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Hypoglycaemic and hypotriglyceridaemic postprandial properties of organic silicon

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ABSTRACT

The positive effects of Si on cardiovascular disease (CVD) and diabetes mellitus (DM) have been mooted. However, the effect of Si on postprandial state has not been evaluated. Postprandial hypertriglyceridaemia and hyperglycaemia are considered risk factors for cardiovascular disease. The effects of Si supplementation on postprandial hypertriglyceridaemia and hyperglycaemia were tested in two groups of 6 healthy male Wistar rats after acute and 1-week administrations. In the postprandial study rats were administered 1 ml of olive oil and glucose solution (0.5 g/kg bw) by oral gavage. The results indicate that Si reduced glucose and triglycerides digestion and absorption from the first dose, although the effects were stronger after 1-week treatment. This study clearly suggests Si supplementation can be a powerful tool in the management of postprandial hypertriglyceridaemia and hyperglycaemia.

1. Introduction

There is growing evidence that the postprandial state is an important factor in chronic diseases. Particularly, postprandial hypertriglyceridaemia and hyperglycaemia are considered risk factors for cardiovascular disease (CVD) and metabolic syndrome (SM) in that they induce endothelial dysfunction and oxidative stress (Ceriello et al., 2002). Postprandial hyperglycaemia is related to macro and microvascular complications in type 2 Diabetes mellitus (DM2) patients (Ceriello, 2005). Similarly, postprandial hypertriglyceridaemia is associated with atherosclerosis and macrovascular disease in DM2 patients (Kumar, Madhu, Singh, & Gambhir, 2010).

Nowadays, people in Western countries eat several times per day; they usually consume high-calorie foods and are in permanent postprandial state. This situation leads in turn to cellular dysfunction and disease. Thus, intervention to reduce the intensity and length of the postprandial period has been suggested (Burton-Freeman, 2010).

Silicon (Si) is an essential micronutrient (Carlisle, 1972) present mainly in plant foods, water, and beer (Jurkić, Cepanec, Pavelić, & Pavelić, 2013). Si supplementation has been linked to the prevention of DM2 and CVD among others properties (Martin, 2013). Nevertheless, the specific mechanisms involved in those effects have not been completely described. Our previous articles (Garcimartín, Santos-López, Bastida, Benedí, & Sánchez-Muniz, 2015; Garcimartín, Merino et al., 2015) demonstrated that when included in a meat matrix, Si alleviated the deleterious effects of a high-saturated/high-cholesterol diet on lipoprotein profile and liver antioxidant defences of one-year-old Wistar rats. However, the impact of Si on the postprandial state, which could contribute to such effects, has not been evaluated. Therefore, we investigated the ability of Si to reduce postprandial hyperglycaemia and hypertriglyceridaemia in healthy Wistar rats.

2. Materials and methods

Silicon determination. The amount of Si in tap water, food and in the assayed Silicium organique G57™ was analysed by ICP-OES (Perkin Elmer Optima model 3200 RL, Boston, MA, USA) following the method of Granero, Vicente, Aguilar, Martínez-Para, and Domingo (2004).

2.1. α-Glucosidase activity

α-Glucosidase activity was measured *in vitro* according to the Garcimartín, Benedí, Bastida, and Sánchez-Muniz (2015) method.

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The inhibitory capacity of organic Si (Silicium organique G57™, Glycan Group, Geneva, Switzerland) was evaluated at a 40 mg/ml of maltose as substrate of reaction. The final concentration of Si in the experiment was 55 μg/ml.

2.2. In vivo experimental design

Two-month-old male Wistar rats, weighing approximately 200 g, were housed in groups under controlled temperature (22.3 ± 1.9 °C) and light (12 h light–12 h dark cycle) in the Centro de Experimentación Animal of the Alcalá University, Madrid, Spain (register number # ES280050001165). The study was approved by the Spanish Science and Technology Advisory Committee and by an ethics committee of the Universidad Complutense of Madrid (Spain). Experiments were performed in compliance with Directive 86/609/EEC of 24th November 1986 (modified by Directive 2003/65/CE) for the protection of scientific research animals.

2.2.1. Acute administration

Animals were divided in two groups of six rats each corresponding to control and Si treatment. Postprandial study was performed after an overnight fast. Control animals were administered by oral gavage 1 ml of olive oil and glucose solution (0.5 g/kg bw). Si group received also the olive oil and glucose solution together with 2 mL of organic Si containing 200 mg/L of Si element, which corresponds to a dose of Si of 2 mg/kg wb/day. This dose was selected after considering the Si intake registered in some Asians countries in comparison with Western countries (Jugdaohsingh et al., 2002). Blood samples were taken from the tail vein at 0, 1, 2, 3 and 4 h.

2.2.2. Subchronic administration

The same rats from the acute study received once-a-day treatment (2 mL of organic Si by oral gavage), during other 6 days. Tap water and food (Global diet 2014, Harlan, Barcelona, Spain) were provided *ad libitum*. The amount of Si analysed by ICP-OES was 1.2 mg/L in tap water and 5.0 mg/kg in the diet. Considering an average consumption of 10 mL/100 g bw/day of water and 10 g/100 g bw/day of food, both Control and Si groups received a basal amount of 0.6 mg of Si/kg bw/ day. Furthermore, the Si group got an extra Si administration of 2 mg/kg bw/day.

The postprandial study was repeated the last day corresponding with the seventh administration. After 4 h rats were anaesthetized with isoflurane (5%), blood from the descending aorta extracted and the small intestine removed and properly frozen and kept at −80 °C till analysis.

2.3. Plasma analysis

Plasma was isolated by centrifugation at 1500g at 4 °C. Triglycerides and glucose were tested spectrophotometrically (LT-4000, Labtech International Ltd., United Kingdom) by enzymatic colorimetric tests (Spinreact S.A., Barcelona, Spain).

2.4. SGLT1 levels

Sodium-dependent glucose transporter 1 (SGLT1) levels were measured in duodenum and jejunum by Western Blot following Garcimartín, Merino et al. (2015) protocol. Membranes were incubated overnight at 4 °C with 1/1000 polyclonal anti- SGLT-1 (H-85) antibody (sc-98974, Santa Cruz Biotechnology, Quimigen, Madrid, Spain).

2.5. Statistical analyses

Data are expressed as the mean ± standard error. Statistical analysis was performed using the version 19.0 of SPSS (SPSS Inc., Chicago, Illinois, USA). The general linear model of repeated measures was used to evaluate the differences in α-glucosidase activity, and postprandial glucose and triglycerides concentration. Comparisons between groups or studies were made by unpaired Student's *t* test. Differences were considered significant at $p < 0.05$.

3. Results

3.1. α-Glucosidase activity

Si significantly reduced (at least $p = 0.032$) the *in vitro* α-glucosidase activity from 15 to 90 min. The glucose concentrations were diminished by 15% in comparison with control at 45 min ($p < 0.001$) (Table 1). A linear adjustment of glucose formation-time was found in the two samples ($p < 0.001$). Si showed 17% lower slope than control.

3.2. Hypoglycaemic effect of Si

Fig. 1A shows plasma glucose concentration profile corresponding to the acute administration. Si administration changed the postprandial curve of glucose respect to control ($p < 0.001$, repeated measures). Si significantly decreased glucose concentration by 10–18% at 3 h and 4 h ($p = 0.020$ and $p = 0.005$, respectively).

After 1-week of Si administration (Fig. 1B), postprandial glucose was significantly reduced respect to control group ($p < 0.001$, repeated measures), starting at 1 h and keeping it until the end of the study ($p < 0.005$, unpaired Student's *t* test). In this postprandial experiment the 4 h determination was not performed, as anaesthesia has been suggested to affect glycaemia (Zuurbier, Keijzers, Koeman, Van Wezel, & Hollmann, 2008).

The comparison of 0–3 h period between both studies did not show any significantly difference in the control group. On the other hand, significant differences were found in Si-group at 0, 1, 2 and 3 h between the acute and subchronic administration ($p \leqslant 0.001$, unpaired Student's *t* test).

3.3. SGLT-1 levels

Compared to control, Si treatment decreased SGLT-1 levels in duodenum and jejunum portions ($p < 0.01$) by 20% (Fig. 2A and B).

3.4. Effect of Si on triglycerides levels

Acute administration of Si (Fig. 3A) significantly reduced the postprandial triglyceridaemia respect to control ($p < 0.001$, repeated measures), specifically at time 2 and 3 h ($p < 0.001$, unpaired Student's *t* test). On the postprandial study after 1 week treatment (Fig. 3B), Si group showed lower postprandial triglyceridaemia than control group ($p \leqslant 0.001$, repeated measures) since the first hour ($p < 0.005$, unpaired Student's *t* test). Si administration delayed from 2 h to 3 h the pic level observed in the control group.

Table 1
α-Glucosidase activity. Glucose formation (mg/dL).

	Control	Si	*p* (Student's *t* test)
0 min	12.43 ± 1.55	10.36 ± 1.69	0.121
15 min	62.32 ± 3.22	55.03 ± 3.50	0.022
30 min	102.59 ± 4.78	94.39 ± 1.29	0.016
45 min	145.32 ± 1.05	126.26 ± 4.55	<0.001
60 min	176.50 ± 2.38	160.39 ± 5.29	0.001
75 min	203.63 ± 6.51	179.03 ± 6.30	0.002
90 min	218.98 ± 4.11	204.73 ± 8.24	0.032
Slope	27.09 ± 4.04	22.48 ± 3.29	<0.05
R^2	0.974	0.979	

Data are expressed as the mean ± standard deviation.

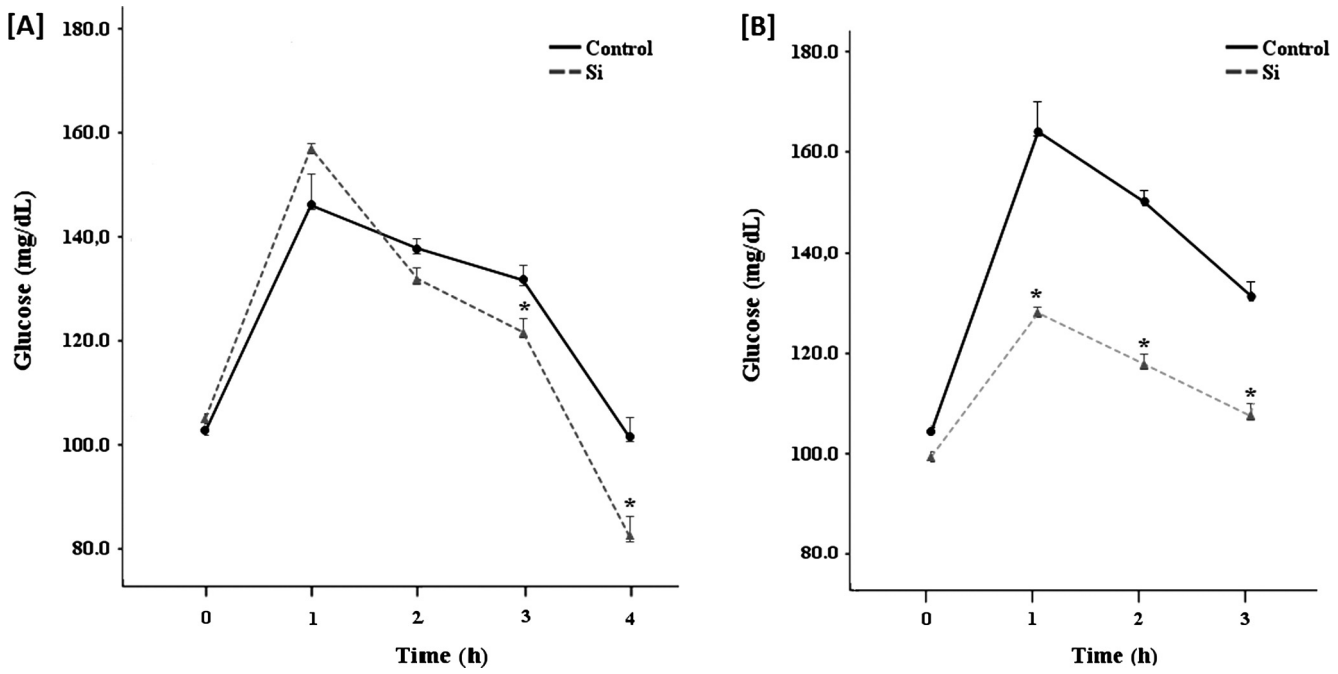

Fig. 1. Postprandial glucose level after oral administration of glucose (500 mg/kg bw) in healthy male Wistar rats. Blood glucose levels (mg/dL) were plotted *versus* time (hours). (A) Acute administration of Si (2 mg/kg bw). (B) After 1 week administration of Si (2 mg/kg bw). n = 6 rats per group. $^{*}p < 0.05$.

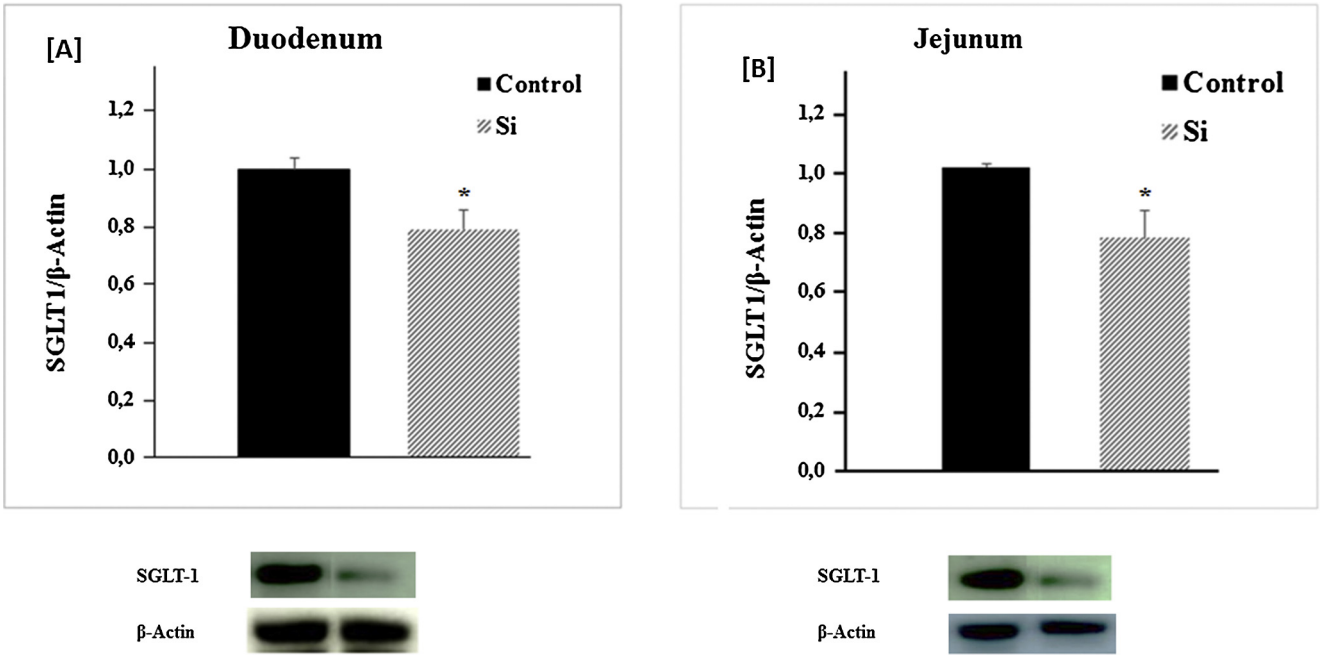

Fig. 2. Effect of 1 week Si administration (2 mg/kg bw) on SGLT1 levels measured by western blot in duodenum and jejunum portions. n = 6 rats per group. $^{*}p < 0.05$.

Significant differences were observed between acute and subchronic studies in Si group fasting levels ($p = 0.002$, unpaired Student's *t* test), and at 1–3 h of postprandial study ($p < 0.01$, unpaired Student's *t* test).

4. Discussion

Our results suggest that Si acts as a powerfully hypoglycaemic and hypotriglyceridaemic agent in healthy young Wistar rats. Furthermore, this study demonstrates new mechanisms linked to Si, and highlights the potential benefits of Si supplementation for CVD and DM2.

The concentration of Si (2 mg/kg bw/day) used in this study was lower than in other studies (Garcimartín, Santos-López et al., 2015; Najda, Gminski, Drożdż, & Flak, 1991; Peluso & Schneemanz, 1994). In humans, this concentration would bring the Si intake of Western populations more into line with the intake of Asians (Jugdaohsingh et al., 2002). Organic Si was chosen because of its water-solubility and it has been considered a suitable source of ortho-silicic acid by EFSA (EFSA Journal, 2016). Moreover, organic Si presents the

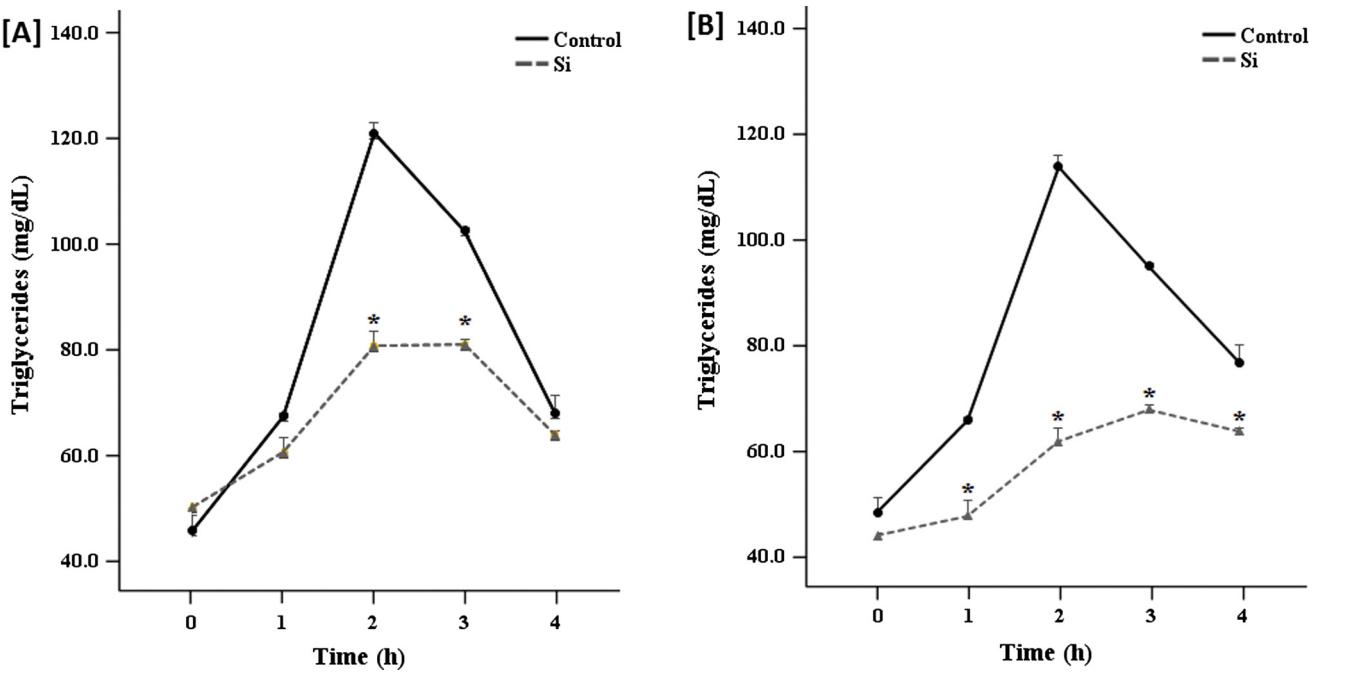

Fig. 3. Postprandial triglyceride levels after oral administration of 1 mL of olive oil in healthy male Wistar rats. Blood triglyceride levels (mg/dL) were plotted *versus* time (hours). (A) Acute administration of Si (2 mg/kg bw). (B) After 1 week administration of Si (2 mg/kg bw). n = 6 rats per group. $^{*}p < 0.05$.

advantage that it can be readily incorporated in a matrix as a functional ingredient, or used directly as a supplement. Taking into consideration the Si content of tap water, food and organic Si it can be calculated that Silicium organique G57™ administrated contributed about 70% to the total Si intake.

Acute administration of Si reduced postprandial hyperglycaemia after 3 and 4 h. This late effect seems to be associated with enhancement of the insulin action. Other minerals (e.g. chromium) have been found to positively interact with insulin (Mertz, 1998). After 1-week-treatment the effects were more evident, which suggests that Si affected gene expression. In fact, lower levels of SGLT1 in duodenum and jejunum portions were found, partially explaining these results, although additional mechanisms should be investigated. Again, inhibition of SGLT1 expression has been found after polyphenol consumption (Solayman et al., 2016). Moreover, significant differences have been reported in fasting glucose in the Si group between the two experiments, possibly related to *in vitro* inhibition of α-glucosidase by Si. Si-enriched spirulina did not affect fasting glucose with respect to the high-fat diet control, but the experimental Si concentration was lower than ours (Vidé et al., 2015). In addition, we demonstrated that the hypoglycaemic effect of Si is especially important in the postprandial state.

Si reduced postprandial triglyceridaemia from the first administration and delayed peaking with respect to the control, suggesting a direct effect on fat digestion or absorption. Again, the two studies show significant differences in the Si group in fasting and postprandial levels, indicating the involvement of other mechanism apart from the inhibition of digestion. These results are in line with our previous article in 1-year-old rats (Garcimartín, Santos-López et al., 2015). There we found that adding Si to a high saturated/high cholesterol diet reduced the effects on triglyceridaemia. Also, the fat content of Chol-Si faeces was higher, probably due to the lower digestion and adsorption demonstrated in the present study. Najda et al. (1991) reported Si-induced hypotriglyceridaemia in healthy rats, but they attributed this effect to changes in the activity of degradation enzymes such as lipoprotein lipases.

We far from know the precise mechanisms by which silicon exerts such hypotriglyceridaemic and hypoglycaemic effects. Although the hypothesis linking Si effects to an electrostatic mechanism cannot be discarded, present results suggest that Si acts regulating the gene-expression of transporters and/or other relevant molecules involved in glucose and lipid metabolisms. Future studies are needed to assess the mechanism involved in the hypotriglyceridaemic effect of Si after 1-week administration and to corroborate that effect in healthy volunteers. In conclusion, this study demonstrated the important role of Si in the postprandial state, reducing the intestinal absorption of glucose and triglycerides. Our new findings support the use of Si as a useful functional ingredient to reduce the risk of chronic disease such as ECV or DM2.

Conflicts of interest

Dr. Alba Garcimartín, Dr. Juana Benedí and Dr. Francisco J. Sánchez-Muniz disclose that they have received research support funding from Glycan Finance corp Ltd (Glycan Group). None of the authors received reimbursement, honoraria, or stipends for their participation in development of these experiments. The research was designed, executed, analysed and communicated only by the six authors. All other authors have no competing interest.

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