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SHORT COMMUNICATION

Lipolytic Activity of Svetol®, a Decaffeinated Green Coffee Bean Extract

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The beneficial health effects of chlorogenic acids (CGAs), major components of coffee beans, are well known and have been attributed to multiple mechanisms of action. However, the lipolytic activity of CGAs does not appear to have been reported. We studied the effects of varying concentrations of Svetol®, a decaffeinated green coffee bean extract enriched in CGAs, on the liberation of free fatty acids from human adipocytes following short-term (2 h) and long-term (192 h) exposure. The results showed that although lipolytic activity observed following short-term incubation could be tentatively linked to residual caffeine traces in the sample, longer-term exposure clearly showed the effects of Svetol® on release of free fatty acids, and this effect was not due to caffeine. The results of this study provide a further mechanism by which to explain the long-term health benefits of CGAs and Svetol®.

Keywords: chlorogenic acid; adipocyte; weight loss; diabetes.

INTRODUCTION

Chlorogenic acids (CGAs), phenolic compounds, which are esters of hydroxycinnamic and quinic acid, are widely dispersed in the plant kingdom and found at elevated levels in coffee beans (Clifford, 1999). Epidemiological studies have shown that consumption of coffee reduces the risk of diabetes development (van Dam *et al*., 2006), and this health benefit has been attributed to the CGA fraction of coffee. Human intervention studies have shown the efficacy of a standardized decaffeinated green coffee bean extract (DGCE) extract, Svetol®, to significantly reduce body weight (Dellalibera *et al*., 2006; Thom, 2007) and post-prandial blood glucose (Thom, 2007; Blum *et al*., 2007) in overweight and obese individuals.

Chlorogenic acids are known to be able to inhibit the glucose-6-phosphatase system (Henry-Vitrac *et al*., 2010) and amylolytic enzymes (Kamitani *et al*., 2009), which may explain improved glucose homeostasis following administration. However, these mechanisms of action do not fully explain body weight reduction and lean:fat mass ratio increases observed following long-term administration of Svetol®. Therefore, CGAs may affect adipocyte metabolism.

Activation of lipolytic activity in adipocyte tissue results in liberation of free fatty acids and glycerol with a concomitant reduction in adipocyte cell volume. Although the *in vivo* lipolytic activity of a green coffee bean extract rich in caffeine and CGAs was previously described (Tanaka *et al*., 2009), the lipolytic activity of CGAs *per se* does not appear to have been reported. Therefore, the objective of this study was to evaluate the lipolytic activity of Svetol®, a commercial DGCE, which contains a specific blend of CGAs and which has been previously demonstrated to aid with weight loss.

MATERIALS AND METHODS

Svetol® was supplied by Naturex Inc. (South Hackensack, NJ) and contained >45% CGAs and >10% 5-caffeoylquinic acid.

Adipose tissue explant preparation. Normal human adipocytes were freshly isolated from surgical samples of healthy abdominal skin (34-year-old woman) as described previously (Rodbell, 1964) and recently detailed by Dallas *et al.* (2008).

Acute evaluation of lipolytic activity. Stock solutions of Svetol® (10 mg/mL) and caffeine as a positive control (10 mM) were prepared immediately prior to the experiment and were added to the isolated adipocytes to obtain a final concentration of 0.04, 0.2 and 1 mg/mL for Svetol® and 1 mM for caffeine (0.194 mg/mL). After 2 h incubation at 37 °C, the concentration of free fatty acids in the supernatant was determined using a FFA-C kit (OXOID, Dardilly, France), an *in vitro* enzymatic colorimetric method assay for the quantitative determination of non-esterified fatty acids, which relies upon the acylation of coenzyme A by the fatty acids in the presence of added acyl-CoA synthetase. Results were expressed as micromoles of free fatty acids or percentage of the negative control. The absence of interference of the test substances on the free fatty acid assay was also determined.

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Sub-chronic evaluation of lipolytic activity. Stock solutions of Svetol® (10 mg/mL) and caffeine as a positive control (10 mg/mL) were prepared immediately prior to the experiment and were added to the isolated adipocytes to obtain a final concentration of 0.01, 0.1 and 1 mg/mL for Svetol® and 1 mg/mL for caffeine. These additions were repeated after 48, 96 and 144 h. At each time point (48, 96 and 144 h) and at the end of the study (192 h), aliquots were taken from the supernatant and were combined prior to being stored at −20 °C for analysis of free fatty acids. Free fatty acids were determined as described earlier.

RESULTS AND DISCUSSION

Short-term treatment (2 h) of human-derived adipocytes with DGCE revealed a dose-dependent increase in free fatty acid liberation, with a free fatty acid content of 47 μM found at 1 mg/mL, a 67% increase over the control (Fig. 1). Caffeine, as expected, elicited a very strong lipolytic response at 1 mM. Although most of the caffeine have been removed from DGCE during industrial processing, up to 2% caffeine may remain. With this in mind, the results were re-analyzed and presented as liberation of free fatty acids expressed as a percentage of the maximum value (caffeine) for each sample based on its inherent caffeine content. The DGCE samples were calculated to potentially contain up to 0.8, 4.0 and 20.0 mg/L caffeine (corresponding to 4.1, 20.6 and 103.0 μM caffeine, respectively), and linear regression identified a relatively good fit between these values and the liberation of free fatty acids obtained with caffeine at a higher dose ($r^2 = 0.9863$; Fig. 1 insert).

There is a strong possibility that the lipolytic activity observed in previous *in vitro* studies of the lipolytic activity of natural plant extracts with residual caffeine content could be largely due to the activity of the inherent caffeine content of the samples, similar to the results obtained herein.

To further elucidate the effects of DGCE on metabolism of triglycerides in human-derived adipocytes, a study of longer duration was conducted using the same model. Analysis of aliquots taken at various time points following

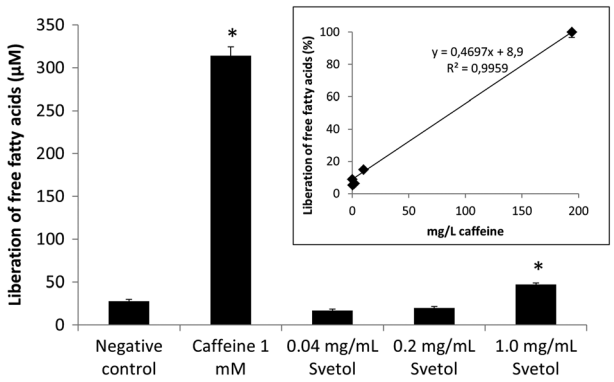

Figure 1. Lipolytic activity of varying concentrations of Svetol® (0.04, 0.2 and 1.0 mg/mL) on the liberation of free fatty acids (μM) from human adipocytes compared with negative and positive (194 mg/mL caffeine) controls following 2 h incubation. Insert: lipolytic activity of samples expressed by caffeine content. Error bars represent standard deviation, $n = 3$; $^*p < 0.05$.

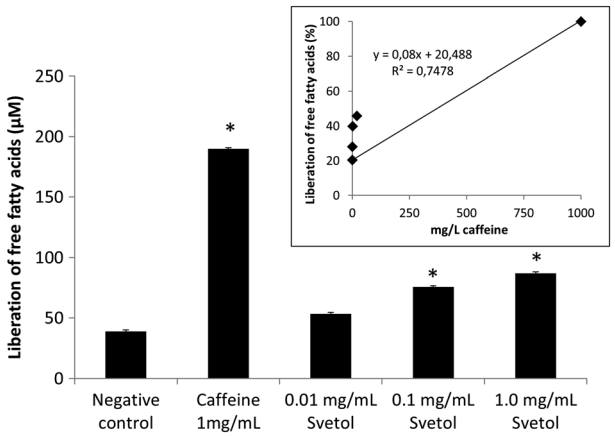

Figure 2. Lipolytic activity of varying concentrations of Svetol® (0.01, 0.1 and 1.0 mg/mL) on the liberation of free fatty acids (μM) from human adipocytes compared with negative and positive (100 mg/mL caffeine) controls from combined aliquots taken during 192 h incubation. Insert: lipolytic activity of samples expressed by caffeine content. Error bars represent standard deviation, $n = 3$; $^*p < 0.05$.

incubation of human-derived adipocytes with varying concentrations of DGCE confirmed the dose–response effect observed in the study of shorter duration (Fig. 2). Liberation of free fatty acids was found to be significantly greater than the control at 0.1 and 1.0 mg/mL DGCE. The results showed a poor correlation between liberation of free fatty acids and caffeine content, with an $r^2 = 0.7478$ (Fig. 2, insert).

Incubation of adipocytes with DGCE for a longer duration of time (192 h) permitted a clear differentiation between the effects of caffeine and other bioactive compounds present in the DGCE. It is also worth noting that the CGA content of the lowest concentration of DGCE reported in this study (0.01 mg/mL Svetol®; 20 μM CGAs) corresponds approximately to the maximum concentration of CGAs observed in plasma (total CGAs 14.8 μM) following single administration of 400 mg of Svetol® (Farah *et al.*, 2008). Thus, we can hypothesize on the biological relevance of the results obtained in the current study.

The demonstration of the lipolytic activity of Svetol® adds further knowledge to the mechanisms underpinning CGA-correlated weight loss, particularly those derived from DGCE (Thom, 2007; Dellalibera *et al.*, 2006). It can be postulated that Svetol® can have a generic effect on glucose control and body weight management, a hypothesis reinforced by the numerous epidemiological studies highlighting the health benefits of consumption of coffee and decaffeinated coffee rich in CGAs (van Dam *et al.*, 2006).

Acknowledgements

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Conflict of Interest

Naturex is involved in the research/development and marketing/sales of Svetol® as an ingredient for the food, cosmetic and nutraceutical industries. Therefore, Naturex has a commercial interest in this publication.

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