ENDOCRINE AND METABOLIC IMPACT OF ORAL INGESTION OF A CAROB-POD-DERIVED NATURAL-SYRUP CONTAINING D-PINITOL: POTENTIAL USE AS A NOVEL SWEETENER IN DIABETES

Juan A Navarro [1,2], Juan Decara [1], Dina Medina-Vera [1,2,3,4], Ruben Tovar [1,2], Antonio J Lopez-Gambero [1,4], Juan Suarez [1,5], Francisco Javier Pavón [1,3], Antonia Serrano [1], Marialuisa de Ceglia [1], Carlos Sanjuan [6], Yolanda Alfonso Baltasar [6], Fernando Rodríguez de Fonseca [1], Elena Baixeras [2,7].

[1]Lab. Medicina Regenerativa, UGC Salud Mental, IBIMA, Hospital Regional Universitario de Málaga, 29010 Málaga, Spain. [2]Facultad de Medicina, Universidad de Málaga, 29010 Málaga, Spain. [3]UGC Corazón, Hospital Universitario Virgen de la Victoria, 29010 Málaga, Spain. [4]Facultad de Ciencias, Universidad de Málaga, 29010 Málaga, Spain.[5]Dpto. de Anatomía Humana, Medicina Legal e Historia de la Ciencia, Universidad de Málaga, 29010 Málaga, Spain. [6]Euronutra S.L. Calle Johannes Kepler, 3, 29590 Málaga, Spain. [7]Dpto. Bioquímica y Biología Molecular, Facultad de Medicina, Universidad de Málaga, 29010 Málaga, Spain.

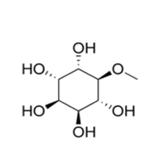
ebaixeras@uma.es

INTRODUCTION

The use of added sugars or non-nutritive sweeteners in processed foods and soft drinks are being blamed for multiple complications associated with obesity and diabetes [1-3]. High fructose content contributes to obesity and liver steatosis, and excessive consumption of non-nutritive sweeteners can generate gut dysbiosis complicating the metabolic control exerted by the liver [1,4-5]. Beyond its evolutionary significance in the selection of foods with a high glucose content as an energy source, the fact is that the consumption of sweets produces a hedonic pleasure in our brain. Then, the challenge stands at: how do we control the use of added sugars while providing a safe, palatable, sweet flavour to foods?. The present work explores an alternative approach, in humans and rodents, for sweetening through the use of a simple carob-pod-derived syrup which contains the inositol D-Pinitol. This inositol is known as an insulin sensitizer in muscle capable of keeping glycaemia while avoiding both unnecessary insulin secretion and the conversion of carbohydrates into fat depots (6).

MATERIAL AND METHODS

Carob Syrup: (InnoSweet®) manufactured by Euronutra SL (Málaga, Spain) containing 45.6% glucose, 47.3% fructose, 0.5% sucrose, and 3.2% D-Pinitol.
Agave Syrup: 75% fructose (control syrup)
Human Volunteers: healthy adult women and men were recruited. Studies were done under fasting conditions.
WISTAR rats, 4-5 week-old male, fasted overnight.
Real-Time qPCR RNA was extracted from rat liver sections (50–80 mg) using the a Trizol®method. PCR reactions were carried out in a CFX96TM Real-Time PCR Detection System (Bio-Rad, CA, USA) for each cDNA template containing the corresponding primer.
Glucose Tolerance Tests (GTT). Rat blood samples were collected from the tail vein at different time points after D-glucose injection. Glucose concentrations were measured with a glucometer (AccuCheck, Roche, Germany).
Statistical Analysis. Graph-Pad Prism 8.0 software was used to analyze the data.

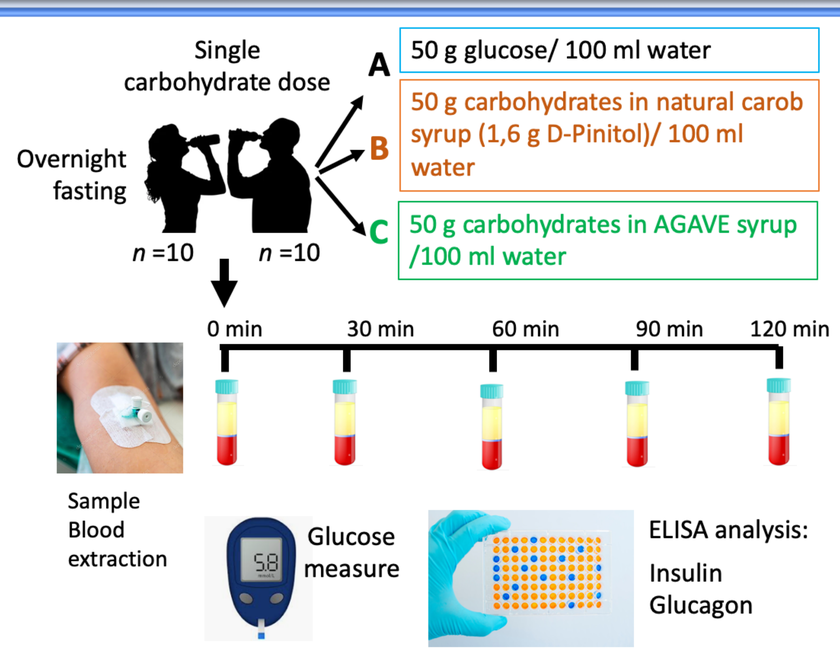


D-(+)-Pinitol


CAROB-POD SYRUP

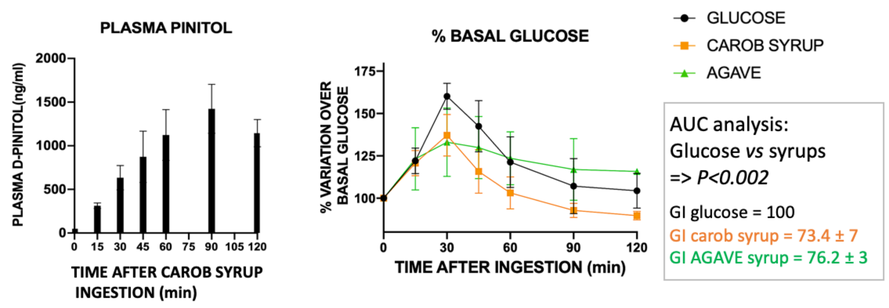
EXPERIMENTAL PROCEDURES IN HUMANS

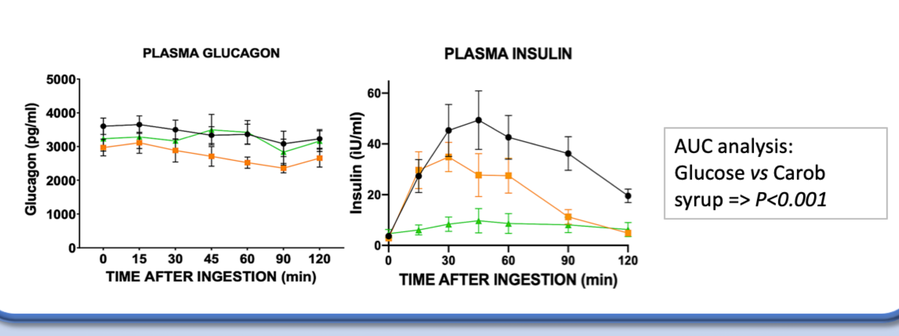
Aims { *1: calculate glycemic index for syrups*
2: analyse glucose homeostasis



RESULTS

Glycemic index and effects on plasma levels of hormones controling glucose homeostasis after acute administration of carob and AGAVE syrups in humans

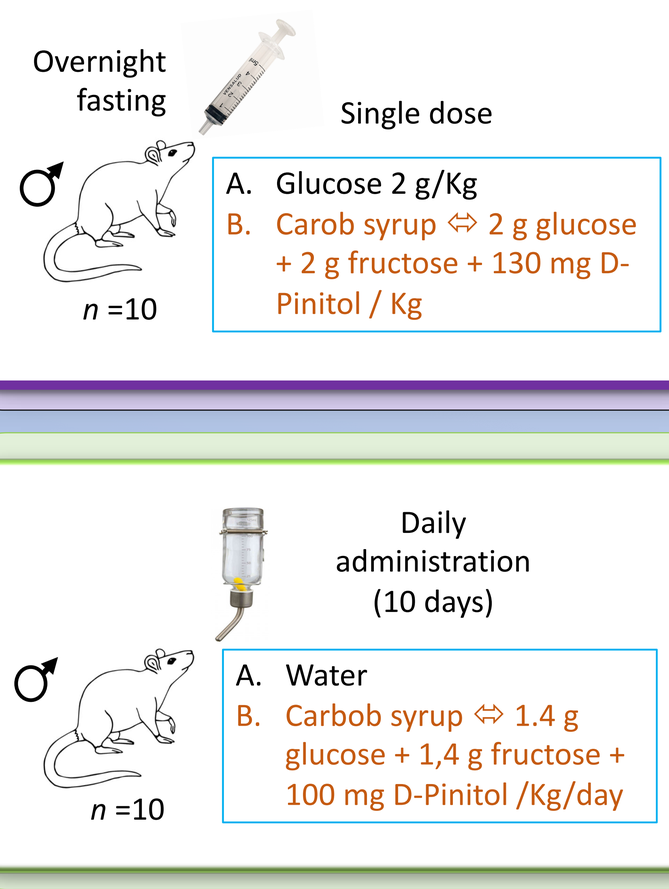


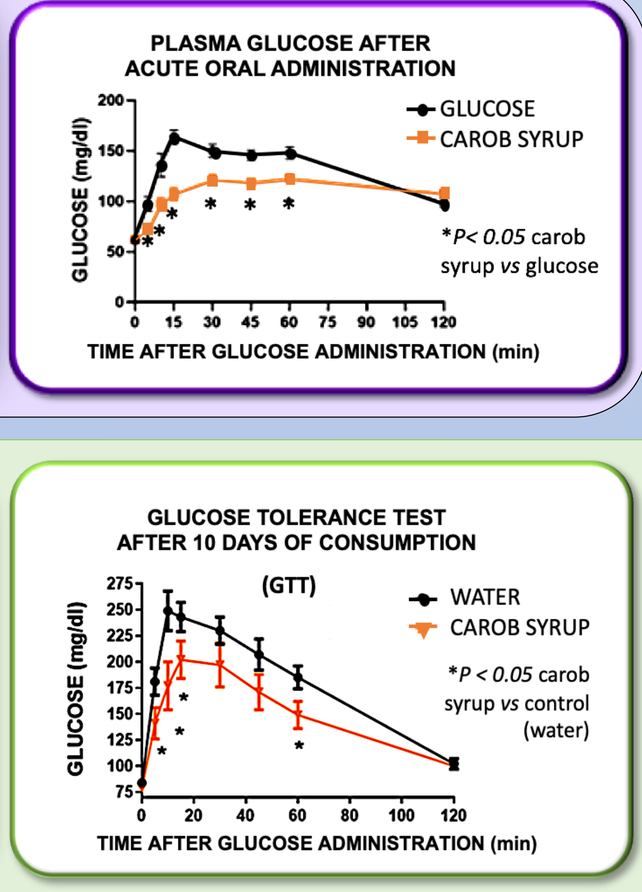


CONCLUSIONS

The acute intake of the carob syrup containing glucose, fructose and D-Pinitol, keeping sweet palatability and the corresponding caloric value, produces shorter in time glucose excursions than those observed for glucose intake alone. Also, both the percentage of change over basal glucose levels and the insulin release induced by the intake of the carob syrup had less intense and shorter durations than those observed for glucose alone. It indicates that the glycemic index of glucose/fructose syrup can be modifyed by adding Pinitol.

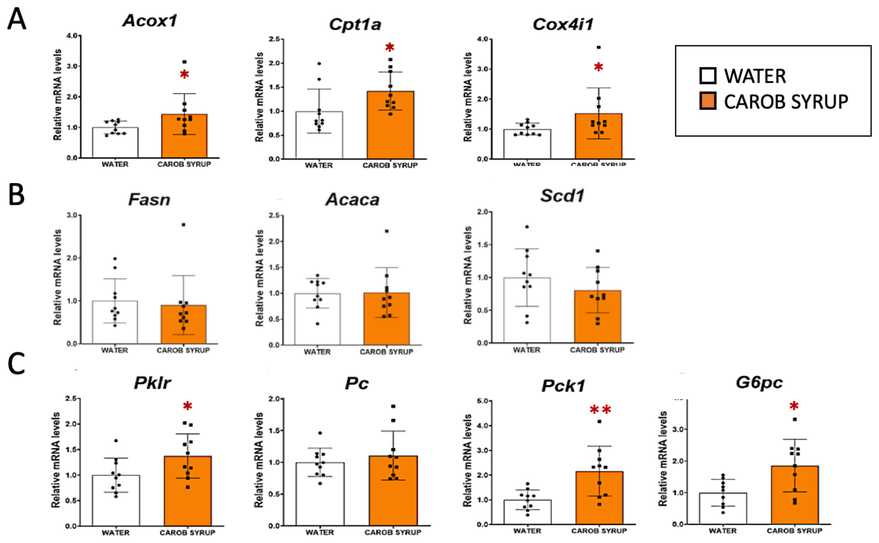
EXPERIMENTAL PROCEDURES IN RATS





RESULTS

Effects of repeated administration for 10 days of carob syrup on the gene expression of the enzymes of the beta-oxidation (A) lipogenesis (B) and gluconeogenic (C) pathways.



Liver biochemistry parameters after 10 days of drinking water or water-diluted carob syrup

	Water	Carob syrup
Total Fat Liver (mg/g)	40.8 ± 1.3	34.8 ± 1.5 (*)
Liver Glycogen (μ/g)	137.7 ± 34.1	76.1 ± 5.2 (*)

CONCLUSIONS

The general profile of carob syrup is that of a safe short-term sweetener; It is capable of favoring the rapid uptake of glucose as well as enhancing the actions of glucagon, seriously compromised in the reduction of hepatic steatosis. Indeed, animals exposed to carob syrup for 10 days show a clear decrease in liver fat and glycogen content, probably as a consequence of a reorientation of hepatic metabolism towards glucose export and lipid oxidation.

Acknowledgements

This work was supported by grants from the following institutions: Ministerio de Economía y Competitividad, Gobierno de España (Grant RTC-2016-4983-1), EU-ERDF-Instituto de Salud Carlos III (Grant PI19/01577), and Consejería de Transformación Económica, Industria, Conocimiento y Universidad de la Junta de Andalucía (Grant P18-TP-5194).

1. Schiano, C *et al Food Res. Int.* **2021**, *142*, 110220.
2. Pang, M.D *et al. Front. Nutr.* **2021**, *7*, 598340. [
3. Greenwood, D.C *et al . Br. J. Nutr.* **2014**, *112*, 725–734.
4. Farup, P.G. *et al. J. Obes.* **2019**, *2019*, 4608315.
5. Bian, X. *et al. Food Chem. Toxicol.* **2017**, *107*, 530–539.
6. Navarro JA *et al*. Nutrients. 2020 Jul 8;12(7):2030. doi: 10.3390/nu12072030.PMID: 32650579.