

Green coffee extract Svetol[®] can manage weight: a review

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INTRODUCTION

The prevalence of excess weight and obesity has developed worldwide to epidemic proportions. A growing number of cases can be seen, as much in the United States as in Europe, in Japan or in developing countries (8). According to the World Health Organisation (WHO), in 2004, 175 million people were suffering from diabetes in the world. Estimates mention more than 366 million people by the year 2030 (21). Except for genetic factors, our diet and the lack of exercise are today the main risk factors that intervene in these degenerative diseases. 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, 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. It is in this context that the decaffeinated green coffee beans extract Svetol has been developed by Berkem. This review presents epidemiological data and the studies carried out on the efficacy and the mechanism of action of Svetol.

ABSTRACT

*This review presents the different works investigated on Svetol[®] - a green coffee bean extract rich in chlorogenic acids with specific ratio between 5-caffeoylquinic acid and other caffeoylquinic acid isomers - in terms of efficacy on weight management and mechanism of action. The two clinical trials indicated a significant decrease ($p < 0.001$ vs placebo group) of weight after 60 days of 400 mg daily supplementation and a significant decrease ($p < 0.05$) of post-load glycaemia compared to the one obtained before supplementation. A complementary *in vitro* study showed that Svetol[®] inhibits the glucose-6-phosphatase (G-6-Pase), hepatic enzyme involved in the glucose release in the bloodstream. Thus, Svetol[®] can reduce weight in humans by regulating the blood sugar concentration via an action on the G-6-Pase.*

EPIDEMIOLOGICAL EVIDENCE

Due to this increasingly worrying public health problem, numerous epidemiological studies have been investigated to establish links between certain dietary habits or life styles and the risk of developing obesity or type 2 diabetes. Here, we are going to focus on the specific link between coffee consumption and the risk of developing type 2 diabetes.

As the Finns are the largest coffee consumers in the world, several teams of scientists studied this population to determine the impact of this consumption on health (4, 19). One of these studies, carried out on 14,629 Finns monitored on average for 12 consecutive years, reported that the relative risk of developing type 2 diabetes decreases by 61% ($p < 0.001$), both sexes considered together, for individuals consuming 10 cups or more per day compared with individuals consuming 2 cups or less. For women, the risk is even reduced by 79% ($p < 0.001$) (19). Similar results have been obtained in Japanese(9) and American (17) populations, which suggests that a high consumption of coffee, non-dependent on the ethnic origin, can reduce the risk of developing type 2 diabetes.

To conclude, during the last 5 years, 8 studies including no less than 202,050 consumers spread over 3 continents - Europe, America and Japan - have clearly brought to light a mean reduction of 40% in the risk of type 2 diabetes in individuals consuming large quantities of coffee (≥ 5 cups/day) (2). Moreover, various authors of epidemiological or clinical studies (9, 15, 20) suggest or agree that the chlorogenic acids - widely present in coffee - do play a highly influential role in protecting against blood sugar problems.

Based on these results and a complete bibliographical study (2), Svetol has been developed and studied in order to propose a possible help for weight management.

HUMAN STUDIES ON SVETOL

Blood Sugar regulation: a prospective study (3)

This prospective study has been investigated in order to evaluate if Svetol could decrease post-prandial blood glucose concentration in humans.

1. Study design

Fifteen 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 (OGTT) before and after supplementation with Svetol. The supplementation consisted in 3 tablets daily - 1 in the morning, 1 at noon and 1 in the evening with food and a glass of water - during forty days. Each tablet contains 200 mg of Svetol. Every participant was given treatment sufficient for 40 days (two jars) when they began the study. The volunteers were asked not to modify their diet and their sporting activity during this period. Before and after the supplementation period, volunteers were submitted to an OGTT.

2. Results

After Svetol's supplementation during forty days, post-load glycaemia decreased significantly compared to the post-load glycaemia obtained before the supplementation ($p < 0.05$, figure 1).

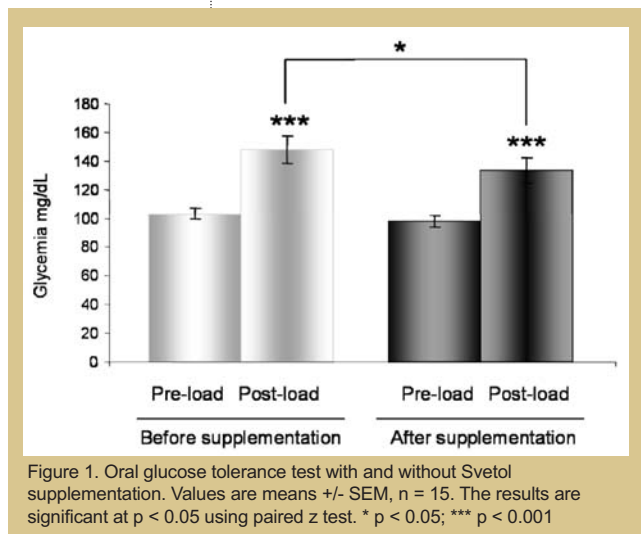


Figure 1. Oral glucose tolerance test with and without Svetol supplementation. Values are means \pm SEM, $n = 15$. The results are significant at $p < 0.05$ using paired z test. * $p < 0.05$; *** $p < 0.001$

Looking at the raw data (not shown), it appeared that 10 volunteers had reductions in their glucose serum levels while five had an increase of this parameter. Sixty-six percent of the participants had an improvement percent ranging from 5% to 100%, with an average at 48%. For these 10 volunteers, the glucose tolerance was highly

and significantly decreased after the Svetol's supplementation compared to the glucose tolerance obtained before the supplementation (figure 2).

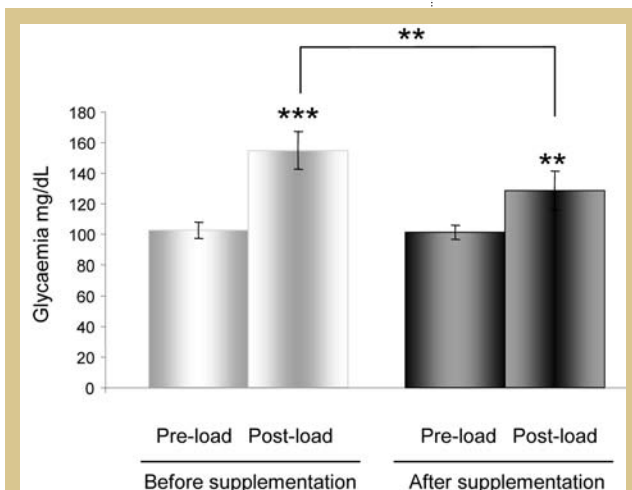


Figure 2. Oral glucose tolerance test with and without Svetol supplementation on 10 subjects responding to the supplementation. Values are means \pm SEM, n = 10. The results are significant at $p < 0.05$ using paired z test. ** $p < 0.01$; *** $p < 0.001$

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

3. Conclusion

To conclude, these preliminary results suggest that Svetol is able to modulate glucose metabolism and that this modulation could have an effect on weight management.

Weight management: a double blind, placebo controlled clinical trial(5)

1. Study design

In order to test the effects of the green coffee extract Svetol on weight loss, fifty volunteers of both sexes, aged from 19 to 75, with body mass index superior to 25 were selected. They were randomised in two groups: control group (n = 20) receiving a placebo, treated group (n = 30) receiving Svetol. Each volunteer took one capsule of Svetol or placebo twice a day with the main meal, for 60 days. Active capsules contained 200 mg of Svetol per capsule. Placebo capsules contained the same components as the active capsules; Svetol was substituted by an identical amount of maltodextrin (200 mg). Changes in weight, body mass index (BMI) and Muscle Mass/Fat Mass ratio (MM/FM) were recorded at T0 and T60.

2. Results

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%) ($p < 0.001$, figure 3). Consequently, body mass index decreased significantly in the Svetol group compared to the control group (not shown). Moreover, MM/FM ratio was significantly increased in the Svetol group compared to the control group: $4.1 \pm 0.7\%$ vs $1.6 \pm 0.6\%$ respectively ($p = 0.01$, figure 3).

3. Conclusion

The significant decrease of weight and body mass index and the significant increase of the MM/FM ratio show that Svetol is able to

exacerbate the effect of a bland low caloric diet in volunteers who are overweight. This effect could be explained by an increase of the consumption of fatty deposits, as shown by the change in the MM/FM ratio, and by preventing them from being accumulated. To conclude, Svetol could be used to aid the recommended diet in a useful and positive manner.

MECHANISM OF ACTION

1. Bibliographical study

On the basis of the epidemiological data reporting a reduced risk of developing type 2 diabetes in high coffee consumers, thanks to

a high content in chlorogenic acids, numerous works have been investigated to understand how these compounds could have such an effect. *In vitro* and *in vivo* studies have shown that pure 5-caffeoylquinic acid - the most represented chlorogenic acid in coffee - inhibits glucose-6-phosphatase (Glc-6-Pase), hepatic enzyme involved in the glucose release from the liver in blood circulation (1, 6, 10, 16). When the glucose level in blood circulation is lower than 1g/L, the hepatic Glc-6-Pase synthesizes glucose by hydrolysing glucose-6-phosphate (G6P) and release glucose into the bloodstream. It's glycogenolysis. If this sequence is interrupted the fatty reserves are used for the production of energy. However no data is available in the current bibliography on the activity of a complex composition such as Svetol.

2. Svetol mechanism of action (12)

Based on this research and the two further

clinical trials carried out on the efficacy of Svetol on post-prandial glycaemia and on weight loss, the activity of Svetol on the glucose-6-phosphatase has been investigated. The aim of this *in vitro* study was to evaluate if Svetol, green coffee extract concentrated in chlorogenic acids with specific ratios between 5-caffeoylquinic acid and other caffeoylquinic acid isomers, could inhibit the activity of hepatic glucose-6-phosphatase. Three concentrations have been tested, equivalent to 157 mg, 315 mg and 472 mg of Svetol per liter of solution. After incubation of human liver microsomes with or without Svetol, we observed that Svetol is able to inhibit competitively the Glc-6-Pase, especially its T1 unit, at 315 mg/L and 472 mg/L.

3. Conclusion

We established for the first time that Svetol - a complex ingredient extracted from selected green coffee beans - is able to inhibit the T1 unit of the Glc-6-Pase in human microsomes in a significant and competitive manner. Moreover, the *in vitro* active doses are equivalent to the daily recommended dose of Svetol.

These results are primarily linked to the post-prandial blood sugar regulation and the fat burning action of Svetol demonstrated in the clinical studies.

DISCUSSION / CONCLUSION

Obesity is a serious public health problem. Overweight and obesity are the cause of health problems of varying degrees of seriousness: asthenia, osteo-articular, psychological and cardio-vascular problems. 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 and the intake of sugar 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 hyperglycaemia) enters into the adipocytes where it is stored as fat reserves (14). 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 glycaemia level.

The aim of these different works (presented above) was to evaluate if the green coffee extract Svetol 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 (1, 6). The significant decrease of weight and fat mass showed that Svetol is able to exacerbate the effect of a bland low caloric

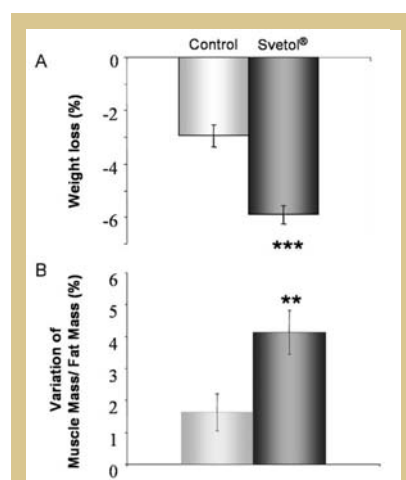


Figure 3. (A) Weight loss (%) and (B) variation of Muscle Mass/ Fat Mass ratio (MM/FM) after 60 days of treatment. Values are means \pm SEM, n = 20 for control group, n = 30 for Svetol group. Means are significantly different (** $p < 0.01$; *** $p < 0.001$ vs control group)

diet in volunteers who were overweight. This effect could be explained by increasing the consumption of fatty deposits, as shown by the change in the MM/FM ratio, and by preventing them from being accumulated (5). From results presented here and bibliography, Svetol could decrease weight by inhibiting the activity of glucose-6-phosphatase (1, 3, 6), and therefore limit the release of glucose into the general circulation (3, 7, 18). 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) utilisation of fat reserves, as a source of energy and therefore, as in the previous case, a case of loss of weight. However, the mechanism proposed depends on the bioavailability of chlorogenic acid. Recent studies have shown that 5-caffeoylquinic acid is absorbed under intact form from the stomach in rats (11). Moreover, in humans, 3-, 4- and 5-caffeoylquinic acids are detected in plasma after coffee consumption (13). These results suggest 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 proposed mechanism.

To conclude, Svetol has demonstrated its validity and could be used to aid the recommended diet in a useful and positive manner.

REFERENCES AND NOTES

- (1) W. J. Arion, W. K. Canfield, F. C. Ramos, P. W. Schindler, H. J. Burger, H.

- Hemmerle, G. Schubert, P. Below, and A. W. Herling, "Chlorogenic acid and hydroxynitrobenzaldehyde: new inhibitors of hepatic glucose 6-phosphatase," Arch Biochem Biophys, 339:2 (1997), 315-322.
- (2) BERKEM Group, Svetol Technical File Vol. Revision05, Nov. 2005.
- (3) J. Blum, B. Lemaire, and S. Lafay, "Svetol®, a decaffeinated green coffee extract, decreases the glycemia after an oral glucose test tolerance," Nutrafoods, Submitted (2007).
- (4) S. Carlsson, N. Hammar, V. Grill, and J. Kaprio, "Coffee consumption and risk of type 2 diabetes in Finnish twins," Int J Epidemiol, 33:3 (2004), 616-617.
- (5) S. O. Dellalibera, B. Lemaire, and S. Lafay, "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, 3 (2006), 1-4.
- (6) H. Hemmerle, H. J. Burger, P. Below, G. Schubert, R. Rippel, P. W. Schindler, E. Paulus, and A. W. Herling, "Chlorogenic acid and synthetic chlorogenic acid derivatives: novel inhibitors of hepatic glucose-6-phosphate translocase," J Med Chem, 40:2 (1997), 137-145.
- (7) A. W. Herling, H. J. Burger, D. Schwab, H. Hemmerle, P. Below, and G. Schubert, "Pharmacodynamic profile of a novel inhibitor of the hepatic glucose-6-phosphatase system," Am J Physiol, 274:6 Pt 1 (1998), G1087-1093.
- (8) I. O. T. IOTF, "www.iotf.org, International Association for the Study of Obesity," (consulted in october 2006).
- (9) A. Isogawa, M. Noda, Y. Takahashi, T. Kadowaki, and S. Tsugane, "Coffee consumption and risk of type 2 diabetes mellitus," Lancet, 361:9358 (2003), 703-704.
- (10) K. L. Johnston, M. N. Clifford, and L. M. Morgan, "Coffee acutely modifies gastrointestinal hormone secretion and glucose tolerance in humans: glycemic effects of chlorogenic acid and caffeine," Am J Clin Nutr, 78:4 (2003), 728-733.
- (11) S. Lafay, A. Gil-Izquierdo, C. Manach, C. Morand, C. Besson, and A. Scalbert,

- "Chlorogenic acid is absorbed in its intact form in the stomach of rats," J. Nutr, 136:5 (2006), 1192-1197.
- (12) S. Lafay, C. Henry-Vitrac, J. Merillon, and X. Vitrac, "Svetol®, a decaffeinated green coffee extract inhibits hepatic Glucose-6-phosphatase," J Agric. Food Chem., Submitted.
- (13) M. Monteiro, A. Farah, D. Moreira, C. Donangelo, and L. Trugo, "Chlorogenic acids are absorbed in humans," Proc. International Conference on Coffee Science (Montpellier, 2006), p. 95.
- (14) R. Murray, D. Granner, P. Mayes, and V. Rodwell, Biochimie de Harper, 25ème Ed, Edition De Boeck ed., Les Presse de l'Université de Laval, 2003.
- (15) A. Reunanen, M. Heliövaara, and K. Aho, "Coffee consumption and risk of type 2 diabetes mellitus," Lancet, 361 (2003), 702-704.
- (16) D. V. Rodriguez de Sotillo and M. Hadley, "Chlorogenic acid modifies plasma and liver concentrations of: cholesterol, triacylglycerol, and minerals in (fa/fa) Zucker rats," J Nutr Biochem, 13:12 (2002), 717-726.
- (17) E. Salazar-Martinez, W. Willett, A. Ascherio, J. Manson, M. Leitzmann, M. Stampfer, and F. Hu, "Coffee consumption and risk for type 2 diabetes mellitus," Ann Intern Med, 140:1 (2004), 1-8.
- (18) C. Simon, A. W. Herling, G. Preibisch, and H. J. Burger, "Upregulation of hepatic glucose 6-phosphatase gene expression in rats treated with an inhibitor of glucose-6-phosphate translocase," Arch Biochem Biophys, 373:2 (2000), 418-428.
- (19) J. Tuomilehto, G. Hu, S. Bidel, J. Lindstrom, and P. Jousilahti, "Coffee consumption and risk of type 2 diabetes mellitus among middle-aged Finnish men and women," JAMA, 291:10 (2004), 1213-1219.
- (20) R. van Dam and E. Feskens, "Coffee consumption and risk of type 2 diabetes mellitus," Lancet, 360:9344 (2002), 1477-1478.
- (21) S. Wild, G. Roglic, A. Green, R. Sicree, and H. King, "Global prevalence of diabetes," Diabetes Care, 27:5 (2004), 1047-1053.

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Degradation Rate by digestive enzyme	Less than 0.4%	Less than 13%	Less than 11%
Acid & heat stability	No decomposition under the Condition of Ph 2.5-8 and heated to 100°C	Not stable under the condition of Ph 4-6 and heated to 80°C	Not stable under the condition of Ph 4-6 and heated to 80°C



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