

Svetol[®], green coffee extract, induces weight loss and increases the lean to fat mass ratio in volunteers with overweight problem

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ABSTRACT

In order to test the effects of Svetol[®], a green coffee extract rich in chlorogenic acids with specific ratio between 5-caffeoylquinic acid and others caffeoylquinic acid isomers, on weight loss, 50 volunteers with body mass index superior to 25 were selected. They were randomized in two groups, control group (n = 20) receiving placebo, treated group (n = 30) receiving Svetol[®]. Each volunteer took one capsule of Svetol[®] or placebo twice a day with main meal, for 60 days. Changes in weight, body mass index (BMI), Muscle Mass/Fat Mass ratio (MM/FM) and self-evaluation of physical aspect were recorded at T0 and T60. After 60 days of treatment, a mean reduction in weight of 4.97 +/- 0.32 kg (5.7%) was observed in the Svetol[®] group compared to control group in which the mean reduction was 2.45 +/- 0.37 kg (2.9%) (p < 0.001). Consequently, body mass index decreased significantly in Svetol[®] group compared to control group. Moreover, MM/FM ratio was increased significantly in Svetol[®] group compared to control group: 4.1 +/- 0.7% vs 1.6 +/- 0.6 respectively (p = 0.01). The significant decrease of weight, body mass index and fat mass showed that Svetol[®] is able to exacerbate effect of a bland low caloric diet in volunteers who have overweight. This effect could be explained by increasing the consumption of fatty deposits, as shown by change in the MM/FM ratio, and by preventing them from being accumulated.

To conclude, Svetol[®] could be used to aid the dietetics prescription in a useful and positive manner.

Key words: chlorogenic acids, Svetol[®], weight, muscle mass/fat mass ratio

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 occurs conjugated with quinic acid as in chlorogenic acid (5-caffeoylquinic acid) (Figure 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 showed 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⁺ electrochemical gradient [6] and inhibits the activity of hepatic glucose-6-phosphatase which is implicated in glucose homeostasis [7, 8].

In vivo, when ingested under coffee form, chlorogenic acid increases the plasma antioxidant capacity [9]. Chlorogenic acid is also able to reverse the prooxidant effects of drugs such as paraquat [10] and have been reported to prevent different cancers and cardiovascular diseases in several experimental studies on animal models [11-15]. Therefore, we hypothesized that chlorogenic acid modulating glucose metabolism and decreasing oxidative stress could limit overweight, obesity development and secondary diseases

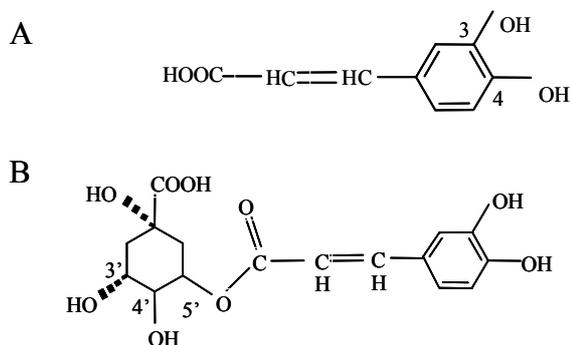


Figure 1: Chemical structure of caffeic (A) and chlorogenic acids (B)

associated with as type 2 diabetes mellitus or cardiovascular problems.

The aim of the present work was to evaluate if Svetol[®], a green coffee extract, could decrease overweight in volunteers who had body mass index (BMI) superior to 25.

SUBJECTS AND METHODS

Chemicals

Svetol[®], decaffeinated green coffee extract, were purchased from Berkem[®] SA (Gardonne, France).

Subjects

Fifty volunteers of both sexes, aged from 19 to 75, were assigned at random to the group of 30 in active treatment, and 20 in placebo treatment. The participants of both groups were homogeneous in weight and muscle mass/fat mass (MM/FM) ratio, characterized by an overweight problem, BMI superior to 25, and the acceptance of a bland low caloric diet. Exclusion criteria were as follows: acute or chronic gastro-intestinal pathologies; gastro-intestinal infections and/or parasitosis; severe hyper-tension (P.A. above 120 mm.); gastro-intestinal cancers; serious or chronic metabolic pathologies; big drinkers; assumption of products for the control of weight and glycaemia; a known intolerance to any of the components of the product under examination.

Svetol[®] supplementation

The product was prepared in jars of 30 capsules absolutely identical. Composition of the product (active capsules) under experimentation was given in **table 1**. Placebo capsules contained the same components as the active capsule, Svetol[®] was substituted by an identical quantity of maltodextrin (200 mg).

	mg/capsule
Svetol [®]	200
Starch	0.04
Magnesium stearate	0.015
Silica micronized	0.008
White gelatine	0.087

Table 1: Composition of the Svetol[®] capsule

Study design

Volunteers took one capsule with each main meal, twice a day, for 60 days. Every participant was given treatment sufficient for 30 days (two jars) when they began the study (T0) and the rest (two jars) at the T30 day.

Data collection and parameters of evaluation

In the course of the first check-up, the following data were gathered: age, height, sex, weight, BMI, MM/FM ratio, self-evaluation of physical aspect. Changes in weight, BMI, MM/FM ratio, self-evaluation of physical aspect were recorded again at T60. An evaluation of compliance and verification of the presence of side effects was undertaken at T30 and T60.

MM/FM ratio was determined by Bioelectric Impedance Analysis. Self-evaluation of physical

aspect was done by scale from 0 = very negative to 10 = excellent.

Evaluation of effectiveness, compliance and tolerability

At the end of treatment, effectiveness, compliance and tolerability were verified with regard to the end-points by comparing the changes in the data recorded at T60 to those at T0.

Therefore, changes of weight, BMI, MM/FM ratio, self-evaluation of physical aspect in the active group were compared to those recorded in the placebo group.

The effectiveness was based on those participants who completed the study. Compliance and tolerability were based on all participants.

Statistical analysis

Numerical values are mean +/- SEM (n = 20 for control group or 30 for treated group). Data were entered into Instat statistical analysis program (Instat, San Diego, CA). Student t-test (parametric test) or Mann-Whitney test (non-parametric test) determined the difference between values. Differences with $p \leq 0.05$ were considered significant.

RESULTS

Weight loss and Body Mass Index

After 60 days of treatment, a mean reduction in weight of 4.97 +/- 0.32 kg (-5.7 +/- 0.3%) was observed in the Svetol[®] group compared to control group in which the mean reduction was 2.45 +/- 0.37 kg (-2.9 +/- 0.4%). These means are significantly different ($p < 0.001$) (**Figure 2A**). Consequently, body mass index decreased significantly in Svetol[®] group compared to control group (-1.9 +/- 0.1 kg/m² vs -0.9 +/- 0.1 kg/m²; $p < 0.001$) (**Figure 2B**).

Muscle Mass/ Fat Mass ratio

In Svetol[®] group, MM/FM ratio was increased significantly compared to control group: +4.1 +/- 0.7% vs +1.6 +/- 0.6 respectively ($p = 0.01$) (**Figure 3**).

Self-evaluation of physical aspect

No significant difference about the appearance was observed between both groups at T60 (6.6 +/- 1.05 vs 6.5 +/- 1.31 for placebo and Svetol[®] groups respectively) but both groups observed an amelioration of the physical appearance between T0 and T60 ($p < 0.05$ for each group).

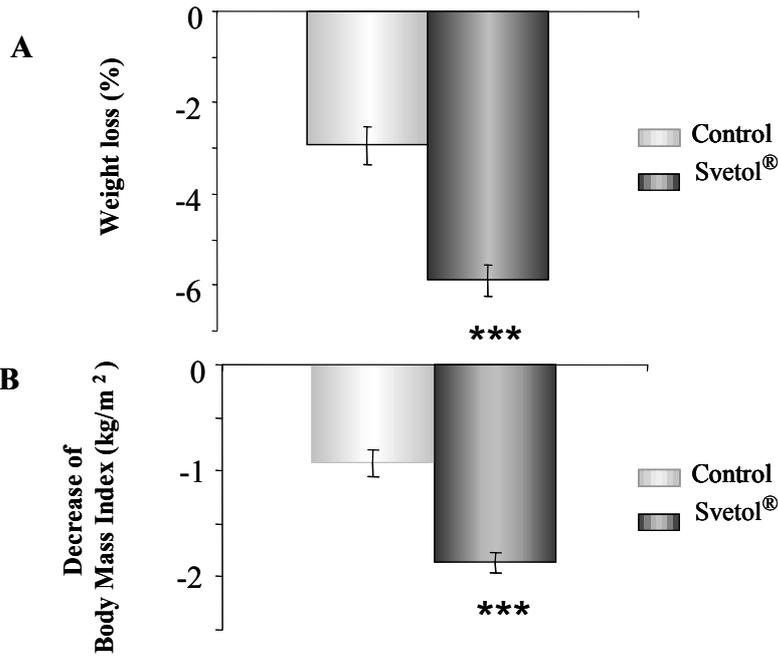


Figure 2: (A) Weight loss (%) and (B) decrease of BMI (kg/m²) after 60 days treatment. Values are means +/- SEM, n = 20 for control group, n = 30 for Svetol[®] group. Means are significantly different (*, p < 0.001 vs. control group).

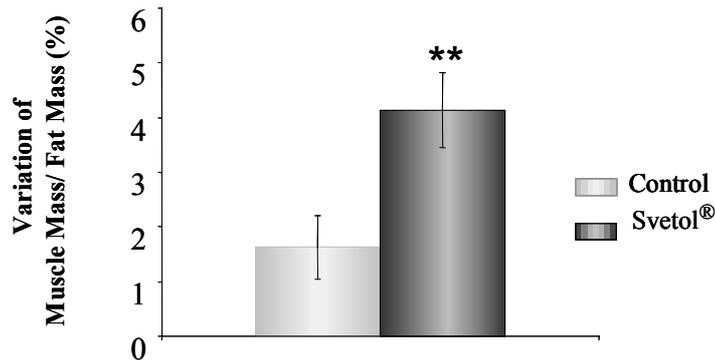


Figure 3: Variation of muscle Mass/ fat Mass ratio after 60 days of treatment (%). Values are means +/- SEM, n = 20 for control group, n = 30 for Svetol[®] group. Means are significantly different (**, p = 0.01 vs. control group).

DISCUSSION

Obesity is a serious public health problem [16]. Overweight and obesity are the cause of health problems of varying degrees of seriousness: asthenia, osteo-articular, psychological and cardiovascular problems.

The reality is that this condition has a negative impact on the quality of life, and in the case of obesity, it can even lead to a reduction in life expectancy.

With the exception of serious neuro-endocrine pathologies the problem is caused mainly by lifestyle. A rational diet in quantity and quality, combined with some physical exercise can help to obtain some loss of weight. A change in lifestyle is

not simple so in order to reach the desired goal of controlling weight pharmaceutical products are used as well as nutritional supplements with various compositions, fat burners, all with the aim of contrasting the lack of balance between the number of calories introduced and the number of those consumed which leads to overweight. There is a relationship between the amount of carbohydrates in the diet and the amount of fats in the adipose reserves since the carbohydrates are responsible for most of the calories introduced [17] and the intake of sugars reduces energy consumption. In normal production and activity of insulin, the calories introduced are burnt up without transforming the lipids into stock. On the other hand, if the amount of glucose present in the blood is in excess with regards to its use and to the hepatic glycogenesis, this excess glucose (owing to the insulin which has been increased by the hyperglycemia) enters into the adipocytes where it is stored as fat reserves [18]. The consequences are: (i) the fat reserves are not used to produce energy; (ii) an increase of adipocytes.

In diets the lower quantity of carbohydrates consumed is a way to “force” the organism to burn up the fat which has been deposited in the adipocytes and therefore to lose weight. It is possible to improve the effect of the lower amounts of carbohydrates consumed by exploiting the hepatic activity to regulate the glycemia level. When glucose level in the blood is lower than 1g/L, the liver synthesized glucose-6-phosphate (G6P) by an hexokinase, hydrolysed G6P by means of a glucose-6-phosphatase and released glucose into the bloodstream. It’s glycogenolysis. If this sequence is interrupted the fatty deposits do not increase, but are instead used for the production of energy.

The aim of the present work was to evaluate if Svetol[®], green coffee extract concentrated in chlorogenic acids with specific ratio between 5-caffeoylquinic acid and others caffeoylquinic acid isomers, could decrease overweight in volunteers by fat burning action as suggested by *in vitro* studies showing inhibition of the activity of hepatic glucose-6-phosphatase by 5-caffeoylquinic acid [7, 8].

The significant decrease of weight and fat mass showed that Svetol[®] is able to exacerbate effect of a bland low caloric diet in volunteers who had overweight. This effect could be explained by increasing the consumption of fatty deposits, as shown by change in the MM/FM ratio, and by preventing them from being accumulated.

From results presented here and bibliography, Svetol[®]'s mechanism could be proposed: first of all, associated with the diet, it inhibits glucose absorption in the small intestine[6]. In addition, by inhibiting the activity of glucose-6-phosphatase [7, 8], it limits the release of glucose into the general circulation [19, 20] and therefore limits

insulinemia. This mechanism engenders two results: (i) less fatty deposits in the adipose tissue and a more difficult access into the adipose cells owing to a reduction in insulin activity; (ii) consumption of fat reserves, where there is a lack of glucose, as a source of energy at the disposition of the organism and therefore, as in the previous case, a case of loss of weight.

However, mechanism proposed depends on bioavailability of chlorogenic acid. Recently, fate and metabolism of chlorogenic acid (5-caffeoylquinic acid) in the gastro-intestinal tract of rats were explored to determine the form under which this ester of caffeic acid is absorbed through the different parts of the gut barrier.

After analysis of the different gastro-intestinal contents, 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 [21]. Consequently, stability of chlorogenic acid in the small intestine is coherent with glucose absorption inhibition in this part of the gut. Moreover, whereas it was shown that chlorogenic acid was hydrolysed into enterocytes before secretion on the serosal side [22], it was absorbed under intact form from the stomach [21] and found in gastric vein and aorta without conjugation (glucuronidation, sulfation or methylation). This result suggests that chlorogenic acid is able to rejoin the liver without modification, which is in accordance with its activity of hepatic glucose-6-phosphatase inhibition.

Thus, chlorogenic acid bioavailability studies supported Svetol[®]'s mechanism proposed.

To conclude, Svetol[®] has demonstrated its validity and could be used to aid the dietetics prescription in a useful and positive manner.

BIBLIOGRAPHY

1. Clifford, M.N., Chlorogenic acids and other cinnamates - Nature, occurrence and dietary burden. *J. Sci. Food. Agric.*, 1999. 79: p. 362-372.
2. Manach, C., et al., Polyphenols - Food sources and bioavailability. *Am. J. Clin. Nutr.*, 2004. 79(5): p. 727-747.
3. Ohnishi, M., et al., Inhibitory effects of chlorogenic acids on linoleic acid peroxidation and haemolysis. *Phytochemistry*, 1994. 36(3): p. 579-583.
4. Rice-Evans, C.A., N.J. Miller, and G. Paganga, Structure-antioxidant activity relationships of flavonoids and phenolic acids. *Free Rad. Biol. Med.*, 1996. 20(7): p. 933-956.
5. Foley, S., et al., Singlet oxygen quenching and the redox properties of hydroxycinnamic acids. *Free Radic Biol Med*, 1999. 26(9-10): p. 1202-8.
6. Welsch, C.A., P.A. Lachance, and B.P. Wasserman, Dietary phenolic compounds: inhibition of sodium-dependant D-glucose uptake in rat intestinal brush border membrane vesicles. *J. Nutr.*, 1989. 119(11): p. 1698-1704.
7. Arion, W.J., et al., Chlorogenic acid and hydroxynitrobenzaldehyde: new inhibitors of hepatic glucose 6-phosphatase. *Arch Biochem Biophys*, 1997. 339(2): p. 315-22.
8. Hemmerle, H., et al., Chlorogenic acid and synthetic chlorogenic acid derivatives: novel inhibitors of hepatic glucose-6-phosphate translocase. *J Med Chem*, 1997. 40(2): p. 137-45.
9. Natella, F., et al., Coffee drinking influences plasma antioxidant capacity in humans. *J Agric Food Chem*, 2002. 50(21): p. 6211-6.
10. Tsuchiya, T., O. Suzuki, and K. Igarashi, Protective effects of chlorogenic acid on paraquat-induced oxidative stress in rats. *Biosci Biotechnol Biochem*, 1996. 60(5): p. 765-8.
11. Mori, H., et al., Inhibitory effect of chlorogenic acid on methylazoxymethanol acetate-induced carcinogenesis in large intestine and liver of hamsters. *Cancer Lett*, 1986. 30(1): p. 49-54.
12. Tanaka, T., et al., Inhibition of 4-nitroquinoline-1-oxide-induced rat tongue carcinogenesis by the naturally occurring plant phenolics caffeic, ellagic, chlorogenic and ferulic acids. *Carcinogenesis*, 1993. 14(7): p. 1321-5.
13. Tanaka, T., et al., Inhibitory effects of chlorogenic acid, reserpine, polyphenolic acid (E-5166), or coffee on hepatocarcinogenesis in rats and hamsters. *Basic Life Sci*, 1990. 52: p. 429-40.
14. Zhou, J., et al., Protective Effect of Chlorogenic Acid on Lipid-Peroxidation Induced in the Liver of Rats by Carbon-Tetrachloride or Co-60-Irradiation. *Journal of Clinical Biochemistry and Nutrition*, 1993. 15(2): p. 119-125.
15. Suzuki, A., et al., Green coffee bean extract and its metabolites have a hypotensive effect in spontaneously hypertensive rats. *Hypertension Research*, 2002. 25(1): p. 99-107.
16. Guy-Grand, B., Obésité: génétique, physiopathologie et thérapeutique à l'aube d'une révolution conceptuelle. 2005: Institut Pasteur, Centre d'information scientifique.

17. Liotta, S., *Obesita e le adiposità localizzate*. 1974, Roma.
18. Anthoni, C. and N. Kolthoff, *Fondamenti di anatomia e fisiologia dell'uomo*, C.E. Ambrosina, Editor. 1977: Milano. p. 433.
19. Herling, A.W., et al., Pharmacodynamic profile of a novel inhibitor of the hepatic glucose-6-phosphatase system. *Am J Physiol*, 1998. 274(6 Pt 1): p. G1087-93.
20. Simon, C., et al., Upregulation of hepatic glucose 6-phosphatase gene expression in rats treated with an inhibitor of glucose-6-phosphate translocase. *Arch Biochem Biophys*, 2000. 373(2): p. 418-28.
21. Lafay, S., et al., Chlorogenic acid is absorbed in its intact form in the stomach of rats. *J. Nutr*, 2006. 136(5); 1192-1197
22. Lafay, S., et al., Absorption and metabolism of caffeic acid and chlorogenic acid in the small intestine of rats. *Br. J. Nutr*, 2006. under press.