mu\text{m}$  nylon syringe filter and dried. Thin-layer chromatography was used to assess the tea's phytochemical profile. After resuspending the dried tea in 60% methanol, 20  $\mu\text{L}$  was added to normal phase silica plates and developed with a solvent system of chloroform and methanol (7:3). Plates were then sprayed with a 1% vanillin solution in sulfuric acid and methanol (1:9), and observed under ultra-violet light.

Four weeks into the study, the tea was concentrated two-fold, and 9 weeks into the study, the tea was concentrated four-fold. The average weight/weight yields were 6.92% for the initial tea concentration, and 7.16%, and 5.73% for the two and four-fold tea concentrations, respectively.

### 2.3. Methods

#### 2.3.1. Animal studies

All animal studies were approved by the Institutional Animal Care and Use Committee at Columbia University Medical Center (#AC-AAAA7756). The C57BLKS/J mice (KS), when made genetically obese via a complete knock-out of the leptin receptor via the *db* mutation, develop severe insulin resistance and progressive insulinopenia (diminishing levels of circulating insulin) resulting in severe hyperglycemia and ultimate premature death due to insulin deficiency (Kodama et al., 1994). In the context of the KS genetic background, hyperglycemia worsens with age secondary to severe obesity-induced insulin resistance and progressive insulinopenia (Leiter, 1997). This particular inbred strain was chosen so that any potential effects of *insulina* tea on either insulin resistance or preservation of beta cell insulin secretion could be detected

A power analysis was conducted to determine the adequate number of animals to use for our studies. Previously published results characterizing the long term treatment (6 weeks) of hyperglycemic mice using a standard oral hypoglycemic agent for the

**Table 1**  
Metabolic data at baseline and 10 weeks. The animals' weight and fed and fasting glucose and serum insulin concentrations were measured at baseline and at 10 weeks. In addition, the HOMA-IR model was used to assess insulin resistance. Experimental and Control groups had significant differences between fasting glucose concentrations, fasting insulin concentrations, and the HOMA-IR values at baseline and 10 weeks (\* $p < 0.05$ , Student's  $t$ -test, two-tailed). Data are presented as mean + standard deviation.

Metabolic parameter	Baseline		10 weeks	
	Tea	Water	Tea	Water
Body weight (g)	25.85 ± 1.94	26.53 ± 2.17	42.10 ± 4.64	41.10 ± 5.63
Fasting glucose (mg/dl)	168 ± 55	171 ± 87	353 ± 126*	339 ± 143*
Fasting serum insulin (ng/ml)	14.4232 ± 6.1799	13.9132 ± 7.3697	4.7743 ± 1.5597*	4.8770 ± 3.0978*
Fed glucose (mg/dl)	241 ± 103	302 ± 147	585 ± 36	559 ± 77
Fed serum insulin (ng/ml)	9.9020 ± 4.7268	9.9928 ± 4.4549	5.0332 ± 2.3356	5.0073 ± 1.7152
HOMA-IR	187 ± 36	175 ± 96	132 ± 36*	140 ± 173

treatment of T2DM, the sulfonylurea, glipizide, showed a ~40% reduction in mean plasma glucose concentrations (Mutalik and Udupa, 2006). For our studies, we used a more conservative goal of achieving a 15% reduction in plasma glucose concentrations in the treatment group in determining adequate sample size. Therefore, assuming mean plasma glucose concentrations of 585 mg/dl with a standard deviation (SD) of 75 mg/dl (mean and SD of control obese animals at ~4 months of age in this study), a sample size of  $n = 4$  for both treated and untreated groups would be adequate to see a statistically significant difference with treatment. We used a sample size of  $n = 6$  for both groups, which should have been adequate to test for moderate effects of the *insulina* tea.

*Insulina* tea or distilled water was administered *ad lib* to 6-week-old male obese KS *db/db* mice. The Experimental (tea) and Control (water) groups consisted of six animals each. The Control group received only water and the Experimental group received only tea throughout the study. At the start of the treatment protocol, Experimental and Control group mice were 5 weeks of age and were metabolically matched at baseline for weight, fed, and fasting glucose concentrations, and fed and fasting serum insulin concentrations using blood collected via tail vein (Table 1). In addition, both groups were matched for relative insulin resistance as estimated by HOMA-IR values, a model used to assess insulin resistance using fasting insulin levels (Wallace et al., 2004) (Table 1).

After baseline measurements of weight, glucose, serum insulin, and insulin tolerance were determined, the mice in the Experimental group were given *ad lib* access solely to *Costus spicatus* tea, which was placed in their water bottles. Similarly, mice in the Control Group were allowed *ad lib* access to water. Throughout the study period, both Experimental and Control animals gained weight at similar rates achieving maximum body weights of ~40 g by 15 weeks of age (Fig. 1A).

All animals were analyzed 1 week pre-treatment, 2, 4, 6, 8, 10 weeks and 1–2 weeks post-treatment. Prior to the start of the 10-week protocol, fasting serum insulin and plasma glucose concentrations were determined on all animals, which were then subjected to intraperitoneal glucose tolerance testing (IP-GTT). Fed plasma glucose and serum insulin concentrations were determined pre-treatment and at 2-week intervals. At the conclusion of the study, IP-GTT and IP-ITT were performed.

### 2.3.2. IP-GTT

Animals were fasted overnight for 12–14 h. Fasting serum insulin and plasma glucose concentrations were determined prior to intraperitoneal injection of 1 mg glucose/gm body weight with sterile 10% glucose. Glucose concentrations were determined at 15, 30, 60, 90, and 120 min post-injection. Serum insulin concentrations were determined at 15 min post-injection.

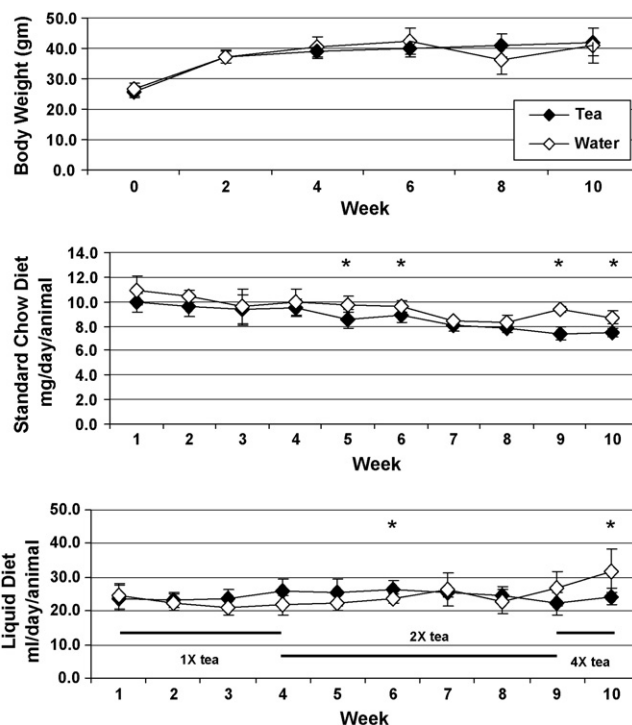
### 2.3.3. Intraperitoneal insulin tolerance testing (IP-ITT)

To determine whether *insulina* tea consumption altered insulin resistance levels between Experimental and Control groups, we

performed IP-ITTs at the conclusion of the 10-week study protocol. Due to the severity of the insulin resistance within these mice, an insulin dose of 8 units/g body weight was administered to achieve adequate glucose lowering. All animals were fasted for 4 h prior to determination of baseline plasma glucose and serum insulin concentrations. Glucose concentrations were determined at 15, 30, 60, 90, and 120 min post-injection.

### 2.3.4. Statistics

Student's  $t$ -test (two-tailed) with a  $p < 0.05$  was used to determine statistical significance.



**Fig. 1.** Body weight, food and liquid consumption of Experimental (tea) and Control (water) mice during the 10-week study protocol: (A) Experimental (tea) and Control (water) mice were weighed at 2-week intervals. Mean body weights of the two groups were not significantly different. Data are presented as mean ± standard deviation. (B) Consumption of standard chow was measured daily per cage, which housed three animals. Data reported here are mean daily consumption per mouse measured over the entire week. Control mice appeared to have slightly greater food consumption over Experimental mice. Significant differences in the consumption between Experimental (tea) and Control (water) mice were seen at weeks 5, 6, 9, and 10 (\* $p < 0.05$ , Student's  $t$ -test, two-tailed). (C) Liquid consumption per cage was measured weekly for the duration of the study. Data are presented as the average volume of liquid consumed per mouse per day. Significant differences in the consumption between Experimental (tea) and Control (water) mice were seen at weeks 6 and 10 (\* $p < 0.05$ , Student's  $t$ -test, two-tailed).

**Table 2**Variations of *insulina* usage. Preparation, dosage, and administration of *insulina* were found to vary among traditional Dominican medicine users and practitioners interviewed.

Participant code	Sex	Amount of plant	Amount of water	Coadjuvants	Preparation time	Dosage	Duration of administration
C-2005-005	M	3–4 leaves (for beginning diabetes); 7–8 leaves (one pound per week)	3 L	cun de amor ( <i>Momordica charantia</i> )	Boil until 1 L is left	Twice a day	Until sugar level is normalized, from then on take only once a day
C-2005-008	M	2–3 leaves	2 cups	–	4 min (do not boil too long because the effect will be lost)	Twice a day	Until blood sugar is under control
C-2006-006	F	4–5 leaves	16 oz	–	Boil until half the amount of water is left	Twice a day	–
G-2005-025	F	1 leaf	1 cup (more or less)	–	5 min	Once a day	Forever
G-2005-050	F	2–3 leaves	1 regular coffee cup	–	Boil for 1 min, turn off fire, cover cup and soak or another 2–3 min	Once–three times a day	15 days – 1 month
G-2005-054	F	10 leaves	2–3 cups	–	Boil until the amount for 1 cup is left	Everytime when thirsty	Depends on sugar level
G-2005-060	F	1 leaf	1 cup	–	Boil water, add leaf, cover cup (infusion, do not boil anymore when leaf is in the water)	Twice a day	Take to control diabetes, when it works keep taking it
G-2005-096	F	2 leaves	2 cups	Cinnamon	10 min	Twice a day	6 months (she now takes pills)
G-2005-110	F	4 leaves	6 cups	–	Boil until the amount of 4 cups is left	Once a day	3 months
G-2005-117	F	10 leaves	2 L	–	Boil until 1 L is left	When thirsty (put in fridge and drink)	
G-2005-129	F	5–6 leaves	8 oz	–	10 min	Once–twice a day	15 years

### 3. Results

#### 3.1. *Insulina* was the second most frequently reported plant to treat diabetes in our survey among 175 Dominicans in New York City

One hundred and twenty-nine participants in the survey (74% of subjects) reported knowing about or using at least one remedy for diabetes. One in four participants (25% of subjects) declared that they had been diagnosed with diabetes, a percentage that is double the New York City average. In total, 90 plants were reported for diabetes and 33 plants were mentioned by at least three participants. A tea of *insulina* was the second most frequently reported plant remedy for either Type 1 (T1DM) or T2DM. The highest ranking plant species in the survey for the treatment of diabetes was *sábila*, *Aloe vera* (L.) Burm. F., (Aloaceae), followed by *insulina* (*Costus* spp., Costaceae), *naranja agria* (bitter orange, *Citrus aurantium* L., Rutaceae), *cundeamor* (*Momordica charantia* L., Cucurbitaceae), *pepino* (cucumber, *Cucumis sativus* L., Cucurbitaceae), and *noni* (*Morinda citrifolia* L., Rubiaceae). The number of people who reported these remedies was 23, 20, 13, 12, 12, and 10, respectively.

Detailed data on the preparation, amount used, and administration regime of *insulina* according to 11 Dominican participants who used this plant in New York City to treat their diabetes is shown in Table 2. The table shows that the amount of plant material and water used, as well as the preparation time, are highly variable. For example, variations in the amount of boiling time for the tea range from 1 to 10 min, with some preparations simply calling for a general decoction. Also variable is the dosage, varying from administration once or twice per day, to anytime thirst occurs (Table 2). In the Dominican Republic, the traditional preparation of *insulina* tea may also involve the use of fresh plant material, as plants used in traditional medicine are typically locally grown and available.

#### 3.2. Continuous consumption of increasingly concentrated *insulina* tea did not improve diabetes progression in obese C57BLKS/J (KS) animals

Although a significant difference was observed between the Experimental group's HOMA-IR values at baseline and 10 weeks ( $187 \pm 36$  vs.  $132 \pm 36$ ,  $p < 0.05$ , Table 1), no significant differences existed between parallel values of the Control group, or between the values of the Experimental and Control groups.

Obese animals consuming regular chow and water (Control group) for 10 weeks progressed from a baseline mean fasting glucose of  $171 \pm 87$  mg/dl to fasting glucose concentrations of  $339 \pm 143$  mg/dl ( $p < 0.05$ ) (Table 1). This significant worsening of their hyperglycemia was reflected in their baseline and 10-week fed glucose concentrations as well. In a similar group of animals consuming *insulina* tea for 10 weeks, a statistically identical picture of glucose homeostasis developed.

In addition, both Experimental and Control groups had comparable concentrations of serum insulin at baseline and after 10 weeks (Table 1). Therefore, *insulina* tea did not appear to improve beta cell function.

In order to control for variables that may impact glucose homeostasis, we followed progression of weight gain, and food and liquid intake for both animal groups. Both groups gained similar amounts of weight during the study protocol (Fig. 1A). Interestingly, there was a consistent trend of slightly decreased food consumption in the Experimental group as compared to the Control group, which became statistically significant in week 5 ( $8.60 \pm 0.75$  mg/day/animal vs.  $9.77 \pm 0.67$  mg/day/animal, respectively), week 6 ( $8.89 \pm 0.58$  mg/day/animal vs.  $9.62 \pm 0.48$  mg/day/animal, respec-

tively), week 9 ( $7.39 \pm 0.52$  mg/day/animal vs.  $9.35 \pm 0.23$  mg/day/animal, respectively), and week 10 ( $7.48 \pm 0.34$  mg/day/animal vs.  $8.69 \pm 0.52$  mg/day/animal, respectively), ( $p < 0.05$ , Fig. 1B). There was a corresponding trend towards decreased total liquid consumption in the Experimental group versus the Control group with significant differences at week 6 ( $26.4 \pm 2.7$  ml/day/animal vs.  $23.6 \pm 1.1$  ml/day/animal) and week 10 ( $24.3 \pm 2.4$  vs.  $31.9 \pm 6.5$  ml/day/animal, respectively), ( $p < 0.05$ , Fig. 1C). This decreased consumption of food and liquid in the Experimental group may reflect decreasing palatability of the more concentrated tea mixture, which was reflected as a relative decrease in appetite. Nevertheless, these differences in food and liquid consumption did not significantly alter weight gain between the two groups.

We also followed weekly glucose and serum insulin concentrations to determine whether a similar pattern of the progression of hyperglycemia and hypoinsulinemia developed between the two groups. From baseline to 10 weeks of the study protocol, worsening levels of hyperglycemia progressed in parallel between Experimental and Control groups. Mean glucose concentrations of the Experimental and Control groups ranged from  $241 \pm 103$  to  $302 \pm 147$  mg/dl, respectively, at the start of the protocol, and progressively increased to mean glucose concentrations of  $585 \pm 36$  and  $559 \pm 77$  mg/dl, respectively (Table 1). There was a significant difference between fasting glucose levels when measured at baseline and 10 weeks, for both the Experimental group ( $p = 0.008$ ), and the Control group ( $p = 0.04$ ).

Consistent with their hyperglycemia, serum insulin concentrations were relatively elevated at 5 weeks of age in both Experimental ( $9.9020 \pm 4.7268$  ng/ml) and Control ( $9.9928 \pm 4.4549$  ng/ml) groups, and progressively declined throughout the 10-week study protocol (Table 1). This progressive decrease in serum insulin concentrations in the face of worsening hyperglycemia reflects the decline in total beta cell mass typically seen in obese KS animals (Leiter, 1997). Serum insulin concentrations were not significantly different between the two groups at 0, 2, 4, 6, 8, and 10 weeks. Additionally, both Experimental and Control groups' fasting serum insulin levels were significantly decreased at 10 weeks, as compared to baseline ( $p = 0.04$  and  $p = 0.03$ , respectively, Table 1).

#### 3.3. *Insulina* tea failed to improve insulin sensitivity in obese KS mice

No differences in glucose concentrations were found at any time point after insulin administration up to 120 min. In addition, total area over the curve (AOC) analysis, which integrates total glucose dispersal over the 2-h study period, shows no significant difference between the two study groups. These data show that *Costus spicatus* tea treatment did not improve insulin sensitivity in these obese mice.

Although glucose tolerance tests were performed on all Experimental and Control mice at the conclusion of the 10-week protocol, extremely elevated fasting glucose concentrations with relatively low serum insulin concentrations at baseline suggested ongoing maximal insulin secretion by the remaining functional beta cells. This was confirmed by post-challenge glucose concentrations which were beyond the range of the glucometer device, and therefore immeasurable. Nevertheless, average fasting glucose and serum insulin concentrations were not different between Experimental and Control groups, suggesting that no measurable beneficial effect on insulin secretion or beta cell function was derived from *Costus spicatus* tea consumption.

Our results showed no improvement in glucose homeostasis in the Experimental group as compared to the Control group. At weekly intervals, there were no differences in average glucose or serum insulin concentrations. At the conclusion of 10 weeks of

drinking *Costus spicatus* tea, the Experimental group was as hyperglycemic as the Control group, with similarly decreased serum insulin concentrations suggesting matched degrees of beta cell failure and loss. In addition, the Experimental group showed no measurable improvement in insulin resistance as shown by insulin tolerance testing and AOC analysis.

#### 4. Discussion

In the obese C57BLKS/J *db/db* mouse model, *Costus spicatus* tea was not effective in improving hyperglycemia or alleviating the severe insulin resistance that develops with obesity.

One challenge in this study was the determination of what should be the optimal *Costus spicatus* tea concentration. Therefore, we chose to start with a baseline dose, guided by local users and vendors of the plant, and concentrated the dose by two-fold and four-fold during the course of the study. This was an attempt to maximize our ability to detect any beneficial effects of the tea within the animal model. Nevertheless, despite utilizing a four-fold concentrated tea during the last 2 weeks of the study protocol, no improvements in glucose or insulin concentrations were seen.

Another potential explanation as to why our studies showed no hypoglycemic activity of the tea may be due to the severity of the insulin resistance associated with this particular animal model. Secondary to the hyperphagia and metabolic effects of disrupting leptin receptor signaling, C57BLKS/J *db/db* mice develop a rapid, and severe obesity-induced insulin resistance (Leiter, 1997). If the anti-hyperglycemic activity of the *Costus spicatus* tea is low, likely no effect would be observed in the severely diabetic animals used in this study.

Although we failed to find other published studies about the hypoglycemic activity of *Costus spicatus*, other species of the genus *Costus* have been shown to demonstrate hypoglycemic activity. An extract of *Costus speciosus* Sm. lowered blood glucose concentrations of streptozotocin-induced hyperglycemic rats (Guzman and Guerrero, 2002). Additionally, a methanol extract of *Costus pictus* D. Don ex Lindl. lowered blood glucose concentrations and increased plasma insulin concentrations in alloxan-induced diabetic rats (Jothivel et al., 2007). A methanol extract of dried *Costus afer* Ker Gawl. also reduced blood glucose concentrations in streptozotocin-induced hyperglycemic rats and stimulated glucose transport in adipocyte cells, suggesting an ability to improve glucose uptake *in vivo* (Anaga et al., 2004).

#### 5. Conclusions

To our knowledge, this is the first animal study of the utility of *Costus spicatus* tea, known by Dominicans in New York City as *insulina*, and commonly used for the treatment of diabetes. Our study in a mouse model of obesity-induced hyperglycemia provides no data to suggest that *Costus spicatus* tea can benefit the treatment of obesity-induced diabetes, the most common form of T2DM. Based on these results, tea of the leaves of *Costus spicatus* should not be recommended as an alternative to standard oral hypoglycemics. Investigations of this sort are critical in light of the many known and unknown herb-drug interactions for common ailments (Fugh-Berman, 2000). Given that Dominican patients have been found to use herbal medicine in conjunction with or instead of conventional treatments (Reiff et al., 2003; Johnson et al., 2006), it is crucial that the botanical identity and efficacy of the herbal treatments be further investigated. Examining potential herb-drug interactions for a widespread and serious disease such as diabetes should be a research priority, given the high prevalence of the disease and herb use in ethnic populations.

Also, based on the prevalence of use of herbal treatments, it is important to understand cultural differences that may impact or influence diabetic patients' perspectives on health care. For example, Hispanic diabetic patients told investigators that they believed that herbal remedies were effective in treating diabetes, and that they wanted their conventional health practitioners to know more about herbal treatments (Poss et al., 2003).

Due to its current, common use in some communities for treating diabetes, it is important to further study *insulina* and its potential utility in the management of hyperglycemia. The effects of tea made from different plant parts, including rhizomes, of *Costus spicatus* and other *Costus* species in the present animal model of obesity-induced diabetes and other diabetes models (T1DM) also deserves further study. Thus, additional study is necessary in order to definitively assess the antidiabetic activity of *insulina*.

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#### References

- Allen, R., Cushman, L.F., Morris, S., Feldman, J., Wade, C., McMahon, D., Moses, M., Kronenberg, F., 2000. Use of complementary and alternative medicine among Dominican emergency department patients. *American Journal of Emergency Medicine* 18, 51–54.
- Anaga, A.O., Njoku, C.J., Ekejiuba, E.S., Esiaka, M.N., Asuzu, I.U., 2004. Investigations of the methanolic leaf extract of *Costus afer* Ker for pharmacological activities *in vitro* and *in vivo*. *Phytomedicine* 11, 242–248.
- Centers for Disease Control and Prevention. Data and trends, [www.cdc.gov](http://www.cdc.gov) (March, 2008).
- Fugh-Berman, A., 2000. Herb-drug interactions. *The Lancet* 355, 134–138.
- Guzman, A.L., Guerrero, R.O., 2002. Efecto hipoglicémico de *Costus speciosus* (Zingiberaceae), en ratas. *Vitea, Revista de la Facultad de Química Farmacéutica* 9, 51–57.
- Hamaguchi, K., Terao, H., Kusuda, Y., Yamashita, T., Bahles, J.A.H., Cruz, M.L.L., Brugal, L.I.V., Jongchong, B.W., Yoshimatsu, H., Sakata, T., 2004. The pc-1 q121 allele is exceptionally prevalent in the Dominican Republic and is associated with type 2 diabetes. *The Journal of Clinical Endocrinology & Metabolism* 89, 1359–1364.
- Hatcher, E., Whittemore, R., 2007. Hispanic adults' beliefs about type 2 diabetes: clinical implications. *Journal of American Academy of Nurse Practitioners* 19, 536–545.
- Inzucchi, S.E., 2002. Oral antihyperglycemic therapy for type 2 diabetes. *Journal of American Medical Association* 287, 360–372.
- Johnson, L., Strich, H., Taylor, A., Timmermann, B., Malone, D., Teufel-Shone, N., Drummond, R., Woosley, R., Pereira, E., Martinez, A., 2006. Use of herbal remedies by diabetic Hispanic women in the southwestern United States. *Phytotherapy Research* 20, 250–255.
- Jothivel, N., Ponnusamy, S.P., Appachi, M., Singaravel, S., Rasilingam, D., Deivasigamani, K., Thangavel, S., 2007. Anti-diabetic activity of methanol leaf extract of *Costus pictus* d. Don in alloxan-induced diabetic rats. *Journal of Health Science* 53, 655–663.
- Kirk, J.K., Passmore, L.V., Bell, R.A., Narayan, K.M.V., D'Agostino, R.B., Arcury, T.A., Quandt, S.A., 2008. Disparities in a1c levels between Hispanic and non-Hispanic white adults with diabetes. *Diabetes Care* 31, 240–246.
- Kodama, H., Fujita, M., Yamaguchi, I., 1994. Development of hyperglycemia and insulin resistance in conscious genetically diabetic (c57bl/ksj-db/db) mice. *Diabetologia* 37, 739–744.
- Leiter, E.H., 1997. Carboxypeptidase e and obesity in the mouse. *Journal of Endocrinology* 155, 211–214.
- Liogier, H.A., 2000. *Diccionario Botánico, Segunda Edición*. Jardín Botánico Nacional Dr. Rafael Ma. Moscoso, Santo Domingo, República Dominicana.
- Mutalik, S., Udupa, N., 2006. Pharmacological evaluation of membrane-moderated transdermal system of glipizide. *Clinical and Experimental Pharmacology and Physiology* 33, 17–26.

- Ososki, A.L., Lohr, P., Reiff, M., Balick, M.J., Kronenberg, F., Fugh-Berman, A., O'Connor, B., 2002. Ethnobotanical literature survey of medicinal plants in the Dominican Republic used for women's health conditions. *Journal of Ethnopharmacology* 79, 285–298.
- Poss, J.E., Jezewski, M.A., Stuart, A.G., 2003. Home remedies for type 2 diabetes used by Mexican Americans in El Paso, Texas. *Clinical Nursing Research* 12, 304–323.
- Reiff, M., O'Connor, B., Kronenberg, F., Balick, M., Lohr, P., Roble, M., Fugh-Berman, A., Johnson, K.D., 2003. Ethnomedicine in the urban environment: Dominican healers in New York City. *Human Organization* 62, 12–26.
- Tucker, K.L., Bermudez, O.I., Gastaneda, G., 2000. Type 2 diabetes is prevalent and poorly controlled among Hispanic elders of Caribbean origin. *American Journal of Public Health* 90, 1288.
- Vandebroek, I., Balick, M.J., Yukes, J., Duran, L., Kronenberg, F., Wade, C., Ososki, A., Cushman, L., Lantigua, R., Mejia, M., Robineau, L., 2007. Use of medicinal plants by Dominican immigrants in New York City for treatment of common health problems: a comparative analysis with literature data from the Dominican Republic. In: Pieroni, A., Vandebroek, I. (Eds.), *Traveling Cultures and Plants: The Ethnobiology and Ethnopharmacology of Human Migrations*. Berghahn Books, New York, pp. 39–63.
- Wallace, T.M., Levy, J.C., Matthews, D.R., 2004. Use and abuse of homa modeling. *Diabetes Care* 27, 1487–1495.
- World Health Organization. Diabetes, <http://www.who.int/mediacentre/factsheets/fs312/en/index.html> (January, 2008).