



IV CONGRESO IBEROAMERICANO DE INGENIERÍA DE LOS ALIMENTOS

Rol del consumo de flavonoides en la modulación de la
respuesta glicémica: estudios preclínicos y experiencias
traslacionales

Adrián Aicardo

Universidad de la República

Organiza:





Diabetes tipo 2 - Realidad epidemiológica

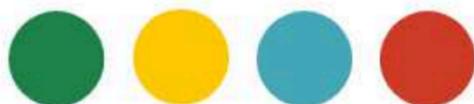
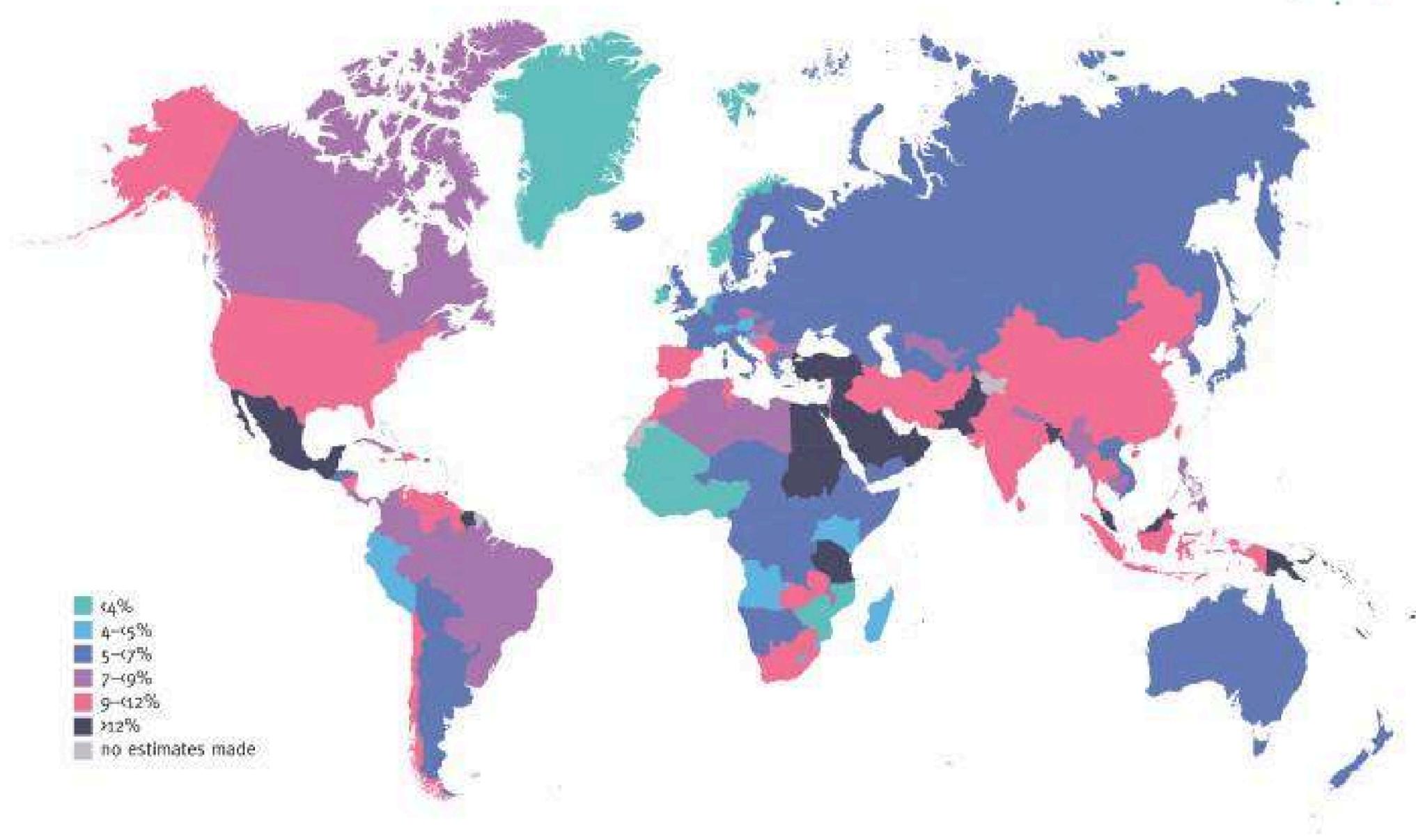
A nivel mundial

Se estima que afecta > 400 millones de personas

Se relaciona a 2 millones de muertes al año

En Uruguay

Prevalencia entre 7-9%





Diabetes tipo 2 - Realidad epidemiológica

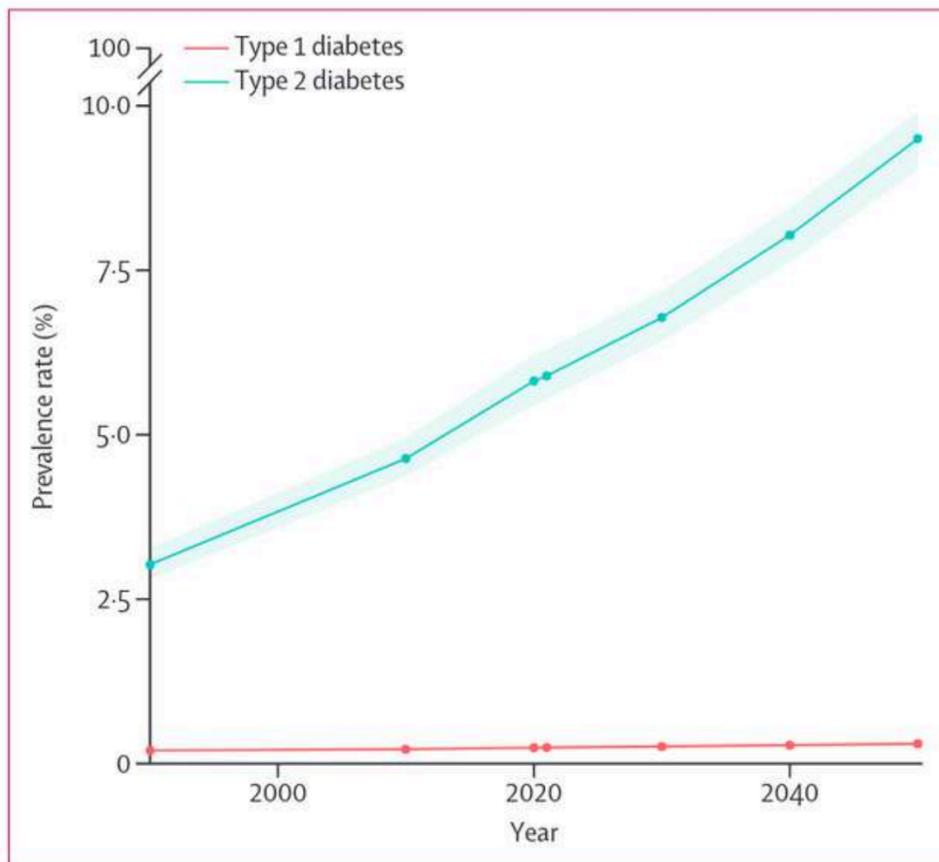
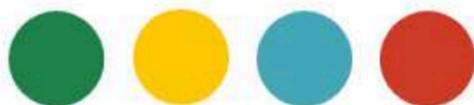


Figure 4: Global age-standardised prevalence of type 1 and type 2 diabetes from 1990 through 2050 forecasts
The shaded area represents 95% uncertainty intervals. Total diabetes is the sum of type 1 and type 2 diabetes.

Se espera que la prevalencia Diabetes mellitus se duplique a nivel mundial para el año 2050

América latina, se estima aumento de prevalencia de 6% a 11%

	DALY count in 2021 (thousands)	Percentage change in DALY count, 1990–2021 (%)
Global	79 200 (67 800 to 92 500)	189.8% (171.1 to 203.4)
Central Europe, eastern Europe, and central Asia	4370 (3670 to 5230)	126.9% (119.3 to 132.4)
Uruguay	38.7 (32.3 to 47.0)	90.9% (76.4 to 111.7)





Diabetes tipo 2 - Relación con alimentación

nature medicine



Article

<https://doi.org/10.1038/s41591-023-02278-8>

Incident type 2 diabetes attributable to suboptimal diet in 184 countries

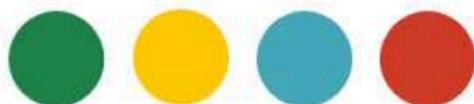
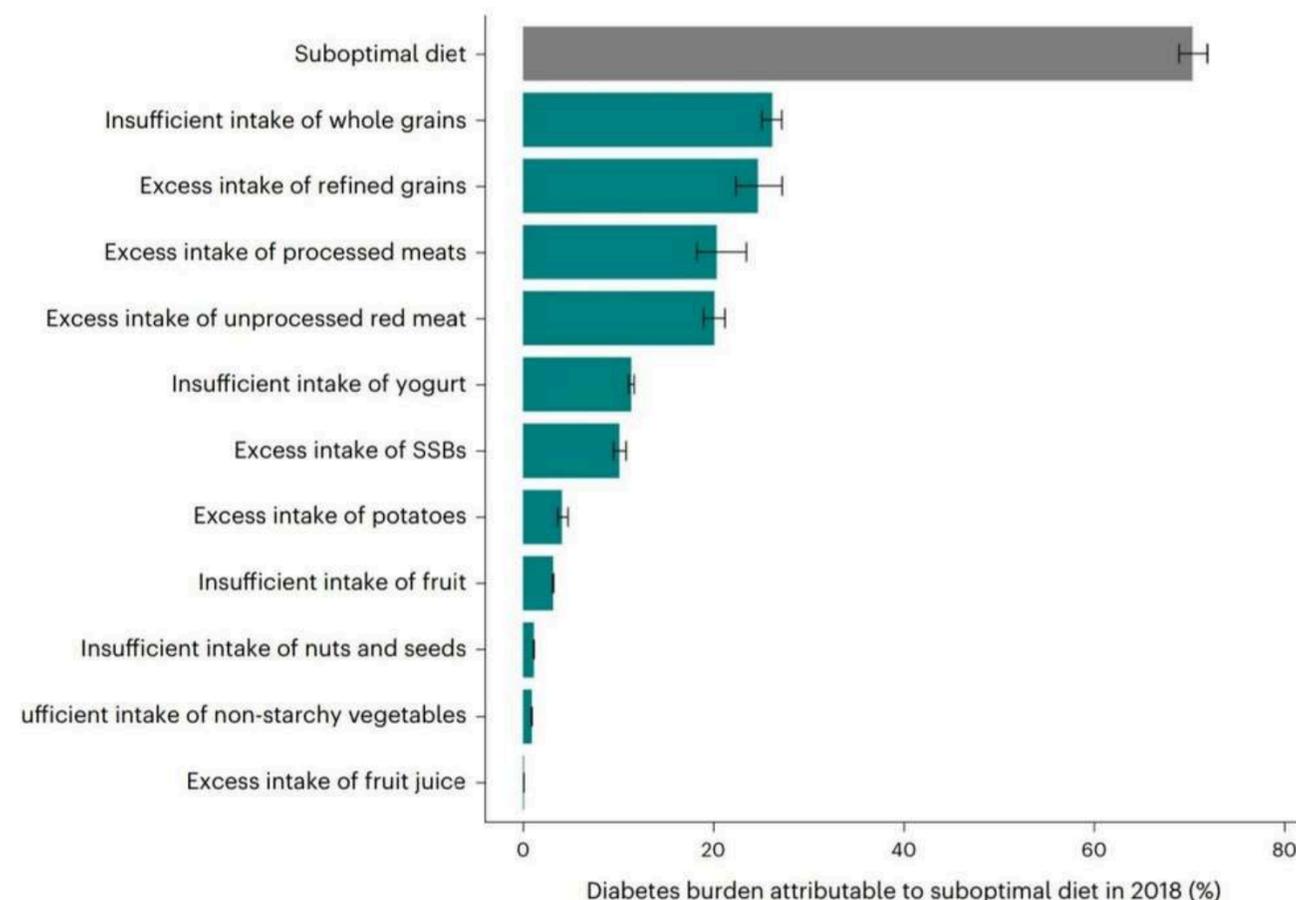
Received: 15 September 2022

Accepted: 28 February 2023

Published online: 17 April 2023

Meghan O'Hearn^{1,2}, Laura Lara-Castor¹, Frederick Cudhea¹, Victoria Miller^{1,3,4}, Julia Reedy¹, Peilin Shi¹, Jianyi Zhang¹, John B. Wong^{5,6}, Christina D. Economos¹, Renata Micha^{1,7}, Dariush Mozaffarian^{1,5,6} & Global Dietary Database*

La incidencia de diabetes tipo 2 es atribuible a dieta subóptima





Diabetes tipo 2 - Relación con respuesta glicémica

Metaanálisis de estudios en cohortes > 100000 participantes cada una

Dietas con alto índice/carga glicémica aumentan riesgo de diabetes tipo 2

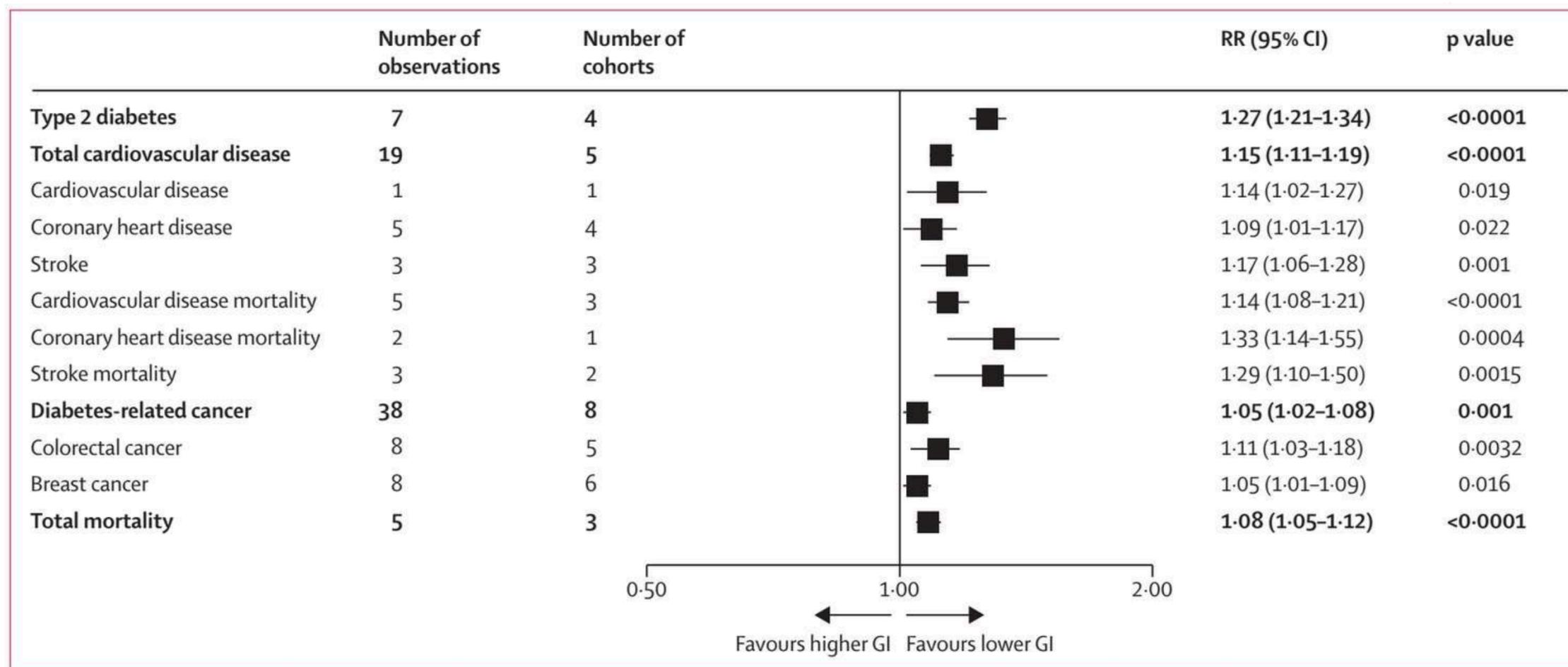
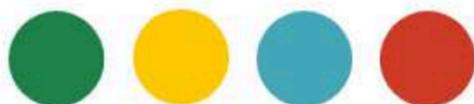


Figure 2: GI exposure and type 2 diabetes, total cardiovascular disease, diabetes-related cancers, and mortality

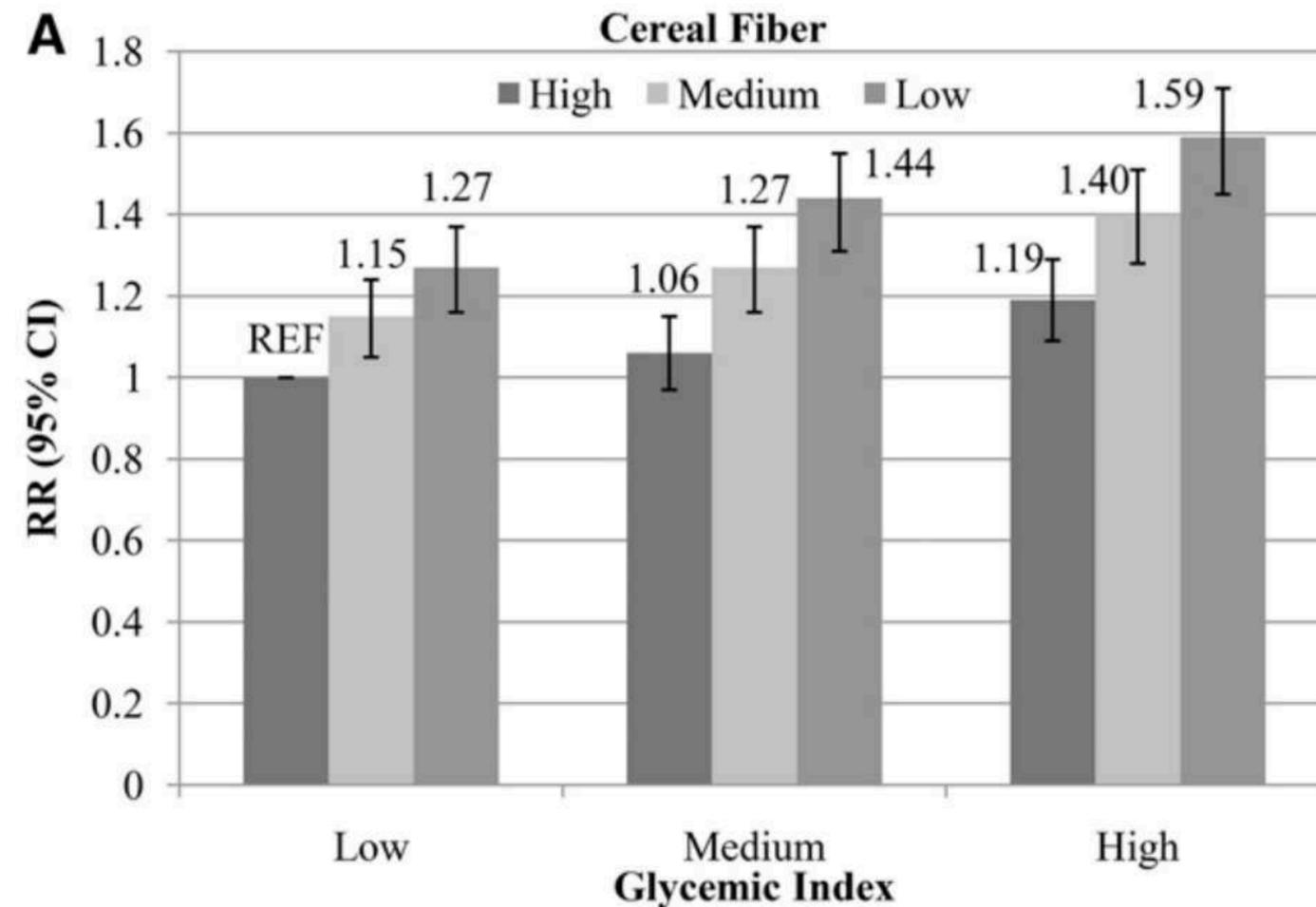
Pooled estimates are expressed as RRs, where black squares represents the pooled RR of GI exposure, with corresponding 95% CIs. Estimates were the comparison between extreme quantiles. The p values represent the analysis performed with the generic inverse variance method with a fixed-effects model (where $p < 0.05$ is significant). RR=relative risk. GI=glycaemic index.





Diabetes tipo 2 - Relación con respuesta glicémica

La combinación de una dieta rica en alimentos con alto IG/CG con baja ingesta de fibra aumenta más el riesgo de desarrollar diabetes tipo 2



.Bhupathiraju, S. N. Am J Clin Nutr . 2014 Jul;100(1):218-32

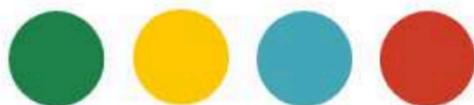
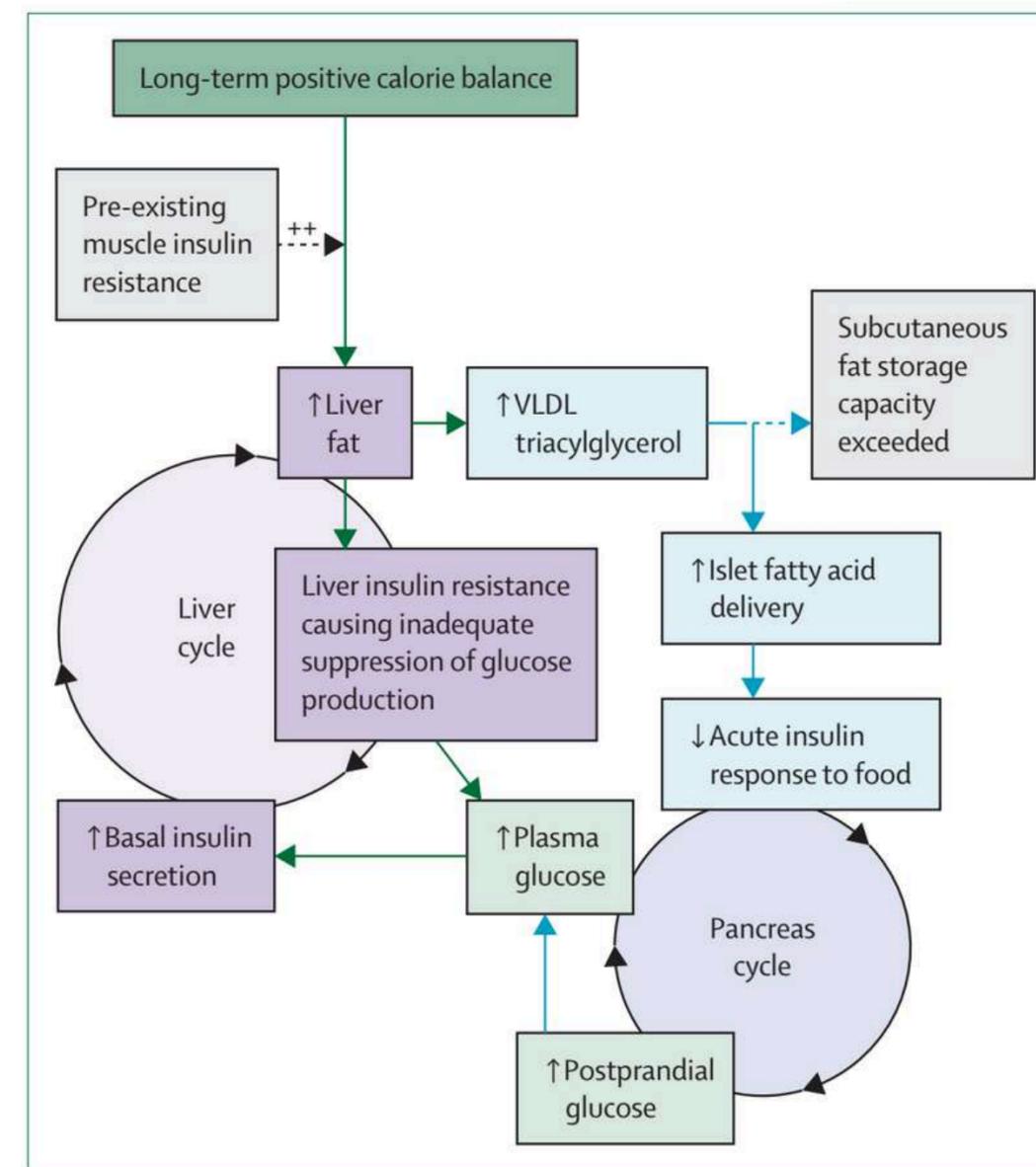


Diabetes tipo 2 - Relación con respuesta glicémica

El desarrollo de diabetes tipo 2 es multifactorial

Diferentes mecanismos etiopatogénicos colaboran para la aparición de:

- Menor acción de la insulina
- Menor secreción de insulina





Ingestas de flavonoides y desarrollo de diabetes tipo 2



Brief Report

Profiles of Polyphenol Intake and Type 2 Diabetes Risk in 60,586 Women Followed for 20 Years: Results from the E3N Cohort Study

Nasser Laouali ^{1,2,*}, Takiy Berrandou ³, Joseph A. Rothwell ^{1,2}, Sanam Shah ^{1,2}, Douae El Fatouhi ^{1,2}, Francesca Romana Mancini ^{1,2}, Marie-Christine Boutron-Ruault ^{1,2} and Guy Fagherazzi ^{1,2,4}

Received: 27 May 2020; Accepted: 25 June 2020; Published: 29 June 2020

60586 mujeres

Seguimiento a 20 años

Antocianinas, catequinas, entre otros

ARTICLE OPEN

Check for updates

Higher habitual intakes of flavonoids and flavonoid-rich foods are associated with a lower incidence of type 2 diabetes in the UK Biobank cohort

Alysha S. Thompson ¹, Amy Jennings ¹, Nicola P. Bondonno ^{1,2,3}, Anna Tresserra-Rimbau ^{1,4,5}, Benjamin H. Parmenter ³, Claire Hill ⁶, Aurora Perez-Cornago ⁷, Tilman Kühn ^{1,8,9,10} and Aedin Cassidy ¹

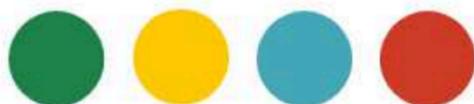
© The Author(s) 2024

113097 mujeres y hombres

Seguimiento a 12 años

Consumo medio flavonoides fue de 805±430mg

Procianidinas, flavan-3-oles, entre otros





Flavonoides y riesgo de diabetes tipo 2

Mecanismos de acción

Mecanismos de acción

Intestinal

Inhibición α -glucosidasa y α -amilasa
Aumentan la producción de incretinas

Pancreático

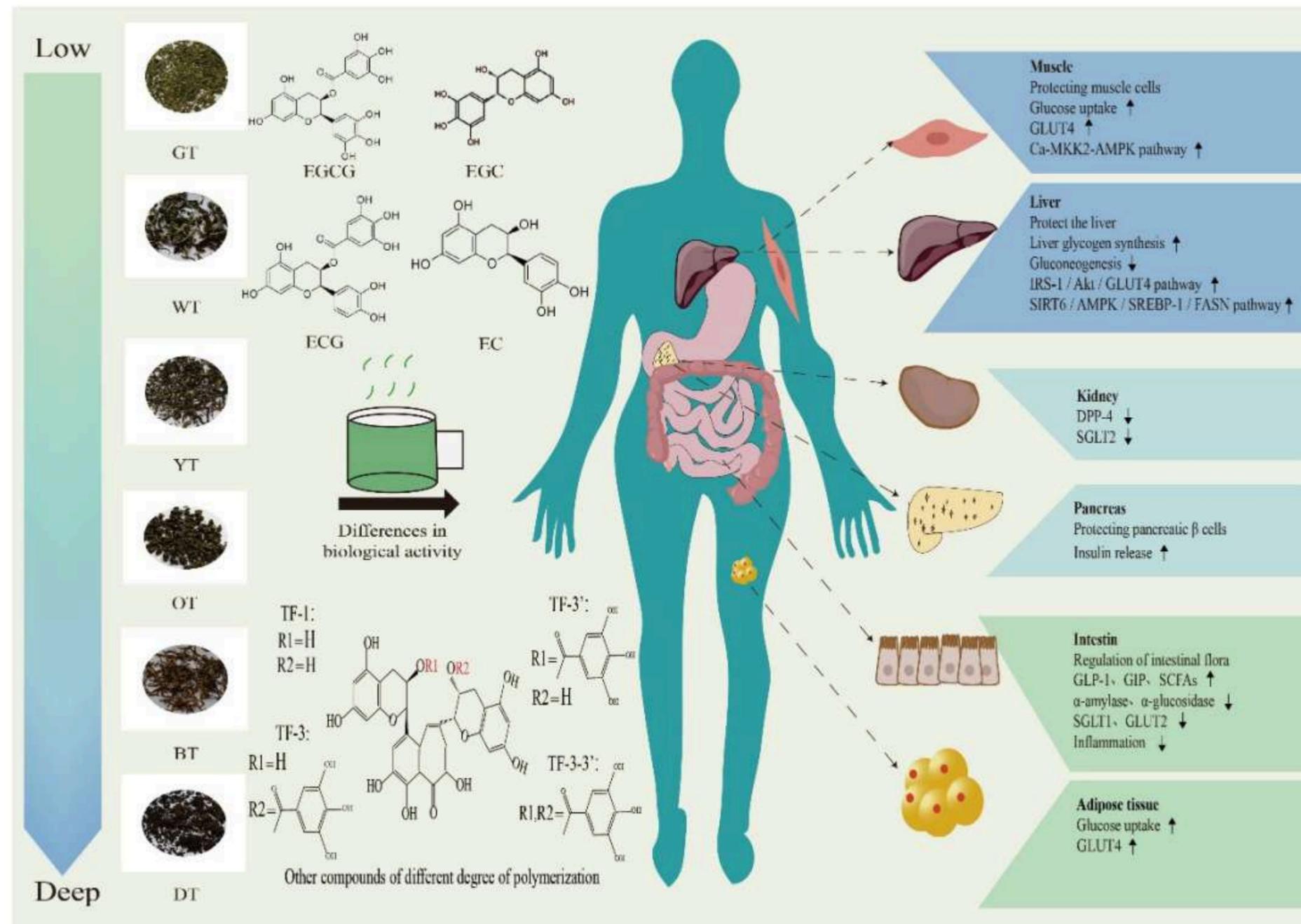
Aumentan expresión de GLUT 2
Estimulan liberación de insulina

Hepático

Reducen la producción de glucosa

Sistémico

Promueven expresión y translocación de GLUT4
Aumentan sensibilidad a insulina
Reducción de citoquinas proinflamatorias
Aumento de adipocinas protectoras





Nivel intestinal

Efectos sobre digestión de carbohidratos



Article

α -Glucosidase Inhibitory Activity of Tannat Grape Phenolic Extracts in Relation to Their Ripening Stages

Auriane Dudoit¹, Nawel Benbouguerra¹, Tristan Richard², Ruth Hornedo-Ortega², Josep Valls-Fonayet², Gaëlle Coussot³ and Cédric Saucier^{1,*}

Received: 17 June 2020; Accepted: 15 July 2020; Published: 22 July 2020

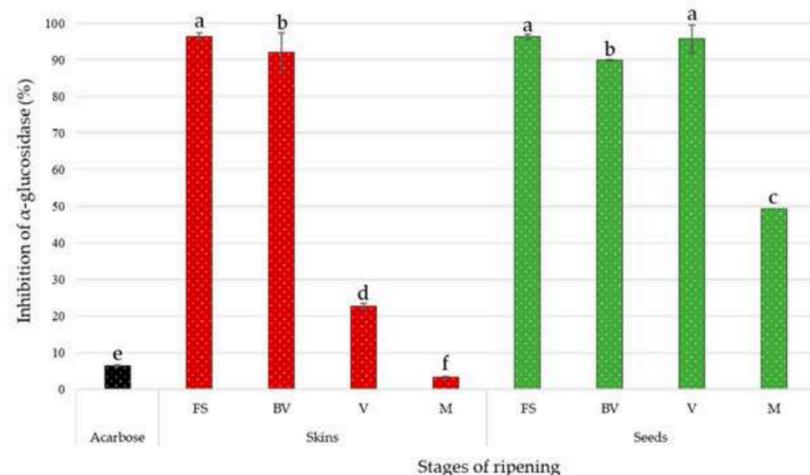


Figure 2. Inhibitory effects of Tannat skin and seed extracts (0.4 g/L) and positive control (acarbose at 0.4 g/L) on α -glucosidase (pH 6.8, T = 37 °C) at different stages of ripening: First Stage (FS), Before Veraison (BV), Veraison (V) and Maturity (M). Values are means of four replicates. Significant differences between treatments at $p < 0.05$ are indicated with letters as measured by Tukey test.

European Food Research and Technology
<https://doi.org/10.1007/s00217-019-03252-w>

ORIGINAL PAPER



Assessment of antioxidant, antidiabetic, antiobesity, and anti-inflammatory properties of a Tannat winemaking by-product

Adriana Maite Fernández-Fernández^{1,3}, Amaia Iriondo-DeHond³, Eduardo Dellacassa², Alejandra Medrano-Fernandez¹, María Dolores del Castillo³



Article

In Vitro Bioaccessibility of Extractable Compounds from Tannat Grape Skin Possessing Health Promoting Properties with Potential to Reduce the Risk of Diabetes

Adriana Maite Fernández-Fernández^{1,2,3}, Amaia Iriondo-DeHond², Tiziana Nardin⁴, Roberto Larcher⁴, Eduardo Dellacassa⁵, Alejandra Medrano-Fernandez¹ and María Dolores del Castillo^{2,*}



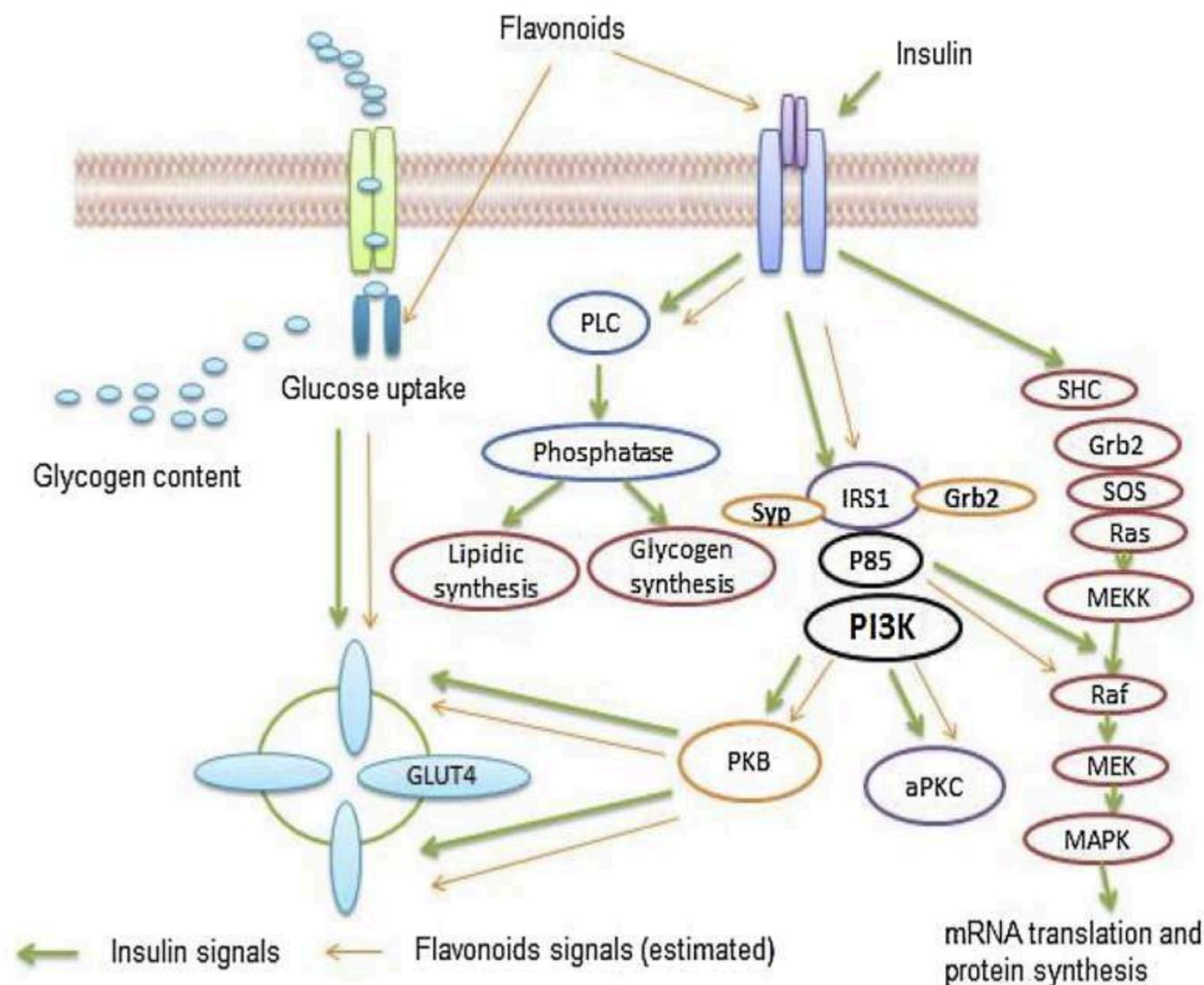


Efectos a nivel sistémico

Sensibilización a la acción de la insulina - Modelos celulares

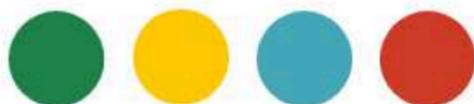
Mejoran la señalización de la insulina en tejidos periféricos aumentando la captación de glucosa desde la sangre

T. Hussain, et al.



Pharmacological Research 152 (2020) 104629

Fig. 3. Molecular mechanism of anti-diabetic properties of flavonoids. This schematic shows that insulin is recognized by insulin receptors and hence it stimulates intrinsic kinase activity that leads to autophosphorylation and recruit substances, for example, IRS1-4 proteins, Cbl and SHC. Phosphorylation of IRS proteins assists proteins with Src homology-2 SH2 domains. Many proteins are considered as adaptor molecules for instance, performing regulatory function of PI3K or adaptor molecule growth factor receptor bound protein-2 (Grb2) that ultimately stimulate Ras-MAPK pathway. Whereas; PI3k enzyme is based on the regulatory (p85) and catalytic (p110) subunits that catalyzes the formation of lipids second messenger PIP3 within cellular milieu, and activates phosphoinositide-dependent kinase (PDKs). PDK targets consist of PKB/Akt and the atypical PKC isoforms. Along with PI3K, stimulation of PKB/Akt and PKCs are contributed in the insulin activated GLUT translocation, glucose uptake and glycogen synthesis.





Efectos a nivel sistémico

Sensibilización a la acción de la insulina - Modelos animales

JOURNAL OF
AGRICULTURAL AND
FOOD CHEMISTRY

Article

pubs.acs.org/JAFC

Oligomeric Cocoa Procyanidins Possess Enhanced Bioactivity Compared to Monomeric and Polymeric Cocoa Procyanidins for Preventing the Development of Obesity, Insulin Resistance, and Impaired Glucose Tolerance during High-Fat Feeding

Melanie R. Dorenkott,[†] Laura E. Griffin,[†] Katheryn M. Goodrich,[†] Katherine A. Thompson-Witrick,[†] Gabrielle Fundaro,[‡] Liyun Ye,[†] Joseph R. Stevens,[‡] Mostafa Ali,[‡] Sean F. O'Keefe,[†] Matthew W. Hulver,^{‡,#} and Andrew P. Neilson^{*†}

- Ratas tratados por 12 semanas con dieta alta en grasas como modelo de obesidad y diabetes tipo 2
- Suplementados con extractos de cacao o fracciones enriquecidas en monómeros, oligómeros o polímeros

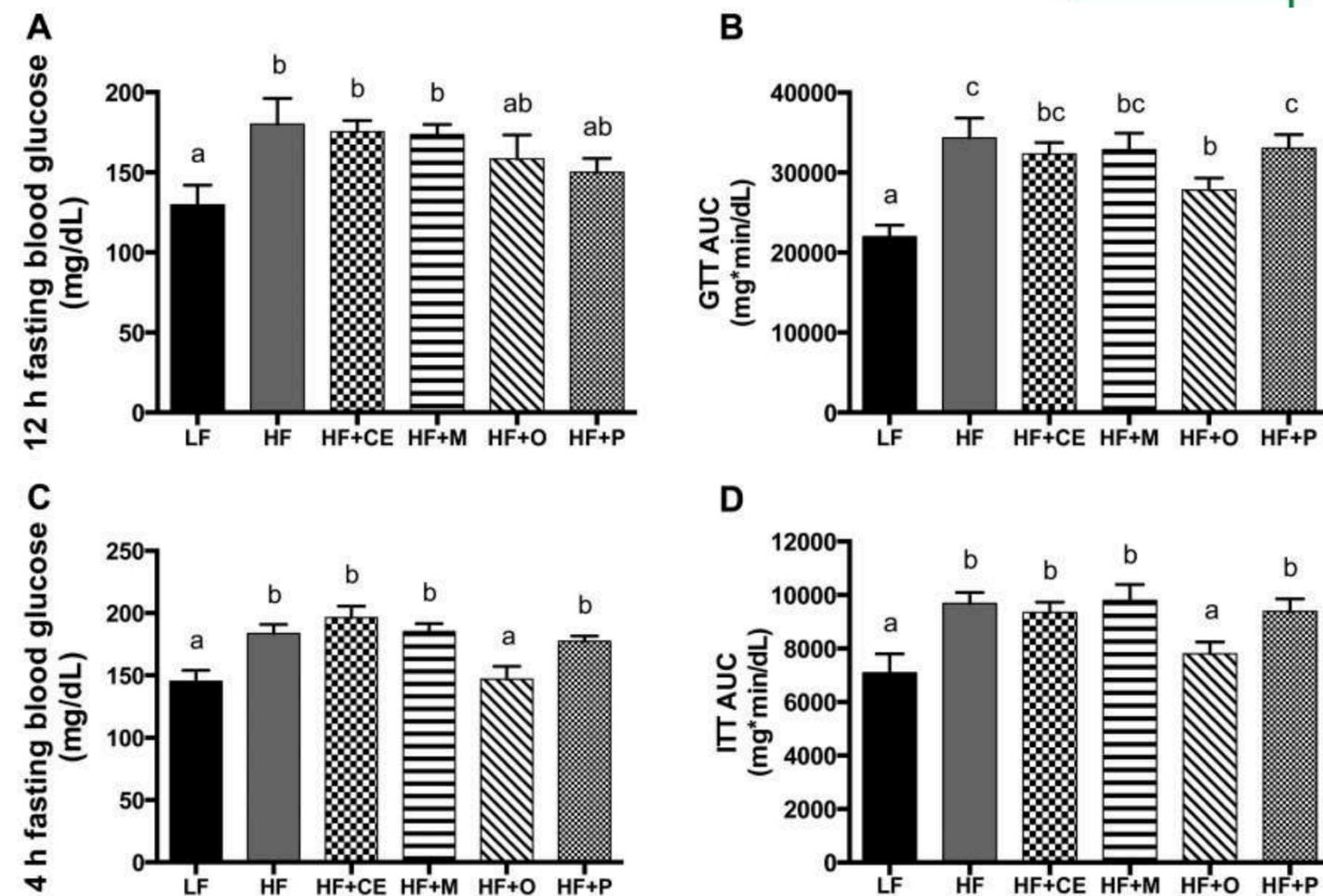


Figure 6. (A) Fasting (12 h) blood glucose levels at week 10; (B) glucose tolerance test (GTT) area under the blood glucose concentration curve (AUC) at week 10; (C) fasting (4 h) blood glucose levels at week 11; (D) insulin tolerance test (ITT) AUC at week 11. Data shown are the mean \pm SEM of $n = 9$ animals/treatment ($n = 8$ for the HF+M group due to loss of one mouse from this group during the feeding study). Significance between treatments was determined with a one-way ANOVA and Fisher's LSD post hoc test ($P < 0.05$). Treatments with different letters are significantly different. LF, low-fat control diet; HF, high-fat control diet; HF+M, high-fat control diet + monomer-rich fraction; HF+O, high-fat control diet + oligomer-rich fraction; HF+P, high-fat control diet + polymer-rich fraction.





Estudios traslacionales





Flavonoides - Orujo de uva Tannat

Characterisation and evolution of grape polyphenol profiles of *Vitis vinifera* L. cv. Tannat during ripening and vinification

E. BOIDO¹, M. GARCÍA-MARINO², E. DELLACASSA³, F. CARRAU¹, J.C. RIVAS-GONZALO² and M.T. ESCRIBANO-BAILÓN²

Article

Antioxidant Capacity and NF-κB-Mediated Anti-Inflammatory Activity of Six Red Uruguayan Grape Pomaces

Emiliana Fariña^{1,†}, Hellen Daghero^{2,†} , Mariela Bollati-Fogolín^{2,*} , Eduardo Boido³, Jorge Cantero^{1,4} , Mauricio Moncada-Basualto⁵ , Claudio Olea-Azar⁶, Fabio Polticelli^{7,8,*}  and Margot Paulino^{1,*}



Antocianinas y control de glucosa plasmática

Estudios en humanos



European Journal of Nutrition
<https://doi.org/10.1007/s00394-020-02379-x>

ORIGINAL CONTRIBUTION



Anthocyanins regulate serum adipon and visfatin in patients with prediabetes or newly diagnosed diabetes: a randomized controlled trial

Liping Yang^{1,2} · Yun Qiu¹ · Wenhua Ling¹ · Zhaomin Liu¹ · Lili Yang¹ · Changyi Wang² · Xiaolin Peng² · Li Wang² · Jianying Chen³

Received: 20 April 2020 / Accepted: 28 August 2020

160 personas con prediabetes o diabetes tipo 2 de reciente diagnóstico

320mg/d extractos rico en antocianinas por 12 semanas

Changes in adipokines and glucose metabolism parameters after 12 weeks of treatment with anthocyanins or placebo

	Anthocyanins (n = 76)		Placebo (n=62)		Difference (CI 95%)	P _t
	Baseline	12 weeks	Baseline	12 weeks		
Glucose metabolism						
HbA1c	6.14 ± 0.6	5.83 ± 0.49 [†]	6 ± 0.6	5.81 ± 0.6 [†]	-0.11 (-0.22, -0.11) *	(
Fasting glucose	6.18 ± 0.9	6.21 ± 0.69	6.17 ± 0.65	6.36 ± 0.75 [†]	-0.16 (-0.44, 0.13) (

Descenso en HbA1c sin cambios sobre glicemia de ayuno



Antocianinas y control de glucosa en diabetes tipo 2

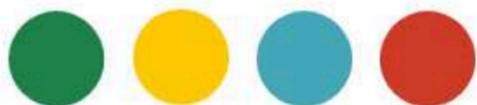
Estudios en humanos

Diferentes metaanálisis han evaluado el efecto suplementación con antocianinas sobre la respuesta glicémica

Neyestani, T. 2023 - 47 estudios - Disminución de glucosa de ayuno y HbA1c

Mao, T. 2023 - 13 estudios - Disminución de glucosa de ayuno y posprandial

Fallah, A. 2020 - 37 estudios - Disminución de glucosa de ayuno y posprandial

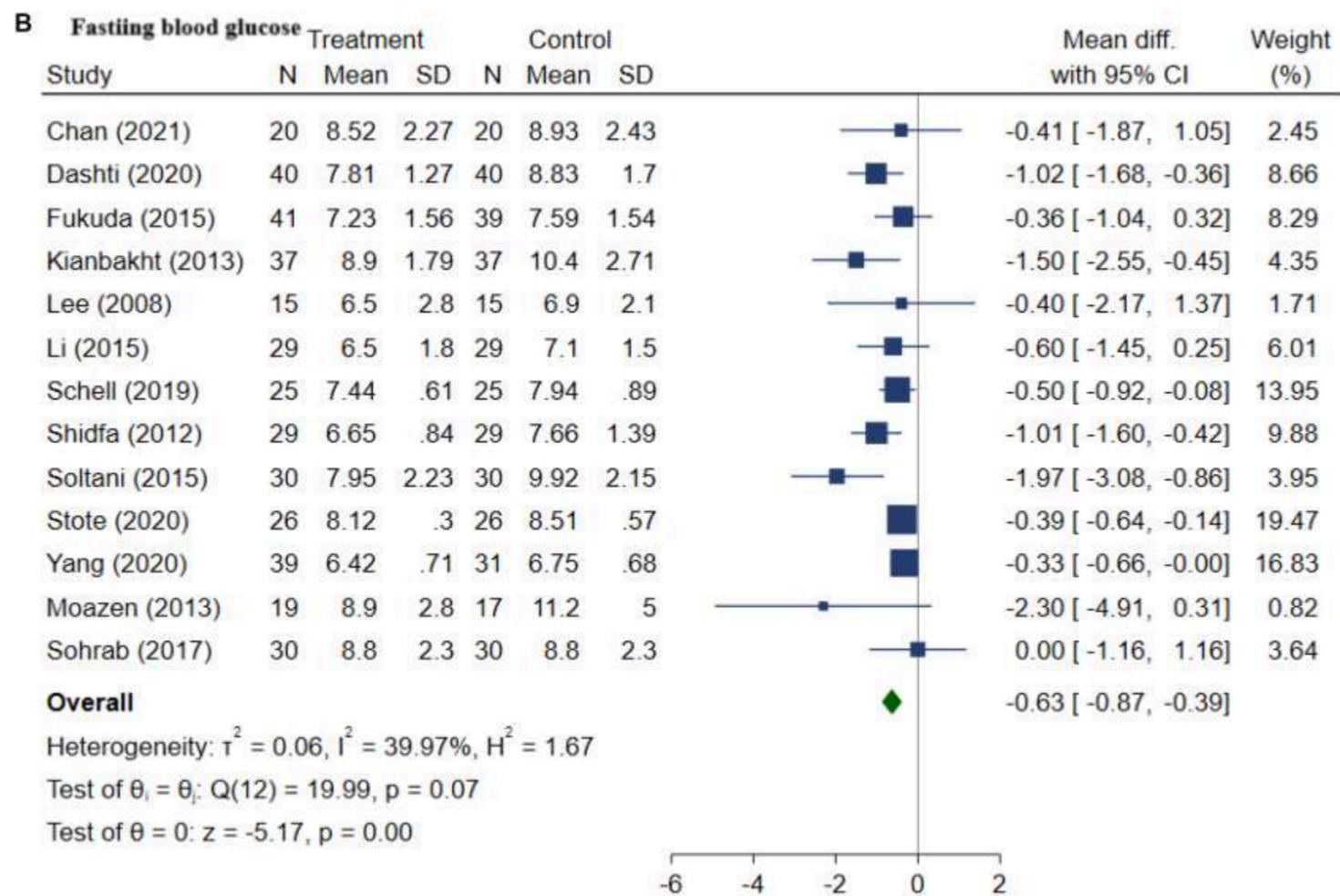




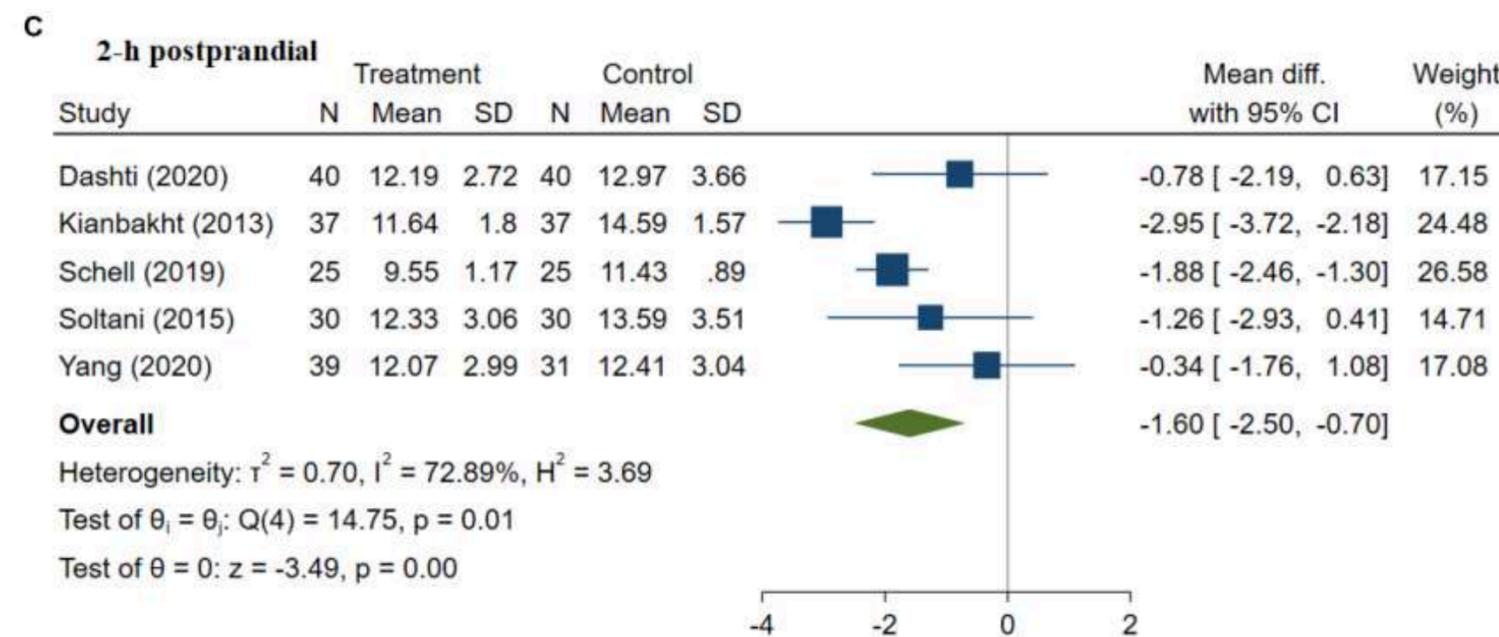
Antocianinas y control de glucosa en diabetes tipo 2

Estudios en humanos

Mao, T. 2023 - 13 estudios - Disminución de glucosa de ayuno y posprandial



Random-effects DerSimonian-Laird model



Random-effects DerSimonian-Laird model



Antocianinas y respuesta glicémica

Estudios en humanos

A randomized placebo-controlled cross-over study on the effects of anthocyanins on inflammatory and metabolic responses to a high-fat meal in healthy subjects

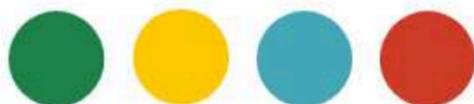
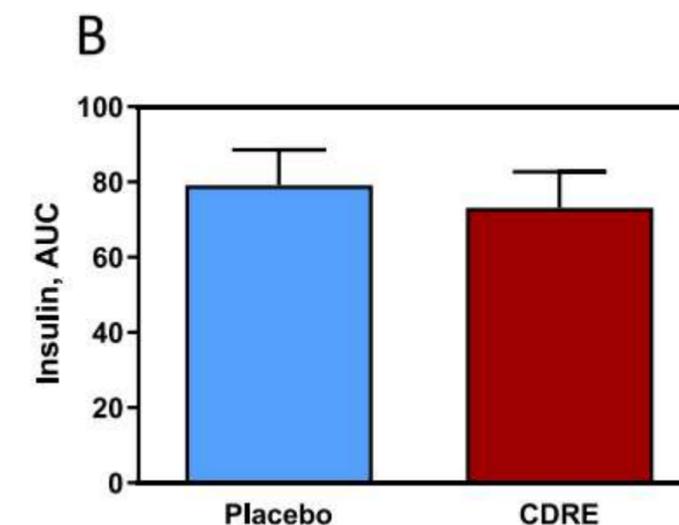
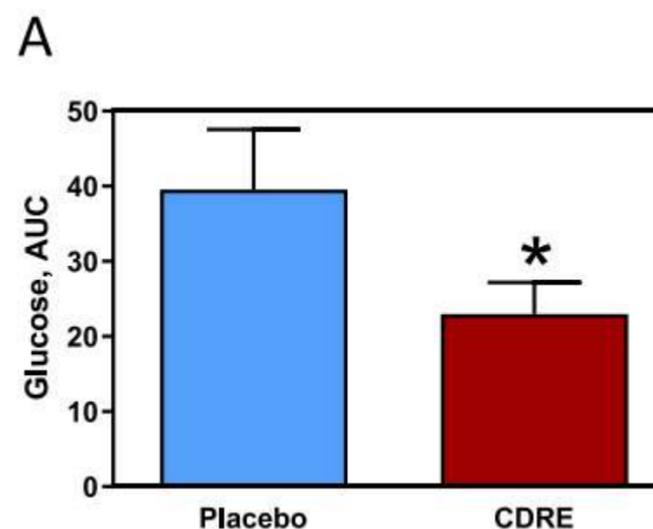
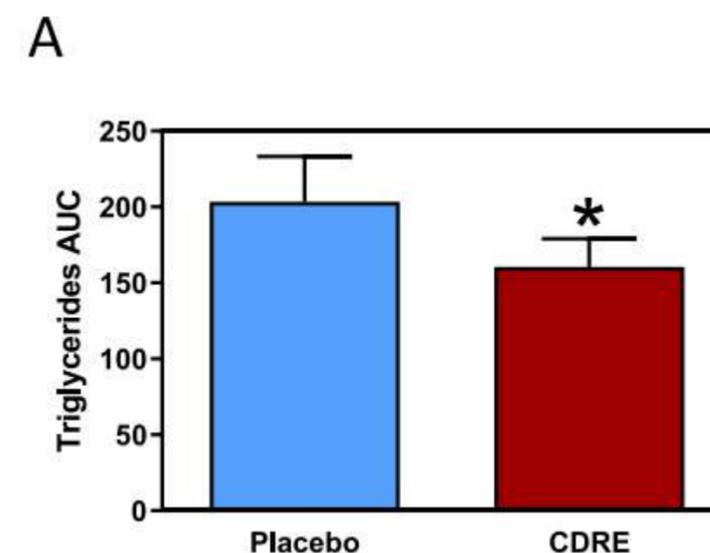
Eleonora Cremonini^{a,b}, Elena Daveri^a, Dario E. Iglesias^a, Jiye Kang^a, Ziwei Wang^a, Russell Gray^c, Angela Mastaloudis^c, Colin D. Kay^d, Shelly N. Hester^c, Steven M. Wood^c, Cesar G. Fraga^{a,e,f,*}, Patricia I. Oteiza^{a,b,**}

Table 1
CDRE anthocyanidin composition^a.

Compound	Content (mg/g of CDRE)
Cyanidins	166.4 ± 0.5
Delphinidins	121.7 ± 0.4
Peonidins	16.7 ± 0.1
Petunidins	5.1 ± .0.1
Malvidin	7.6 ± 0.1
Other anthocyanins	3.0 ± 0.1
Total anthocyanins	320.4 ± 0.7

Values are means ± SE.

^a Detailed concentration of anthocyanins in each individual extract is included in [Supplemental Table S3](#), and (poly)phenol composition of the extracts in [Supplemental Table S4](#).



Orujo de uva y control de glucosa plasmática

Estudios en humanos



Urquiaga et al. *Biol Res* (2015) 48:49

Wine grape pomace flour improves blood pressure, fasting glucose and protein damage in humans: a randomized controlled trial

Inés Urquiaga^{1*}, Sonia D'Acuña¹, Druso Pérez¹, Sara Dicenta¹, Guadalupe Echeverría¹, Attilio Rigotti^{1,2} and Federico Leighton¹



Abstract

Background: The Mediterranean diet is a healthy diet with positive scientific evidence of preventing chronic diseases. Bioactive components support the healthy properties of the Mediterranean diet. Antioxidants and fiber, two components of the Mediterranean diet, are key functional nutrients for healthy eating and nutrition. Wine grape pomace is a rich source of these dietary constituents and may be beneficial for human health. Our hypothesis was that the intake of red wine grape pomace flour (WGPF) prepared from red wine grapes (Cabernet Sauvignon variety) reduced the metabolic syndrome in humans. To evaluate the effect of WGPF on components of metabolic syndrome we design a 16-week longitudinal intervention study. Thirty-eight males, 30–65 years of age, with at least one component of metabolic syndrome, were randomly assigned to either the intervention group (n = 25) or the control group (n = 13). At lunch, the intervention group was given 20 g of WGPF per day, which contained 10 g of dietary fiber, 822 mg of polyphenols and an antioxidant capacity of 7258 ORAC units. Both groups were asked to maintain their regular eating habits and lifestyles. Clinical evaluation, anthropometric measurements and biochemical blood analyses were done at the beginning and the end of the study.

Table 3 Metabolic syndrome components in groups at baseline and 16 weeks

	Experimental		Control	
	Basal (0 weeks)	Final (16 weeks)	Basal (0 weeks)	Final (16 weeks)
Waist circumference (cm)	102.7 ± 9.9	102.5 ± 10.5	98.1 ± 7.0	98.8 ± 7.4
Systolic blood pressure (mmHg)	127.1 ± 11.5 ^a	122.8 ± 8.5 ^b	122.4 ± 12.4	120.0 ± 13.3
Diastolic blood pressure (mmHg)	79.7 ± 8.3 ^a	74.4 ± 5.6 ^b	80.2 ± 6.6	76.4 ± 9.3
Fasting glucose (mg/dL)	92.7 ± 5.8 ^a	89.4 ± 7.9 ^b	88.9 ± 5.8	86.9 ± 5.4
HDL cholesterol (mg/dL)	46.4 ± 10.7	46.5 ± 10.8	41.2 ± 8.6	42.7 ± 14.4
Triglycerides (mg/dL)	147.5 ± 88.2	153.0 ± 98.6	179.8 ± 96.5	157.4 ± 81.6
Number of positive criteria for metabolic syndrome	1.84 ± 1.62 ^a	1.48 ± 1.29 ^b	1.54 ± 1.13	1.54 ± 1.13
Metabolic syndrome prevalence (%)	32	24	23	23

Values are mean ± SD. Student t-test for paired samples was used to analyze differences of means within groups. Student t-test for independent samples was used to analyze differences of means between groups. Wilcoxon signed rank-sum test was used to compare the number of positive criteria for metabolic syndrome. Means within a group with different superscript letters are significantly different; P < 0.05 paired t test



Orujo de uva y control de glucosa plasmática

Estudios en humanos



Original article

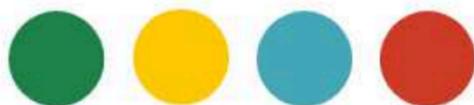
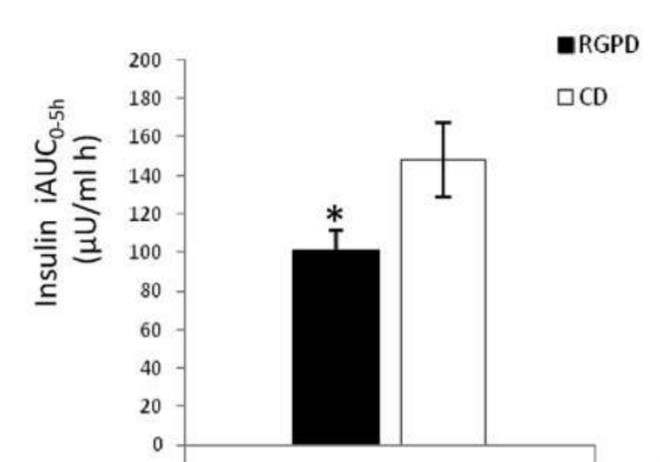
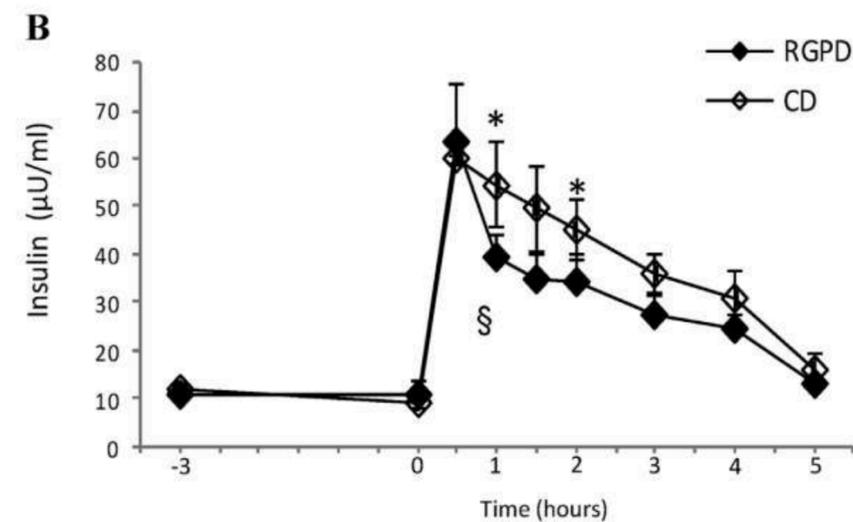
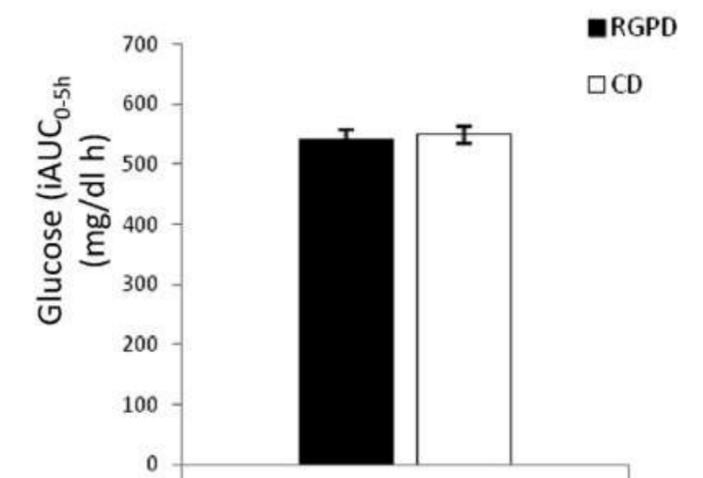
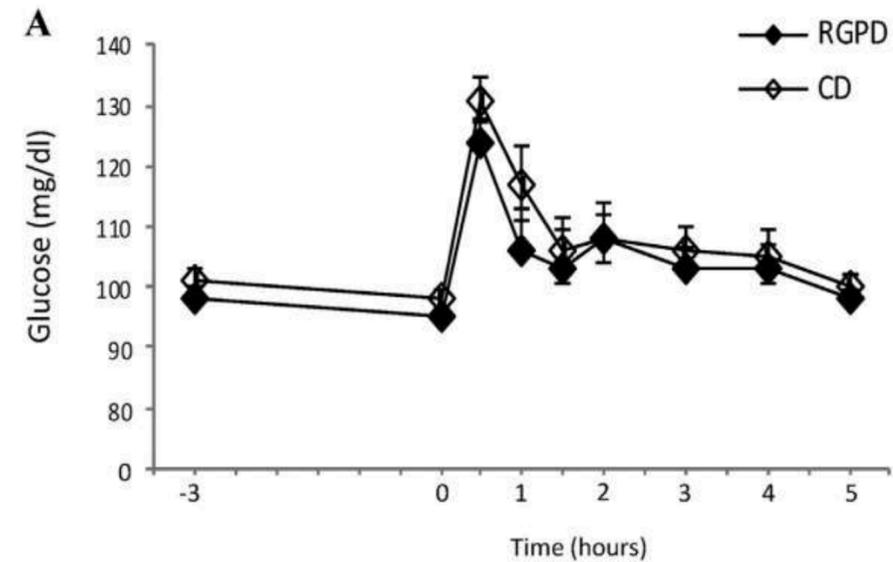
Grape pomace polyphenols improve insulin response to a standard meal in healthy individuals: A pilot study

G. Costabile^a, M. Vitale^{a,*}, D. Luongo^b, D. Naviglio^c, C. Vetrani^a, P. Ciciola^a, A. Tura^d, F. Castello^e, P. Mena^e, D. Del Rio^{e,f,g}, B. Capaldo^a, A.A. Rivellese^a, G. Riccardi^a, R. Giacco^h

12 participantes sanos

250 ml previo a ingesta

1562 gGAE polifenoles totales



Orujo de uva y control de glucosa plasmática

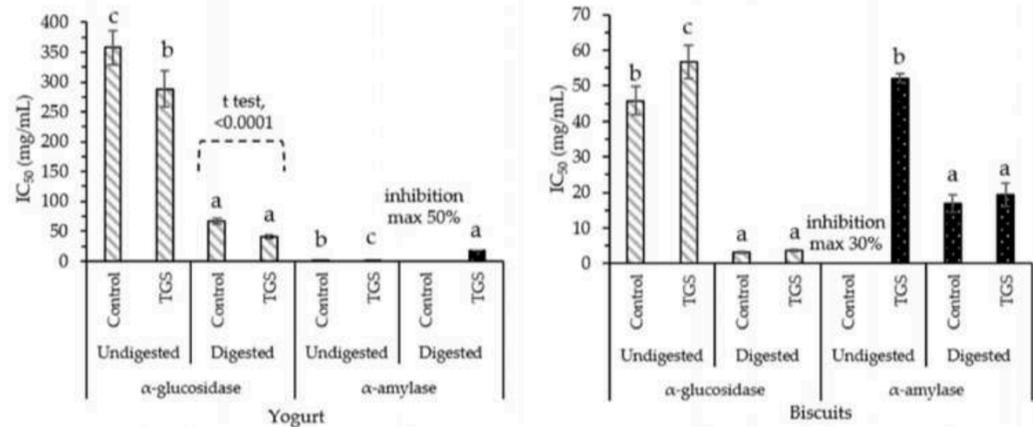
Estudios en humanos



Article

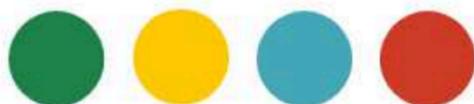
Tannat Grape Skin: A Feasible Ingredient for the Formulation of Snacks with Potential for Reducing the Risk of Diabetes

Adriana Maite Fernández-Fernández^{1,2,3}, Eduardo Dellacassa⁴, Tiziana Nardin⁵, Roberto Larcher⁵, Cecilia Ibañez¹, Dahiana Terán¹, Adriana Gámbaro¹, Alejandra Medrano-Fernández¹ and María Dolores del Castillo^{2,*}



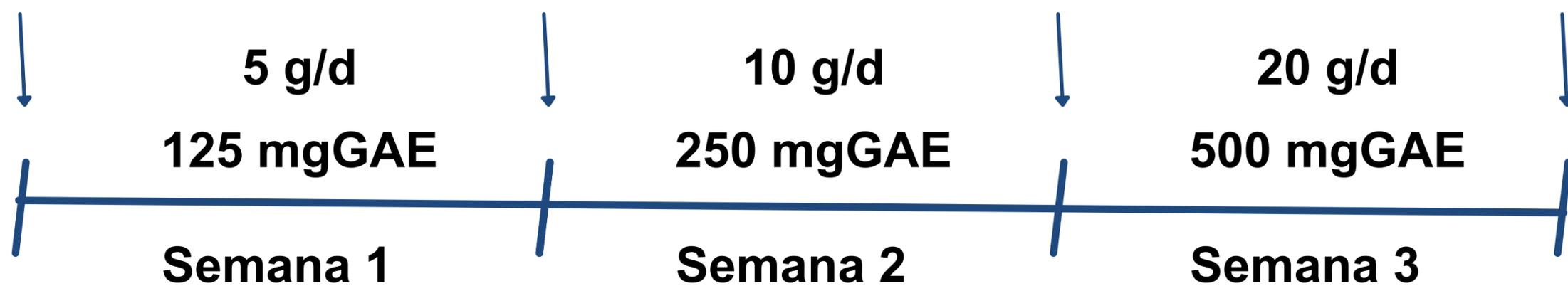
Tannat grape pomace as an ingredient for potential functional biscuits: bioactive compound identification, *in vitro* bioactivity, food safety, and sensory evaluation

Victoria Olt^{1,2}, Jessica Báez^{1,2}, Romina Curbelo³, Eduardo Boido⁴, Miguel Amarillo⁵, Adriana Gámbaro⁵, Silvana Alborés⁶, Natalia Gerez García⁷, María Verónica Cesio⁷, Horacio Heinzen⁷, Eduardo Dellacassa³, Adriana Maite Fernández-Fernández^{1*†} and Alejandra Medrano^{1*†}



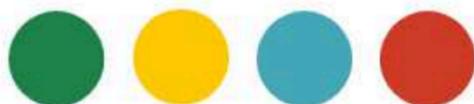


Diseño de estudio de intervención en humanos con polvo de orujo de uva Tannat



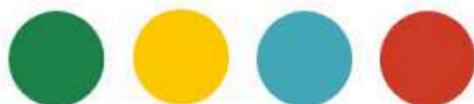
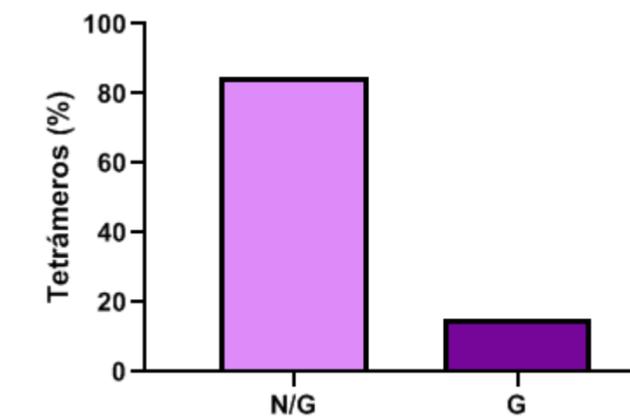
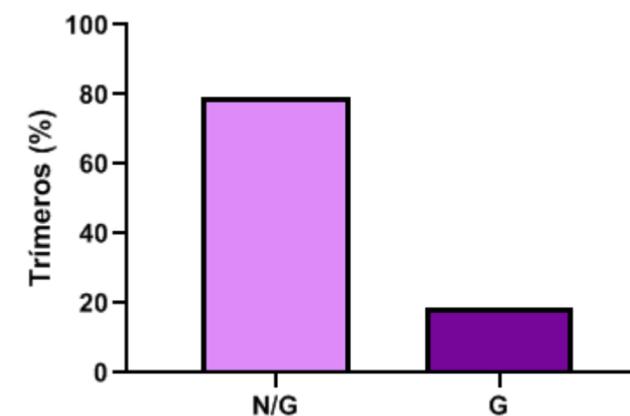
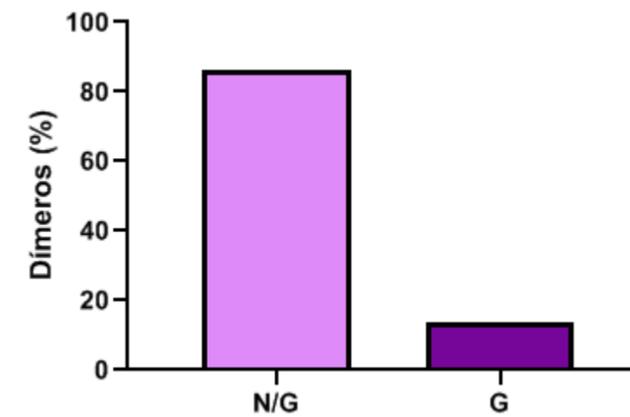
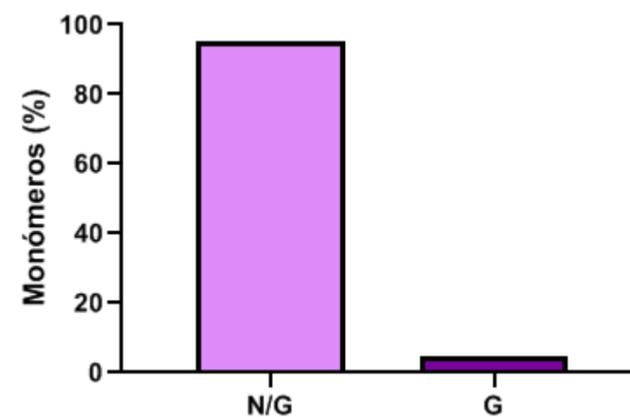
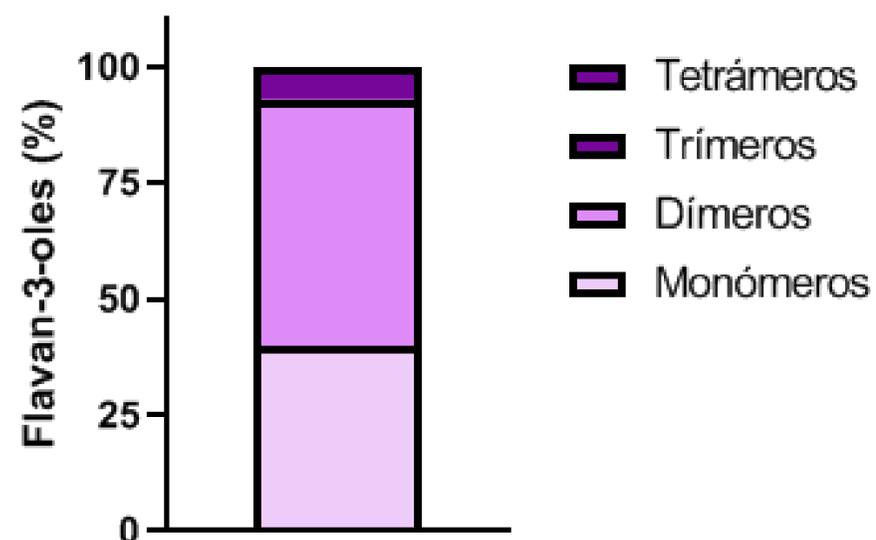
En cada visita:

- Tolerancia a dosis polvo de orujo
- Presión arterial
- Glicemia de ayuno
- Muestra de orina 24hs
- Muestra de plasma





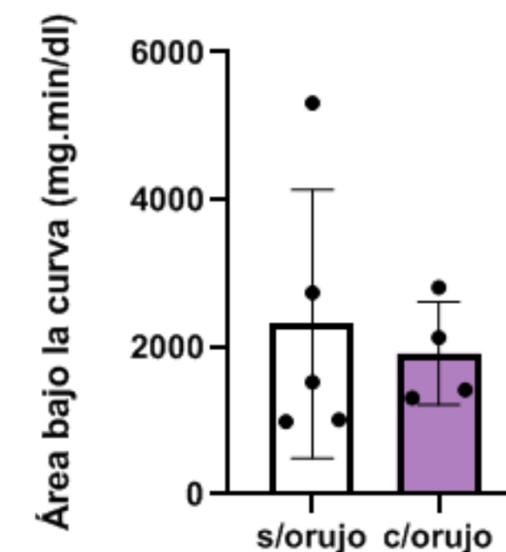
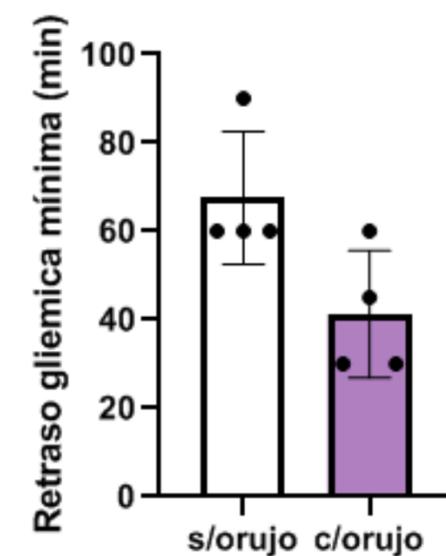
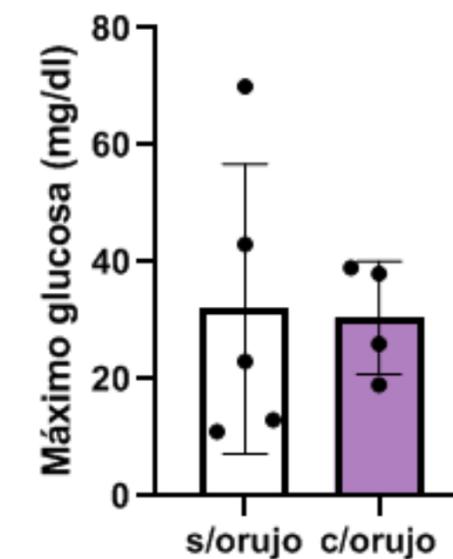
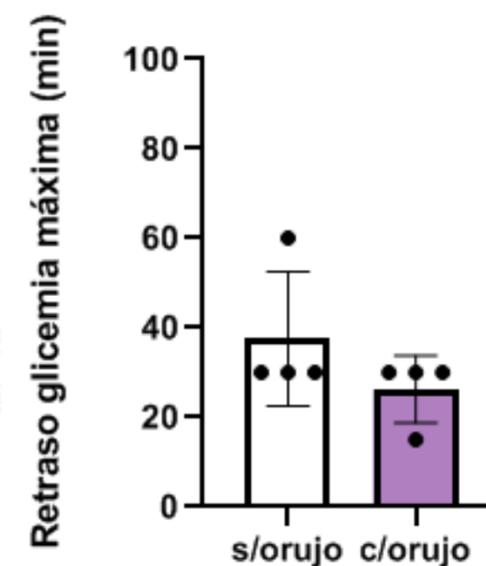
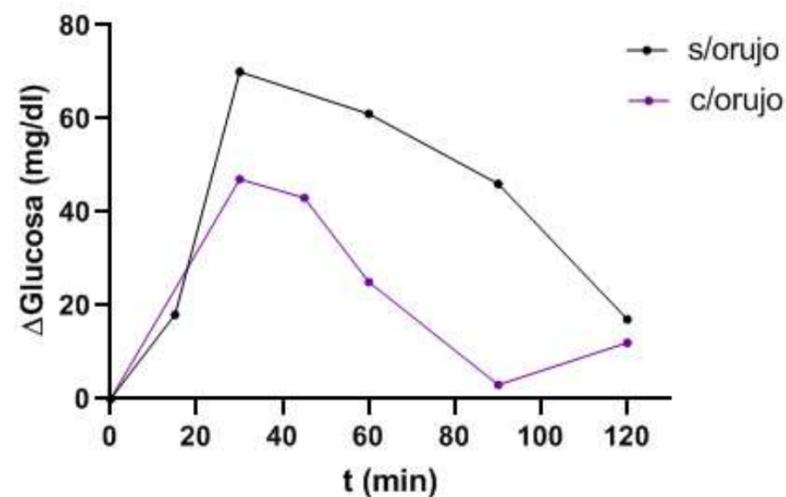
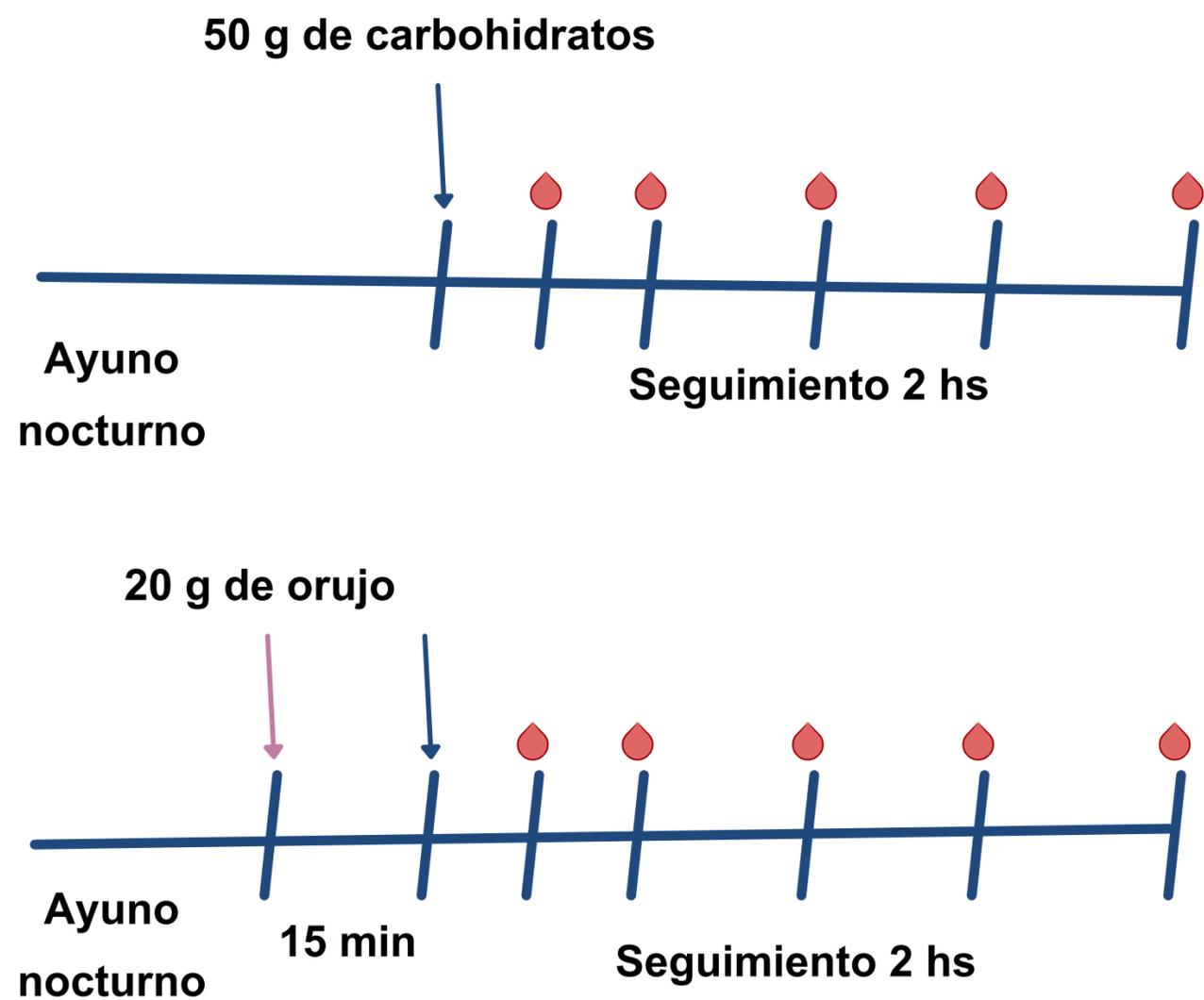
Diseño de estudio de intervención en humanos con polvo de orujo de uva Tannat





Diseño de estudio de intervención en humanos

Modulación de respuesta glicémica con polvo de orujo Tannat





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Mauricio Mastrogiovanni



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