

# EFFECT OF A GREEN DECAFFEINATED COFFEE EXTRACT ON GLYCAEMIA

## A Pilot Prospective Clinical Study

James Blum<sup>1</sup>, Benoit Lemaire, Sophie Lafay<sup>2</sup>

<sup>1</sup> Marshall-Blum, Clinical Outcomes Specialists, Bangor, ME, USA

<sup>2</sup> Berkem Développement, Gardonne, France

### SUMMARY

A green decaffeinated coffee extract\* (GDCE) rich in chlorogenic acids with a specific ratio between 5-caffeoylquinic acid and other caffeoylquinic acid isomers was developed. The aim of the present clinical study was to determine if GDCE could decrease the glycaemia in the post-prandial state in humans. Fifteen healthy women and men aged between 18 and 70 participated to the study. All participants were used as their own control and were submitted to an oral glucose tolerance test before and after supplementation of GDCE. The supplementation consisted of 3 tablets daily for forty days without diet and exercise changes.

Results indicated a significant decrease ( $147.8 \pm 9.3$  vs  $133 \pm 8.7$  mg/dL;  $p < 0.05$ ) in post-load glycaemia compared to the one obtained before supplementation. Moreover, at the end of the study, a weight loss of around 3 pounds was noted.

In conclusion, these preliminary results suggest that GDCE is able to modulate glucose metabolism and that this modulation could have an effect on weight management.

### INTRODUCTION

Hydroxycinnamic acids are one of the major classes of phenolic compounds. They are present in a large variety of fruits and vegetables (1,2). The major representative of hydroxycinnamic acids in food is caffeic acid. It largely oc-

curs conjugated with quinic acid as in chlorogenic acid (5-caffeoylquinic acid) (Fig 1). Coffee, one of the most widely consumed beverages in the world, is the major dietary source of chlorogenic acids.

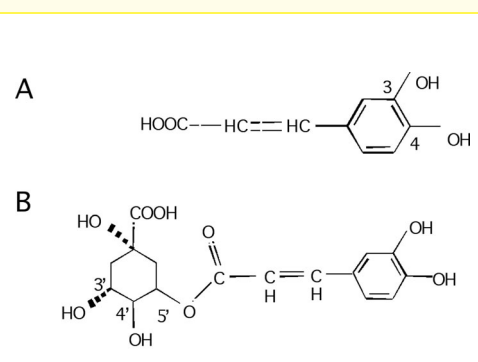
Chlorogenic acid has antioxidant properties as shown by its ability to scavenge various free radicals when tested *in vitro* (3-5). Moreover, chlorogenic acid reduces glucose uptake by favouring the dissipation of the Na<sup>+</sup> electrochemical gradient (1) and inhibits the activity of hepatic glucose-6-phosphatase which is implicated in glucose homeostasis (2, 3).

*In vivo*, when ingested under cof-

### Key words

Green decaffeinated coffee extract  
Coffea canephora robusta  
Glycaemia  
Glucose tolerance test  
Body weight

**Figure 1** Chemical structure of caffeic (A) and chlorogenic acids (B)



**BERKEM Développement**  
Marais-Ouest, 24680  
Gardonne, FRANCE  
tel +33(0)5.5363 81.00  
fax +33(0)5.5327 03.45  
email active.ingredients@berkem.com  
web www.svetol.com

**CEC Publ** Milan, Italy *harnessing Nutraceuticals through Science*

tel +39.02.4152.943  
fax +39.02.416.737  
email info.nutrafoods@cec-editore.com  
website www.cecpublisher.com

\* Svetol® is a green decaffeinated coffee (*Coffea canephora robusta*). extract produced by Berkem Development (Gardonne, France).

fee form, chlorogenic acid increases the plasma antioxidant capacity (4). Chlorogenic acid is also able to reverse the pro-oxidant effects of chemicals, such as paraquat, in rats (5) and has been reported to prevent different cancers and cardiovascular diseases in several experimental studies on animal models (6-10). Therefore, we hypothesized that chlorogenic acid, by modulating glucose metabolism and decreasing oxidative stress, could limit overweight, obesity development and secondary diseases associated with type 2 diabetes mellitus or cardiovascular problems.

The aim of the present study was to evaluate if a green coffee extract (GDCE) rich in chlorogenic acids, with specific ratio between 5-caffeoylquinic acid and other caffeoylquinic acid isomers, could decrease the glycaemia in post-prandial state in humans as suggested by an *in vitro* study with 5-caffeoylquinic acid carried out by Welsch *et al* (1).

## MATERIALS AND METHODS

### Subjects

Initially, eighteen subjects of both sexes, aged from 18 to 70 were enrolled for the trial, with fifteen subjects completing the study. Subjects were recruited from the general population of Bangor, ME, USA. Three subjects, reported some discomfort during the trial, were excluded from the protocol. One individual had a urinary tract infection, another had serial headache over a four-day period, and the third reported nausea associated with a 6-pound weight gain. The subjects with the urinary tract infection and the headache reported an abatement of their symptoms following discontinuation of the product.

### Exclusion criteria

Subjects who were under the age of 18 or over the age of 70, those who were non-compliant with testing and taking treatment regimens, those who were nursing, pregnant, or trying to become pregnant, those with insulin-dependent diabetes, those with uncontrolled hypertension, those with a known intolerance to any of the components of the product, those with severe co-morbid disease, that included cardiac, pulmonary, renal, hepatic, or active cancer (this determination was subject to the study physician), those who consumed medications or other herbal preparations, those with alcohol abuse as determined by provider interviews or medical history.

### Preparation of the green coffee extract

The GDCE (Svetol®, Berkem Development, Gardonne, France) was prepared in jars of 60 tablets. Composition of the product under experimentation is given in *Table 1*.

**Table 1** Composition of the GCDE tablets

Content	mg/tablet
Green coffee extract	200.00
Tricalcic phosphate	28.00
Magnesium stearate	5.6
Microcrystalline cellulose	246.4

### Study design

Volunteers took 3 tablets daily, 1 tablet in the morning, 1 tablet at noon and 1 tablet in the evening with food and a glass of water for forty days. Each tablet contained 200 mg of GDCE. Each participant was given treatment sufficient for 40 days (two jars) when they began the study. The volunteers were asked not to modify their diet nor their sports activity during this period. Before and after the supplementation period, volunteers were submitted to an oral glucose tolerance test (GTT).

### Glucose tolerance test

Subjects were asked to fast before (at least 8 h before) and during this test. They had a baseline glucose serum measurement taken when they arrived at the clinic (Herbal Research Clinic, Bangor, ME, USA). Then, each subject was given a standard glucose sugar load, consisting of eighteen jelly beans.

A follow-up serum glucose measurement was taken at 1 h (2 draws total). Subjects were asked to refrain from eating, drinking (with the exception of water), smoking or leaving the premises for the duration of the test.

This prospective, non-randomized, non-blinded, open label, pilot clinical trial had IRB approval (Fox Commercial IRB, Springfield, IL, Candace Woods, Executive Director: IRB # 020411-001).

### Body weight measurements

Body weight measurements were taken at the beginning and at the end of the study.

### Statistics

Numerical values are mean  $\pm$  SEM. Data were entered into XLStat statistical analysis program. The paired z-test determined the difference between values. Differences with  $p \leq 0.05$  were considered significant.

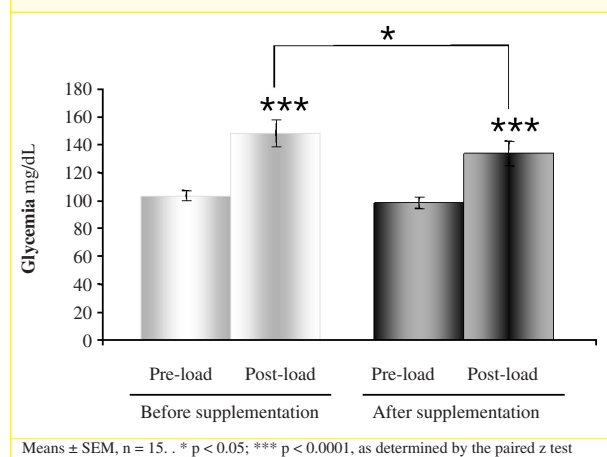
## RESULTS

Pre-load glycaemia, with or without supplementation, did not differ significantly ( $98 \pm 3.8$  vs  $103.2 \pm 3.6$  mg/dL respectively) (Fig 2).

After GDCE supplementation for 40 days, post-load glycaemia decreased significantly compared to the post-load glycaemia obtained without the supplementation ( $147.8 \pm 9.3$  vs  $133 \pm 8.7$  mg/dL;  $p < 0.05$ , Fig 2).

Moreover, at the end of the supplementation, a mean weight loss of around three pounds for the entire group was noted without diet and exercise changes.

**Figure 2** Oral glucose tolerance test with and without GDCE supplementation



## DISCUSSION

Several previous epidemiologic studies have shown that individuals with an average to high daily consumption of coffee reduced their risk of developing type 2 diabetes (11-14). Weight loss may be linked with this health effect because one prospective epidemiologic study found that consumption of coffee was followed by lower diabetes risk, but only in participants who had lost weight (15). Three clinical studies distinguished the effect of caffeinated and decaffeinated coffee (16-18) and suggested that there are non-caffeine compounds such as chlorogenic acids in coffee that enhance glucose tolerance. *In vitro* and *in vivo* studies carried out with the 5-caffeoylquinic acid, the main chlorogenic acid in coffee, showed that this phenolic acid is able to modulate glucose metabolism (1, 2, 18-21). More particularly, Welsch *et al* (1) showed that 5-caffeoylquinic acid reduced glucose uptake by favouring the dissipation of the  $\text{Na}^+$  electrochemical gradient, which provides the driving force for active glucose accumulation. Another study showed that 5-caffeoylquinic acid inhibited the glucose-6-phosphatase T1 transporter in intact rat microsomes (2).

On the basis of all these findings, a chlorogenic acid-implicated mechanism can be proposed to explain the epidemiological results and the link with a weight loss. 5-Caffeoylquinic acid in the diet could inhibit glucose absorption in the small intestine (1), thus limiting insulinemia and promoting lipolysis. In addition, when glycaemia decreases to under 1 g/L, the hepatic release of glucose into the general circulation might be limited by inhibiting the activity of glucose-6-phosphatase (2, 3, 22, 23).

The consequence of these two actions may lead to a breakdown of fat reserves as a source of energy leading to weight loss. However, the proposed mechanisms depend on the bioavailability of chlorogenic acid. Recently, the fate and metabolism of chlorogenic acid (5-caffeoylquinic acid) in the gastrointestinal tract of rats were explored to determine the form under which this ester of caffeic acid is absorbed through the gut barrier. After analysis of the content in the different parts of the gastrointestinal tract, it appeared that chlorogenic acid is stable in the stomach and the small intestine but cleaved into caffeic acid in the caecum by the microflora (24). Consequently, stability of chlorogenic acid in the small intestine is coherent with glucose absorption inhibition in this part of the gut.

Few clinical studies have been carried out on glucose metabolism and coffee (17,18,25) and none were done with green (not roasted) coffee which contains higher chlorogenic acids concentration compared to roasted coffee (26).

The present study was carried out to see if GDCE was able to decrease glycaemia in the post-prandial state in humans as suggested by the literature, this being the first step of the weight loss mechanism.

The significant decrease of post-load glycaemia after the GDCE supplementation with respect to that before supplementation is in agreement with results obtained in *in vitro* or clinical studies (17,18, 25) with 5-caffeoylquinic acid or with coffee beverage respectively. Johnston *et al* (18) compared the effect of caffeinated and decaffeinated coffee consumption on 9 healthy volunteers and showed that decaffeinated coffee is able to modulate gastrointestinal hormone secretion (glucagon-like peptide 1 and glucose dependent insulinotropic

polypeptide) and is correlated with glucose uptake, insulin secretion and thus, post-prandial glycaemia. Johnston *et al* (18) suggested that the gastrointestinal hormone profiles after consumption of decaffeinated coffee are consistent with delayed intestinal glucose absorption and decreased glycaemia. This mechanism could be proposed to explain the effect of the GDCE on the post-load glycaemia. These results could explain why in epidemiological studies, regular coffee consumption is associated with a decrease of insulin-resistance characterizing the type 2 diabetes. However, other studies must be done with GDCE to validate this hypothesis.

Although the principal criterion of this study was not the weight loss, we noted a slight weight decrease (3 pounds) at the end of GDCE supplementation suggesting that modulation of glucose metabolism could have an influence on weight management. After this prospective clinical trial, we set up a randomized, double blind, clinical study using GDCE on volunteers with overweight problems. This study (27), showed that volunteers were able to lose weight (mean of 11 pounds) and increase lean mass/fat mass ratio in a significant manner when they consumed 400 mg of GDCE in association with a bland low caloric diet during 8 weeks compared to the placebo group.

## CONCLUSION

The prospective study presented shows that a decaffeinated green coffee extract with a specific ratio between 5-caffeoylquinic acid and the other chlorogenic acids, is able to decrease the glycaemia in a post-prandial state in humans. These results, associated with the weight loss seen in the randomized double blind clinical study (27), supports the fact that GDCE is able to have a fat burning action via glucose metabolism regulation.

## REFERENCES

- 1 Welsch CA, Lachance PA, Wasserman BP (1989) Dietary phenolic compounds: inhibition of sodium-dependant D-glucose uptake in rat intestinal brush border membrane vesicles *J Nutr* 119(11) 1698-1704
- 2 Arion WJ *et al* (1997) Chlorogenic acid and hydroxynitrobenzaldehyde: new inhibitors of hepatic glucose 6-phosphatase *Arch Biochem Biophys* 339(2) 315-322

- 3 **Hemmerle H et al (1997)**  
Chlorogenic acid and synthetic chlorogenic acid derivatives: novel inhibitors of hepatic glucose-6-phosphate translocase  
*J Med Chem* 40(2) 137-145
- 4 **Natella F et al (2002)**  
Coffee drinking influences plasma antioxidant capacity in humans  
*J Agric Food Chem* 50(21) 6211-6216
- 5 **Tsuchiya T, Suzuki O, Igarashi K (1996)**  
Protective effects of chlorogenic acid on paraquat-induced oxidative stress in rats  
*Biosci Biotechnol Biochem* 60(5) 765-768
- 6 **Mori H et al (1986)**  
Inhibitory effect of chlorogenic acid on methylazoxymethanol acetate-induced carcinogenesis in large intestine and liver of hamsters  
*Cancer Lett* 30(1) 49-54
- 7 **Tanaka T et al (1993)**  
Inhibition of 4-nitroquinoline-1-oxide-induced rat tongue carcinogenesis by the naturally occurring plant phenolics caffeic, ellagic, chlorogenic and ferulic acids  
*Carcinogenesis* 14(7) 1321-1325
- 8 **Tanaka T et al (1990)**  
Inhibitory effects of chlorogenic acid, reserpine, polyphenolic acid (E-5166), or coffee on hepatocarcinogenesis in rats and hamsters  
*Basic Life Sci* 52 429-440
- 9 **Zhou J et al (1993)**  
Protective effect of chlorogenic acid on lipid-peroxidation induced in the Liver of rats by carbon-tetrachloride or Co-60-irradiation  
*J Clin Biochem Nutr* 15(2) 119-125
- 10 **Suzuki A et al (2002)**  
Green coffee bean extract and its metabolites have a hypotensive effect in spontaneously hypertensive rats  
*Hypertension Research* 25(1) 99-107
- 11 **Rosengren A et al (2004)**  
Coffee and incidence of diabetes in Swedish women: a prospective 18-year follow-up study  
*J Intern Med* 255(1) 89-95
- 12 **van Dam R, Hu F (2005)**  
Coffee consumption and risk of type 2 diabetes: a systematic review  
*JAMA* 294(1) 97-104
- 13 **Wu T et al (2005)**  
Caffeinated coffee, decaffeinated coffee, and caffeine in relation to plasma C-peptide levels, a marker of insulin secretion, in U.S. women  
*Diabetes Care* 28(6) 1390-1396
- 14 **Bidel S et al (2006)**  
Effects of coffee consumption on glucose tolerance, serum glucose and insulin levels - A cross-sectional analysis  
*Horm Metab Res* 38(1) 38-43
- 15 **Greenberg JA et al (2005)**  
Coffee, tea and diabetes: the role of weight loss and caffeine  
*Int J Obes (Lond)* 29(9) 1121-1129
- 16 **Naismith DJ et al (1970)**  
The effect, in volunteers, of coffee and decaffeinated coffee on blood glucose, insulin, plasma lipids and some factors involved in blood clotting  
*Nutr Metab* 12(3) 144-151
- 17 **Batram DS et al (2006)**  
The glucose intolerance induced by caffeinated coffee ingestion is less pronounced than that due to alkaloid caffeine in men  
*J Nutr* 136(5) 1276-1280
- 18 **Johnston KL, Clifford MN, Morgan LM (2003)**  
Coffee acutely modifies gastrointestinal hormone secretion and glucose tolerance in humans: glycemic effects of chlorogenic acid and caffeine  
*Am J Clin Nutr* 78(4) 728-733
- 19 **Hsu FL, Chen YC, Cheng JT (2000)**  
Caffeic acid as active principle from the fruit of *Xanthium strumarium* to lower plasma glucose in diabetic rats  
*Planta Med* 66(3) 228-230
- 20 **Andrade-Cetto A, Wiedenfeld H (2001)**  
Hypoglycemic effect of *Cecropia obtusifolia* on streptozotocin diabetic rats  
*J Ethnopharmacol* 78(2-3) 145-149
- 21 **Rodriguez de Sotillo DV, Hadley M (2002)**  
Chlorogenic acid modifies plasma and liver concentrations of: cholesterol, triacylglycerol, and minerals in (fa/fa) Zucker rats  
*J Nutr Biochem* 13(12) 717-726
- 22 **Herling AW et al (1998)**  
Pharmacodynamic profile of a novel inhibitor of the hepatic glucose-6-phosphatase system  
*Am J Physiol* 274(6 Pt 1) G1087-G1093
- 23 **Simon C et al (2000)**  
Upregulation of hepatic glucose 6-phosphatase gene expression in rats treated with an inhibitor of glucose-6-phosphate translocase  
*Arch Biochem Biophys* 373(2) 418-428
- 24 **Lafay S et al (2006)**  
Absorption and metabolism of caffeic acid and chlorogenic acid in the small intestine of rats  
*Br J Nutr* 96 1-8
- 25 **Feinberg L et al (1968)**  
Effects of coffee consumption on oral glucose tolerance curves in normal human subjects  
*Metabolism* 17 916-922
- 26 **Trugo LC, Macrae R (1984)**  
A study of the effect of roasting on the chlorogenic acid composition of coffee using HPLC  
*Food Chem* 15(3) 219-227
- 27 **Dellalibera SO, Lemaire B, Lafay S (2006)**  
Le Svetol®, un extrait de café vert décaféiné, induit une perte de poids et augmente le ratio masse maigre sur masse grasse chez des volontaires en surcharge pondérale  
*Phytothérapie* 4 1-4