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ORIGINAL ARTICLE

## Herbal tea in the treatment of diabetes mellitus

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**Edmond A. Ryan, MD**  
**Sharleen Imes, MSc**  
**Clarissa Wallace, MD**  
**Sherman Jones**

Dr. Ryan and Ms. Imes are with the Department of Medicine, University of Alberta, Edmonton, Alta. Dr. Wallace is currently with the Department of Medicine, Royal Columbian Hospital, New Westminster, BC. Mr. Jones is deceased. He was with the Alexis band, Alberta

Medical subject headings: alternative medicine; beverages; diabetes mellitus, non-insulin-dependent; fructosamine; hemoglobin A; medicine, herbal; medicine, traditional; metformin

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### Abstract

**Objective:** To evaluate the effects of a native herbal tea in patients with type 2 diabetes.

**Design:** Randomized, placebo-controlled, single-blind study.

**Setting:** The Metabolic Centre at the University of Alberta Hospitals.

**Subjects:** Forty volunteers with type 2 diabetes.

**Interventions:** After a 1 month "run-in" period, subjects drank 250 mL/d of either the herbal tea or a placebo tea for 10 days, and were followed up for a further 4 weeks.

**Outcome measures:** A responder analysis defined as a 10% change in mean blood glucose levels based on 4 capillary glucose readings daily. Secondary end points included changes in HbA<sub>1c</sub>, fructosamine and response to a meal challenge using Ensure.

**Results:** The responder analysis showed no benefit from the herbal tea. Fructosamine levels before and after tea therapy decreased significantly in both study groups. Mean HbA<sub>1c</sub> levels and incremental areas under the glucose curve (AUC) in the meal challenge did not change in either study group. These data were reanalysed in hyperglycemic subjects with HbA<sub>1c</sub> levels greater than 120% of normal. The responder analysis and HbA<sub>1c</sub> levels did not change in either group. Mean (and standard deviation) fructosamine levels, before and after tea therapy, were significantly lower in the herbal tea group than in the placebo tea group (361 [98] versus 338 [100]  $\mu\text{mol/L}$ ,  $p < 0.01$  compared with 338 [60] versus 323 [49]  $\mu\text{mol/L}$ ,  $p = 0.08$ ). In the hyperglycemic subgroup the mean AUC during the meal challenge, before versus after tea therapy, was 776 (369) versus 639 (331)

mmol/L ( $p = 0.22$ ) in the herbal tea group and 433 (125) versus 420 (173) mmol/L ( $p = 0.90$ ) in the placebo group.

**Conclusions:** Although the responder analysis failed to show an effect of the herbal tea, the data suggest there may be a short-term benefit from the tea in subjects with poor glycemic control.

### Résumé

**Objectif :** Évaluer les effets d'une tisane naturelle chez des patients atteints d'un diabète de type 2.

**Conception :** Étude randomisée à simple insu avec placebo.

**Contexte :** Centre métabolique aux hôpitaux de l'Université de l'Alberta.

**Sujets :** Quarante volontaires atteints d'un diabète de type 2.

**Interventions :** Après une période de «rodage» d'un mois, les sujets ont ingéré 250 mL/j de la tisane ou d'un placebo pendant dix jours puis ont fait l'objet d'un suivi pendant quatre semaines.

**Mesures de résultats :** Analyse de la réponse au traitement, définie comme étant un changement de 10 % des taux moyens de glucose sériques, à partir de quatre lectures capillaires par jour. Mesure des résultats secondaires à la fin du traitement, y compris variation des taux d'HbA<sub>1c</sub> et de fructosamine et réaction à une provocation par ingestion d'Ensure.

**Résultats :** L'analyse de la réponse au traitement a révélé que la tisane n'avait eu aucun effet bénéfique. Dans les deux groupes de l'étude, les niveaux de fructosamine avant et après la thérapie à la tisane ont diminué de façon

marquée. Les niveaux moyens d'HbA<sub>1c</sub> et les surfaces d'augmentation sous la courbe (SSC) du taux de glucose dans le nouveau régime n'ont pas varié chez l'un ou l'autre groupe. On a analysé à nouveau ces données chez des sujets hyperglycémiques dont le niveau de HbA<sub>1c</sub> était supérieur de 120 % à la normale. L'analyse des répondeurs et les niveaux de HbA<sub>1c</sub> n'ont pas changé dans l'un ou l'autre groupe. Les niveaux moyens (et l'écart type) de fructosamine, avant et après la thérapie à la tisane, étaient significativement moins élevés dans le groupe ayant ingéré la tisane que chez le groupe placebo (361 [98] contre 338 [100] µmol/L,  $p < 0,01$  compara-

tivement à 338 [60] contre 323 [49] µmol/L,  $p = 0,08$ ). Dans le sous-groupe hyperglycémique, la SSC moyenne pendant le régime, avant et après la thérapie à la tisane, s'est établie à 776 (369) contre 639 (331) mmol/L ( $p = 0,22$ ) dans le groupe ayant consommé la tisane, et à 433 (125) contre 420 (173) mmol/L ( $p = 0,90$ ) dans le groupe placebo.

**Conclusions :** Même si l'analyse de la réponse n'a révélé aucun effet attribuable à la tisane, les données laissent croire que l'ingestion de tisane chez des sujets qui contrôlent mal leur glycémie peut leur être bénéfique à court terme.

## Introduction

Approximately 1.3 million or 5% of Canadians have type 2 diabetes mellitus.<sup>1</sup> The care of diabetes and its associated complications, such as cardiovascular disease, translate into a major financial burden for federal and provincial health care services. Native communities across Canada are experiencing a surge in the prevalence of type 2 diabetes, with age-adjusted rates ranging from 9% to 26%.<sup>2-5</sup> Type 2 diabetes is being diagnosed in Aboriginal children as young as 7 years,<sup>4,6</sup> and native people of all ages appear to be at disproportionate risk for the serious complications of diabetes.<sup>7</sup> Native healing practice traditionally includes the use of plant remedies, and Aboriginal people in Canada and the United States have accumulated an enormous store of valuable information about the medicinal properties of the continental flora.<sup>8-12</sup>

Herbal remedies are becoming increasingly popular with the public as they are perceived as being beneficial, free of side effects and complementary to Western medicines. This growing interest in alternative therapies is stimulating research into traditional practices, and focusing attention on the need for outcome studies and quality-control standards in the rapidly expanding herbal-drug industry.<sup>13</sup> In view of the challenge that health care issues in the native population present, there is an urgent need for scientifically valid but culturally sensitive interventions and treatments for this high-risk group.<sup>14</sup>

Anative Sioux healer (S.J.) from the Alexis band in Alberta has been treating diabetes mellitus in his community with a tea made from 2 locally grown plants. The objective of this study was to investigate

the safety and hypoglycemic effects of this herbal tea in patients with type 2 diabetes in a placebo-controlled, single-blind study design.

## Methods

### Subjects

Forty non-native volunteers with type 2 diabetes mellitus entered the study. There were 10 men and 10 women in each of the herbal tea and placebo tea groups. There was no significant difference in HbA<sub>1c</sub> levels, age or duration of disease between the 2 groups (Table 1). The number of subjects who controlled their diabetes with diet only, oral hypoglycemic agents or insulin was similar in the 2 study groups (Table 1).

Table 1: Subject characteristics at study entry

Characteristic	Herbal tea, n = 20	Placebo tea, n = 20
HbA <sub>1c</sub> , %	7.9 (2.0)	8.3 (1.8)
Age, yr	58.6 (10.6)	58.4 (7.0)
Duration of disease, yr	10.0 (6.9)	9.0 (6.3)
Body mass index	30.4 (7.1)	33.1 (8.3)
Diabetes control regimen, no. of subjects		
Diet only	2	1
Oral hypoglycemic agents	9	7
Insulin	8	10
Insulin and oral hypoglycemic agents	1	2

Data for HbA<sub>1c</sub>, age, duration of disease and body mass index are means and standard deviations. None of the differences were significant.

### Study protocol

The study was approved by the Research Ethics Committee of the University of Alberta, and the study subjects provided written informed consent. The study began with a 4-week "run-in" period during which subjects tested and recorded their capillary blood glucose levels 4 times daily using home glucose monitors. Those on diet alone or oral hypoglycemic agents tested themselves before breakfast and 2 hours after each major meal, those on insulin tested before meals and at bedtime. Blood-testing strips were provided to all enrolled subjects. The subjects were then randomly allocated to either the herbal tea group or the placebo tea group in a single-blind design.

The herbal tea was prepared using 2 locally grown plants (*Populus tremuloides*, trembling aspen, and *Heracleum lanatum*, cow parsnip) harvested by the native healer. The plants were placed in a steam kettle with water and heated with stirring for 1 hour. The placebo tea was made by brewing a combination of Chinese green tea, mint and fennel seeds. The subjects were instructed to drink one-quarter cup of the tea, diluted with hot water to make a cup of beverage, with each meal and an evening snack. The tea-drinking phase of the study lasted for 10 days.

The subjects completed a 2-hour meal tolerance test at home both immediately before the tea-drinking period and again at the end of this 10-day period. For this, the subjects tested their capillary blood sugar levels in the fasting state and then at 1 hour and 2 hours after consuming 375 mL of Ensure, a liquid meal replacement (Abbott Laboratories, St-Laurent, Que.).

At the beginning of the run-in period, screening blood samples were drawn for complete blood count, platelet count, determination of liver enzymes, and measurement of creatinine, total protein and total bilirubin, HbA<sub>1c</sub> and fructosamine levels. Just before starting the tea, HbA<sub>1c</sub> and fructosamine levels were remeasured. After the 10 days of tea drinking, the screening blood tests and fructosamine tests were repeated. After 4 weeks of follow-up, the HbA<sub>1c</sub> determination was repeated.

Subjects continued to test their blood glucose levels throughout the 10-day tea drinking period and during the 4 weeks of follow-up. No adjustments

were made to the therapeutic regimen of the study subjects unless symptomatic hypoglycemia occurred or a capillary glucose reading of less than 3.5 mmol /L was observed without other explanation.

### Analytical methods

Complete blood count and platelets were measured using the Coulter STKS instrument (Coulter, Hialeah, Fla.). Alkaline phosphatase, alanine transaminase, serum creatinine, total protein, total bilirubin and HbA<sub>1c</sub> levels were assayed with the Hitachi 917 chemistry analyser (Boehringer Mannheim, Indianapolis, Ind.). Fructosamine values were measured using the colourimetric method on a Hitachi 717 chemistry analyser (Boehringer Mannheim). Capillary glucose levels were measured by the subjects using a variety of home glucose monitors including One Touch (LifeScan Ltd., Burnaby, BC), Glucometer Elite (Bayer Inc., Etobicoke, Ont.), Advantage (Boehringer Mannheim) and Precision QID and Companion II (Medisense, Bedford, Mass.).

A 2-way paired *t*-test was used to compare blood results from the 2-week interval before the tea was used with the tea-drinking period. Data are presented as the mean (and standard deviation). A probability value of less than 0.05 was considered significant. The analysis was conducted by an investigator blinded to the treatment groups. The primary end point for analysis was a responder analysis, defined as a 10% change in the mean blood glucose levels based on 4 capillary glucose readings daily. Secondary end points included change in HbA<sub>1c</sub> and fructosamine levels and the response to the meal challenge using Ensure.

Data from 4 subjects (all in the herbal tea group) was excluded from primary end-point analysis by the blinded investigator. One patient had a urinary tract infection, a second changed the dose of glyburide during the tea-drinking period, a third had very labile glucose levels and a fourth changed the dose of diuretic during the study. For analysis of the meal challenge, data from the 2 latter subjects were included; in the third subject with labile glucose levels, the capillary glucose level was stable for 2 days before the tests, and in the fourth subject the diuretic dose was unchanged for these 2 tests.

## Results

Screening blood chemistry for safety showed no toxic effects of the herbal tea. Hemoglobin levels decreased in both study groups, from 148.6 (12.8) g/L before tea therapy to 145.1 (11.5) g/L after tea therapy ( $p < 0.05$ ) in the placebo group, and from 147.8 (10.5) g/L before tea therapy to 145.0 (11.9) g/L after tea therapy ( $p < 0.05$ ) in the herbal tea group. Serum creatinine levels decreased in the herbal tea group from 84.7 (15.3)  $\mu\text{mol/L}$  before tea therapy to 77.8 (19.2)  $\mu\text{mol/L}$  after tea therapy ( $p < 0.01$ ), but this change is likely not clinically significant. One patient experienced gastrointestinal discomfort with the herbal tea but was able continue with the tea consumption. No other adverse events occurred. Body weight remained stable during the study, 79.3 (17.6) kg before versus 79.7 (17.4) kg after tea therapy in the herbal tea group and 93.1 (20.7) kg before versus 93.0 (20.7) kg after tea therapy in the placebo group.

The responder analysis showed no benefit from the herbal tea: 19% of herbal tea subjects showed improved blood glucose levels compared with 35% of placebo tea subjects ( $p = 0.24$ ). Table 2 outlines the effects of the herbal tea on parameters of blood glucose control. HbA<sub>1c</sub> values, measured immediately before tea therapy versus 4 weeks after finishing the tea did not change significantly in either group. Fructosamine levels measured immediately before drinking the tea and repeated after the treatment significantly decreased in both groups. The AUC in the meal challenge test was decreased after drinking the herbal tea (632 [442] versus 495 [309] mmol/L) and this difference was close to being significant ( $p = 0.08$ ). There was no change in incremental AUC in the placebo group. The capillary glucose levels after

the meal tolerance test showed a reduced 1-hour rise after consumption of the herbal tea (7.2 [4.7] before versus 5.7 [2.9] mmol/L after tea therapy,  $p = 0.09$ ), compared with the placebo group (5.0 [2.0] before versus 5.3 [1.9] mmol/L after tea therapy,  $p = 0.55$ ).

These data were reanalysed in subjects with a HbA<sub>1c</sub> values greater than 120% of normal, in the event that subjects with poor glycemic control might show a response to the herbal tea. Those subjects with a HbA<sub>1c</sub> levels above 7.3% were included in this analysis. Equal proportions of patients in each study group fell into this subgroup, 56% of the herbal tea subjects and 60% of the placebo tea subjects. The responder analysis in this subgroup showed no specific benefit from the herbal tea: 38% of subjects in both study groups showed an improvement. However, 25% of the placebo tea subjects had a deterioration of the blood glucose levels compared with 11% in the herbal tea group. Table 3 shows the effects of the herbal tea on other parameters of blood glucose control in patients with a HbA<sub>1c</sub> greater than 120% of normal. HbA<sub>1c</sub> values did not change significantly in either study group. Fructosamine levels before and after tea therapy did not change significantly in the placebo tea group but did decrease significantly in subjects receiving the herbal tea (361 [98] versus 338 [100]  $\mu\text{mol/L}$ ,  $p < 0.01$ ). The mean incremental AUC from the meal challenge did not change in the placebo group. In the herbal tea group, there was a decrease in the AUC (776 [369] versus 639 [331] mmol/L), although this change was not statistically significant ( $p = 0.22$ ). The absolute rise in 1-hour capillary glucose values was unchanged in the placebo group (5.6 [1.5] mmol/L before versus 5.8 [1.7] mmol/L after tea therapy) compared with a decrease in subjects drinking the herbal tea (8.7 [4.2] mmol/L before versus 7.3 [2.9] mmol/L after tea therapy).

**Table 2: Effects of herbal tea in subjects with type 2 diabetes**

Measurement	Herbal tea			Placebo tea		
	No.	Before	After	No.	Before	After
HbA <sub>1c</sub> , %*	14	7.5 (1.8)	7.9 (1.6)	19	8.1 (1.5)	8.3 (1.3)
Fructosamine, $\mu\text{mol/L} \dagger$	15	315 (89)	303 (83)	20	308 (62)	297 (54)
AUC, mmol/L‡	12	632 (442)	495 (309)	15	404 (162)	399 (168)

Data are means (and standard deviation) and the values for each parameter before tea therapy are not different between the 2 groups.

\*Post-tea samples were drawn 4 weeks after finishing the tea therapy.

†Positive samples were drawn 2 weeks after starting the tea therapy.

‡AUC is incremental area under the glucose curve after a meal tolerance test.

§ $p < 0.05$  before v. after tea therapy in the herbal tea and placebo tea groups; the other comparisons are not significantly different.

However, this reduction was not statistically significant ( $p = 0.2$ ) and, unfortunately, only 5 subjects in this herbal tea subgroup correctly completed both meal tolerance tests.

## Discussion

Plants and herbs have been used medicinally for diabetes for more than 2000 years.<sup>15</sup> More than 1200 plants and plant extracts throughout the world have been purported to benefit patients with diabetes mellitus.<sup>16</sup> Hypoglycemic properties of some herbal extracts have been examined in animal models and in patients having type 2 diabetes, and a number of hypoglycemic compounds have been isolated from plants.<sup>17-19</sup> Despite numerous interesting observations, to date metformin is the only approved drug for treatment of diabetes that is derived from a medicinal plant (*Galega officinalis*, French lilac) that was historically used to treat diabetes.<sup>15</sup> In North America, the field of ethnobotanical research has lagged behind the rest of the world. Despite the fact that the North American flora contains a large number of medicinal plants discovered by and in continual use by the Aboriginal people, only a few screenings of indigenous medicinal plants have been undertaken.<sup>8-12</sup> Evidence of the safety and efficacy of these herbal medicines remains mostly anecdotal; there is a paucity of clinical scientific evaluations of these medicines. Such studies are important since natural remedies are not always benign.<sup>20,21</sup> Nonetheless, plant remedies remain the cornerstone of treatment in underdeveloped regions and among the Aboriginal peoples of the world.

For this study, we collaborated with a Sioux healer (S.J.) who had been using a herbal tea to treat native

people with type 2 diabetes in his community. His treatment also included a spiritual healing component. It was his experience that some people were able to remain off insulin, with good blood glucose control, for over 7 years. In our study, the subjects were advised to maintain the same dose of insulin or oral hypoglycemic agents throughout the course of the trial and to contact the study physician if hypoglycemia or hyperglycemia occurred. No patient came off insulin during the study.

Our modest results compared with the healer's apparent success underline the potentially powerful placebo effect of traditional healing methods, which typically involve empathy with the patient, individualization of treatment, and one-on-one time spent with the patient. The power of positive suggestion and relevant lifestyle changes may also contribute to the success attributed to traditional healing methods. In our experience, 2 small pilot trials completed before the present study did, indeed, show very promising effects of this herbal tea. The first trial was placebo-controlled, but subjects became accidentally unblinded to the treatment group when speaking to each other about the taste of the tea early on in the study. The significant reductions in dose of hypoglycemic agents and insulin seen in the subjects drinking the herbal tea could possibly be attributed, at least in part, to a strong placebo effect of this treatment. The subjects of the second pilot trial remained blinded throughout the study, and a moderate benefit was seen in the form of improved blood glucose control and reduced need for hypoglycemic pills or insulin. To improve the design for the present study, a 1-month run-in period was added to establish regular home capillary blood monitoring and eating habits and ensure a stable therapeutic regimen that

Table 3: Effects of herbal tea in subjects with type 2 diabetes and HbA<sub>1c</sub> greater than 120% of normal (including those with a level greater than 7.3%)

Measurement	Herbal tea			Placebo tea		
	No.	Before	After	No.	Before	After
HbA <sub>1c</sub> , %*	7	8.6 (2.0)	8.7 (1.8)	11	8.9 (1.4)	9.0 (1.1)
Fructosamine, µmol/L†	8	361 (98)	338 (100)§	12	338 (60)	323 (49)
AUC, mmol/L‡	5	776 (369)	639 (331)	8	433 (125)	420 (173)

Data are means (and standard deviation).

\*Post-tea samples were drawn 4 weeks after finishing the tea therapy.

†Post-tea samples were drawn 2 weeks after starting the tea therapy.

‡AUC is incremental area under the glucose curve after a meal tolerance test.

§ $p < 0.01$  after v. before tea therapy in the herbal tea group; the other comparisons are not significantly different.

could be maintained for the duration of the study. In this way a reliable baseline period before tea therapy was established with which to gauge the effects of the herbal tea treatment. Properly designed studies can allow for the possibility that alternative therapies may be particularly good at inducing a placebo response.<sup>22</sup> Indeed, in our study, 35% of subjects experienced improved blood glucose levels while drinking the placebo tea. It is unlikely that our placebo tea had any specific medicinal effect on glucose control, but of course we cannot completely exclude such a possibility. The meters used in this study did not have built in memory chips, so patient manipulation of the self-monitoring results cannot be excluded, but we believe our placebo control design negates this weakness.

Our analysis of a subgroup of the study population is warranted given the heterogeneous nature of diabetes. A greater response to hypoglycemic treatment is not surprising in those with poorer glycemic control and underscores the need for well-matched study groups. Our data showed that the herbal tea was associated with a significant reduction in fructosamine levels in this subgroup, reflecting a short-term improvement. Fasting blood glucose values were similar between the herbal tea and placebo groups at the start of the meal tolerance tests done before and after tea therapy, so the benefit may reflect a decreased post-prandial glucose curve. Diabetic control has been cited as a factor in interpreting therapeutic benefits in other papers, for example the inverse relationship of HbA<sub>1c</sub> and the effect of linolenic acid on diabetic neuropathy.<sup>23</sup> Lack of attention to such details could result in false-negative results in otherwise promising avenues of research.

In the present study, the responder analysis failed to show any effect of the herbal tea. However, the data suggested a benefit in patients with poor glycemic control, possibly by lowering post-prandial glucose levels. Further work will be necessary to confirm this tea's effectiveness in those with elevated glucose readings. Given that Aboriginal people carry a disproportionate burden of diabetes and its complications, it is certainly worth our efforts to continue to investigate traditional healing methods and seek ways to meld culturally acceptable treatments with Western views of scientifically-based medicine.

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**Reprint requests to:** Dr. Edmond A. Ryan, 362 Heritage Medical Research Centre, University of Alberta, Edmonton AB T6G 2S2