

**CLINICAL TRIAL ON THE EFFECTS OF SWEETENERS
DERIVED FROM THE STEVIA PLANT ON GLUCOSE LEVELS**

**IN CONJUNCTION WITH THE ENDOCRINOLOGY/METABOLISM
AND DIABETIES UNIT OF THE "EVGENIDEIO CLINIC"**

Objective: To study the acute effect of stevia plant extracts on glucose, insulin and GLP-1 levels after eating a mixed meal.

Subjects: 42 subjects (16 men, 26 women), age 20-60 with metabolic syndrome and pre-diabetes were studied. The study was performed by the Evgenideio Clinic.

Method: In order to achieve the objective of this clinical study, the subjects made 2 visits to the Evgenideio Clinic. At the first visit, the participants were given a solution (intervention) containing stevia plant extract corresponding to 60 mg of stevia equivalents 45 minutes before the mixed meal. At the second visit, a placebo solution (a solution which had the same composition as the intervention solution but without the addition of stevia plant extracts) was given to participants before the mixed meal. During both visits, blood samples were taken at -45, 0, 30, 60, 120, 180 and 240 minutes. Glucose, insulin, c-peptide and GLP-1 were found in all samples. Glucagon, insulin, c-peptide and GLP-1 were measured at -45, 0 and 30 minutes, and MATSUDA, GIR, HOMA indicators were also studied, as were Δ (30 - 0 minutes) insulin / Δ (30 - 0 minutes) glucose, Δ (-45 - 0 minutes) insulin / Δ (-45 - 0 minutes) glucose, both after consumption of the placebo solution and after consumption of the intervention solution (where Δ = difference).

The mixed meal consumed by the people who participated in this study consisted of: two slices of white bread (60g), cheese (30g), ham (30g), margarine (10g) and commercial orange juice (250ml).

The patients did not take any medicines on the morning of the test and arrived without having eaten. They remained on the site of the clinical trial throughout the procedure and did not smoke.

Results: Serum glucose, insulin, c-peptide and GLP-1 results as determined at different times and during consumption of the placebo solution and during consumption of a solution containing extracts from the stevia plant are listed below:

- Glucose: There was no significant difference in glucose levels at the different times, other than in the glucose value at time -45 minutes ($p < 0.05$) (before taking the stevia or the placebo). It is interesting that a marginal statistically significant difference in the change in glucose $\Delta\text{Glu } 0 - (-45)$ ($p = 0.06$) was observed between the stevia and the placebo.
- Insulin: There was no significant difference in insulin levels at the different times. A marginal statistically significant difference in the change in insulin $\Delta 60-0$ ($p = 0.06$) and $\Delta 60-30$ ($p < 0.05$) was observed between the stevia and the placebo. Compared to when the placebo solution was consumed, there was a delay in the peak insulin secretion following consumption of the stevia solution.
- c-peptide: c-peptide followed the same pattern as insulin, as the only time when values differed statistically between taking the solution with stevia plant extracts and taking the placebo solution was 30 mins ($p = 0.056$).
- GLP-1: GLP-1 values did not differ statistically between taking the solution with stevia plant extracts and taking the placebo solution at any of the various times.
- Glucagon: Taking the solution with stevia plant extracts under fasting conditions significantly reduced glucagon levels relative to taking the placebo solution at 45 minutes, without, however, there being any statistically significant reduction in glucose levels, although there was a trend towards lower glucose levels after taking the stevia solution. This statistically significant decrease in glucagon was not maintained after the mixed meal as consumed.

Further statistical analysis of the above results showed that there is no significant difference in static insulin resistance and insulin sensitivity indices, or in dynamic insulin sensitivity markers between taking a solution with stevia plant extracts and taking a placebo solution before eating a mixed meal.

Conclusions: Acute consumption of a solution with stevia plant extracts of an amount corresponding to 60 mg of steviol equivalents **did not negatively affect the glycemic profile of patients with metabolic syndrome**, and also it did not alter insulin, c-peptide or GLP-1 excretion significantly after eating a mixed meal. Administration of a 60 mg steviol equivalent solution (which corresponds to an amount someone might normally consume) led to a reduction - although not statistically significant - in fasting glucose after 45 minutes without stimulating insulin secretion but reducing glucagon excretion. **This action is desirable** as increased secretion of glucagon helps to deregulate fasting glucose and postprandial glucose.