

# The effects of flavanols on the enteroendocrine system: Proanthocyanidins on food intake

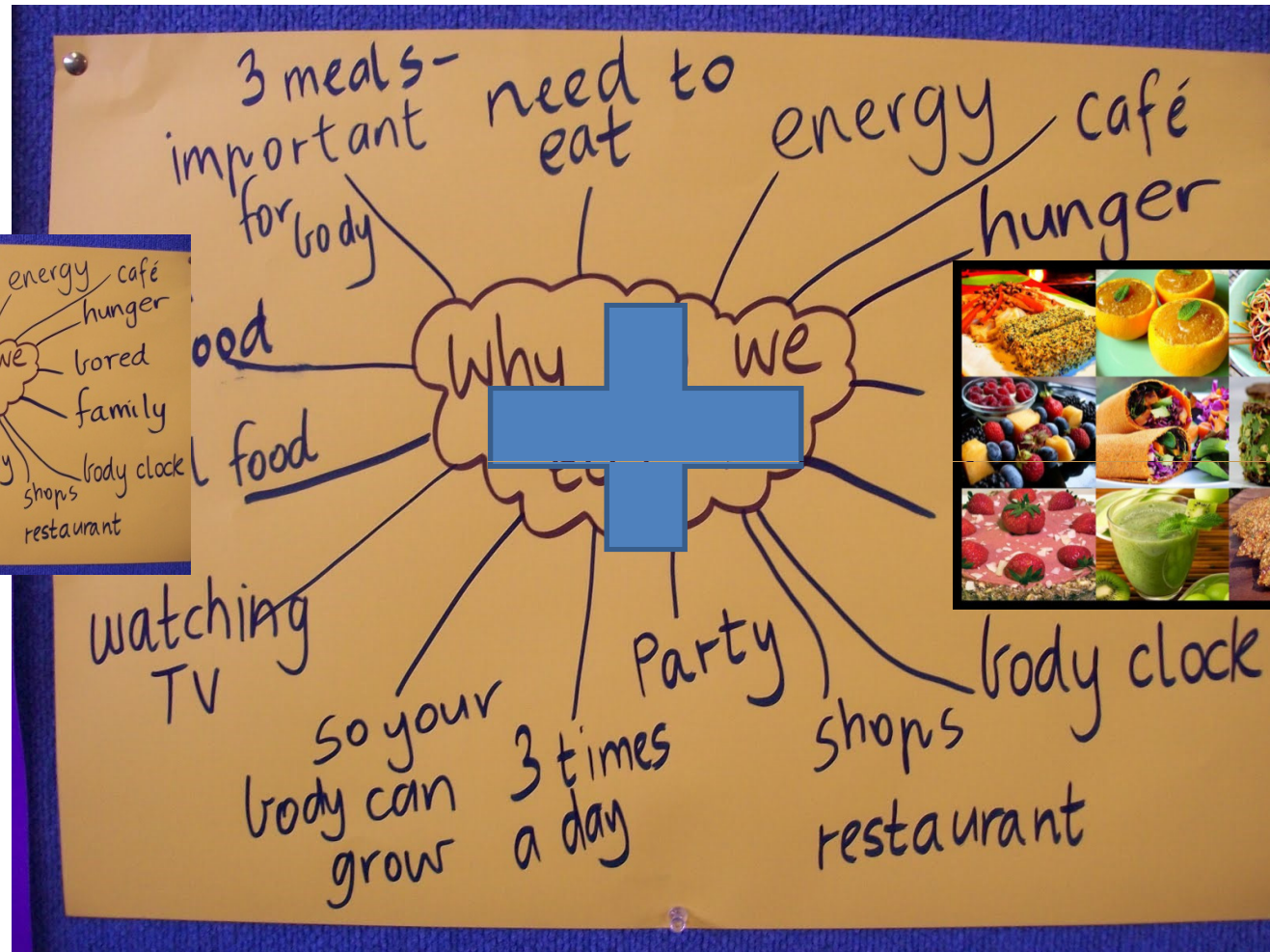
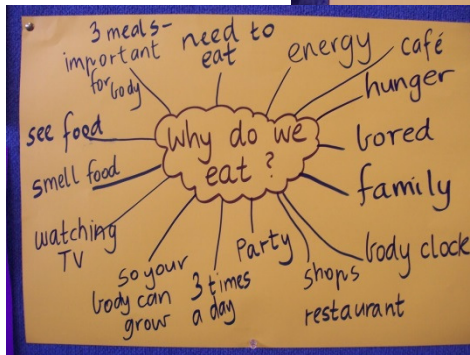
Montserrat Pinent, Joan Serrano, Àngela Casanova-Martí, Katherine Gil-Cardoso, M Teresa Blay, Ximena Terra, and **Anna Ardévol** ( [anna.ardevol@urv.cat](mailto:anna.ardevol@urv.cat) )

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Tarragona, Spain.



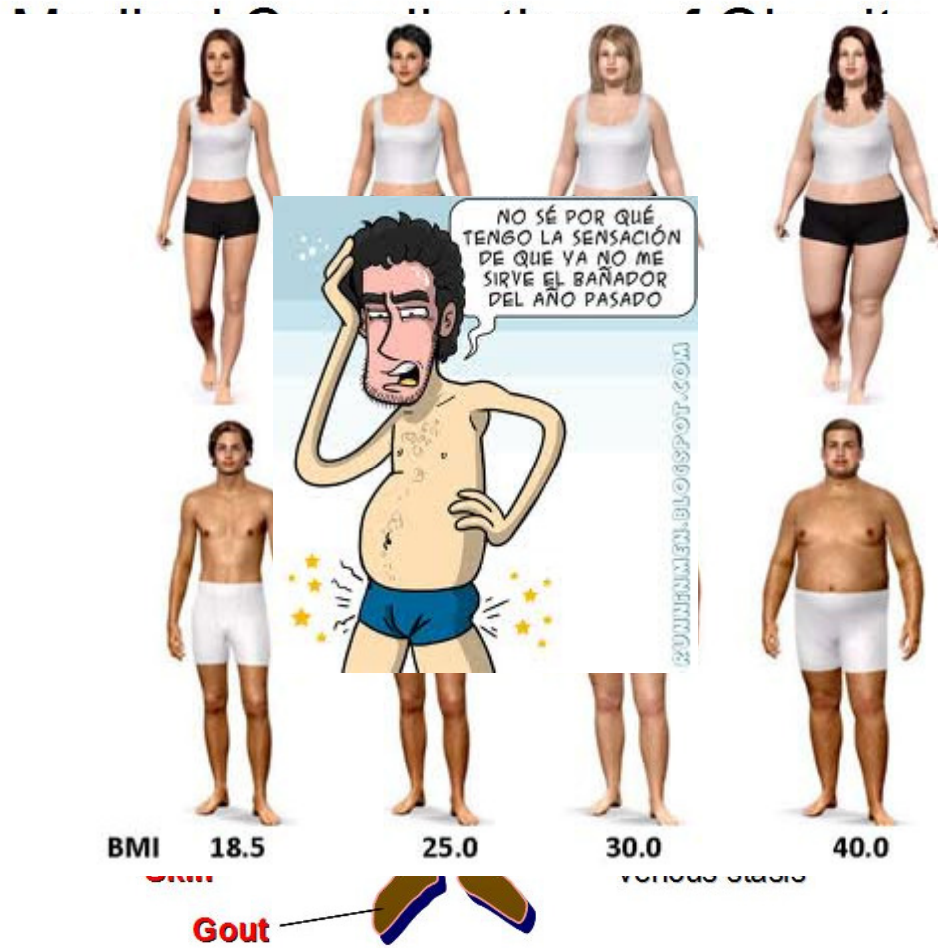


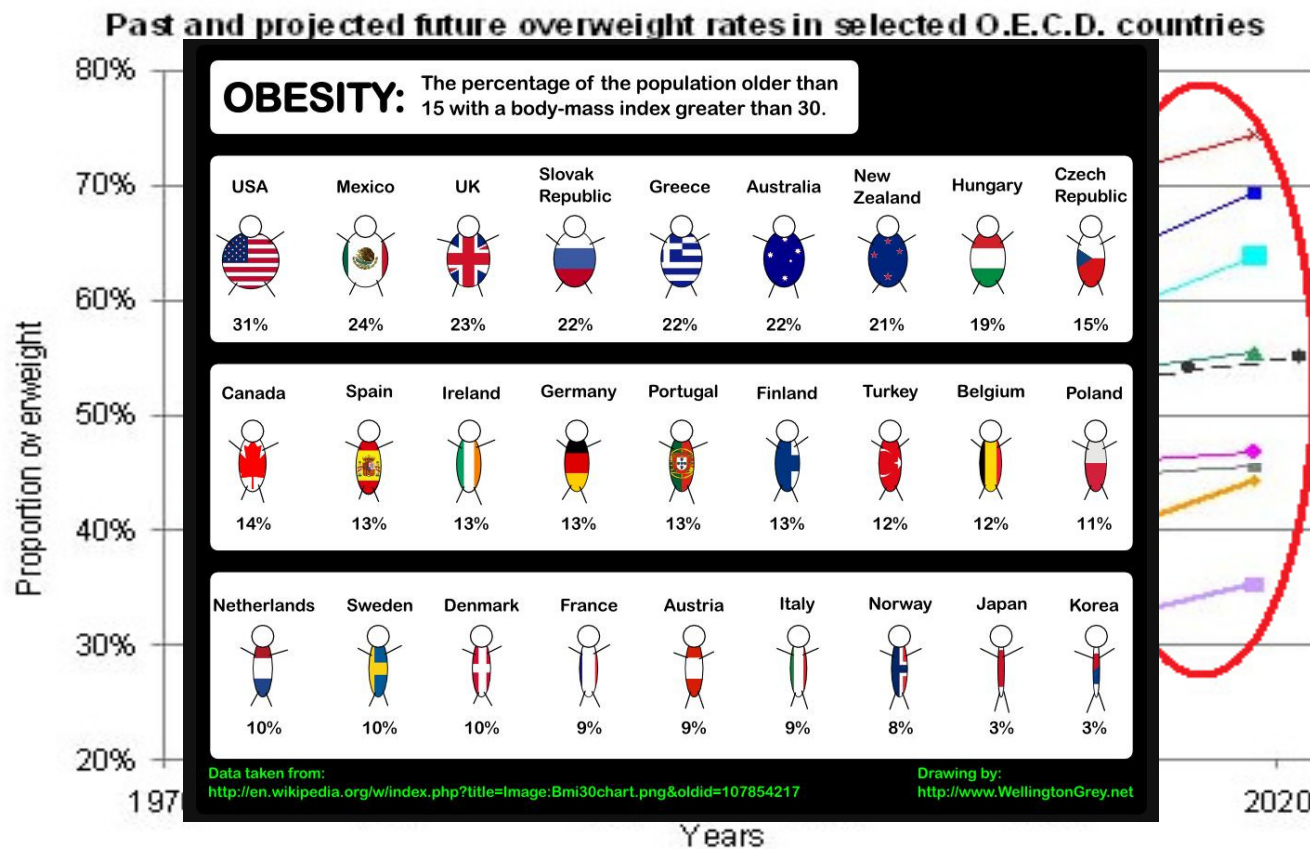
The problem  
addressed is:





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Organization for Economic Cooperation and Development



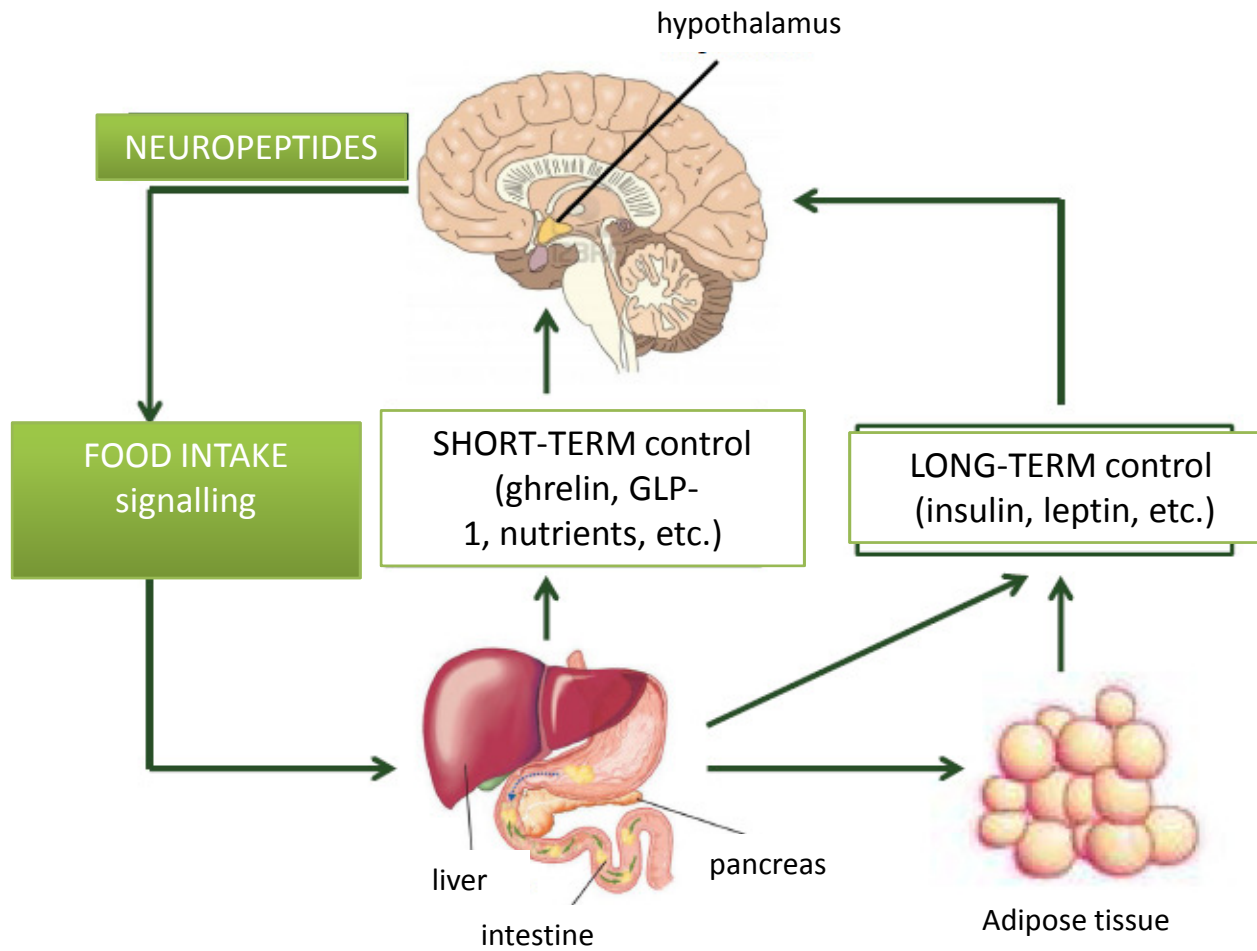


The USA and UK estimate that 40-50% of pets  
“exceed their ideal body condition.”

→ Our proposal is:

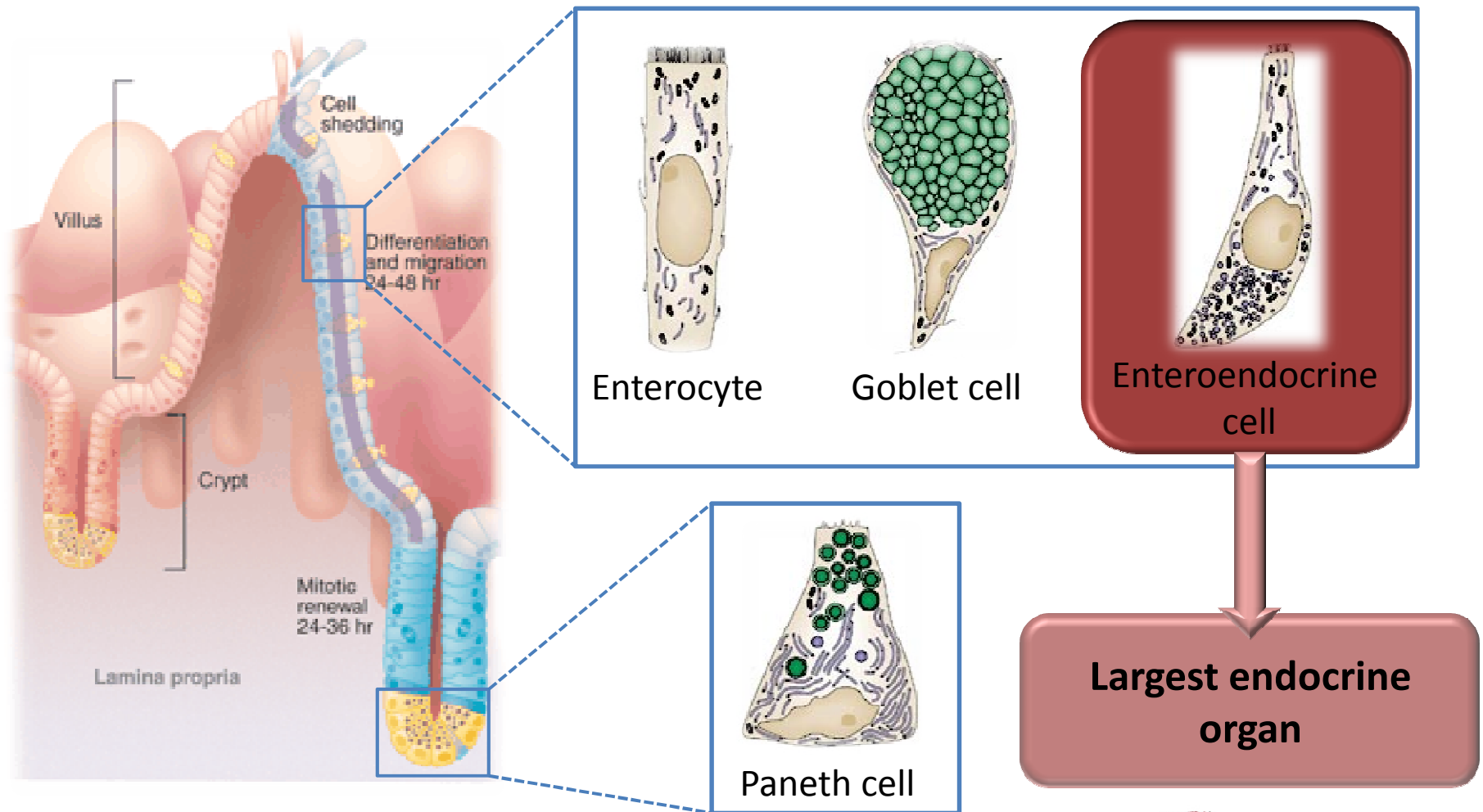
- Decreasing energy intake to help control body weight
- Approaching a market interested in maintaining the feeling of satiety to help curb energy intake

## *Food intake control*





## Enteroendocrine cells



## Enteroendocrine cells



Epithelial localization

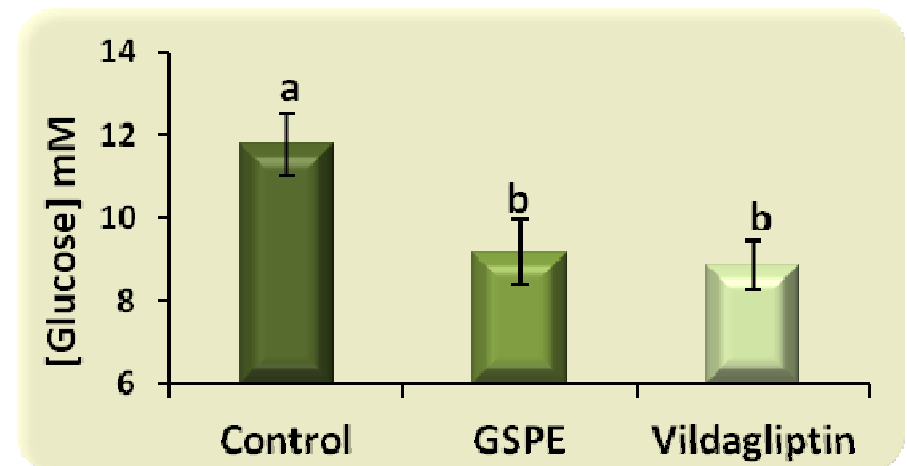
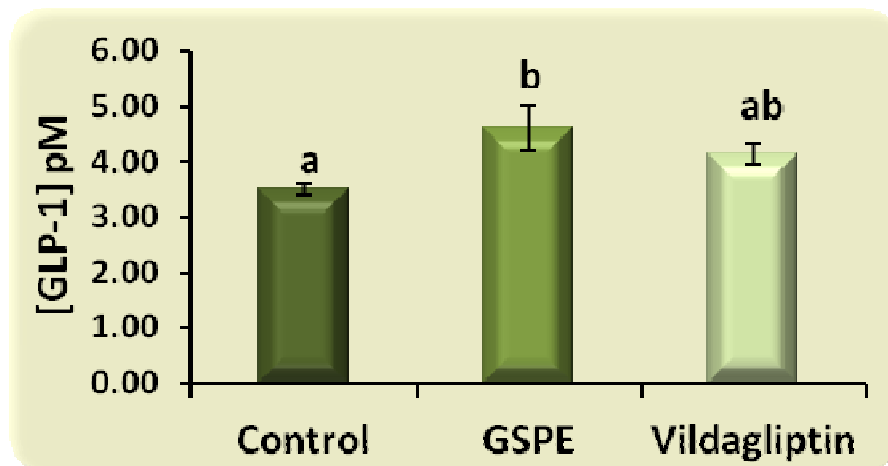
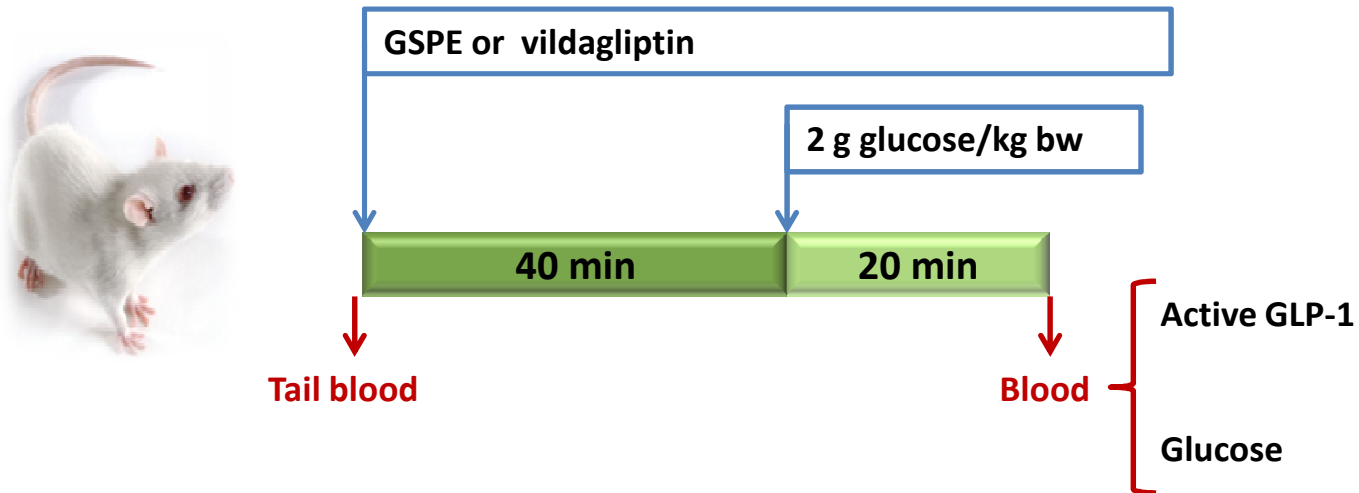
**CLOSED**

**OPEN**

Morphology, hormone product(s), distribution

Cell type	Highest density	Peptide released
G-cells	Stomach	Gastrin
X-cells	Stomach	Ghrelin
ECL-cells	Stomach	Histamin
Unnamed cells	Stomach and duodenum	Gastrin Releasing Peptide (GRP)
S-cells	Duodenum and jejunum	Secretin
I-cells	Duodenum and jejunum	Cholecystokinin (CCK)
K-cells	Duodenum and jejunum	Glucose-dependent insulintropic polypeptide (GIP)
N-cells	Ileum	Neurotensin
L-cells	Ileum and colon	Glucagon-like peptides (GLP's), Peptide YY (PYY)
D-cells	Entire GI tract	Somatostatin
EC-cells	Entire GI tract	5-hydroxytryptamin (5-HT, Serotonin)

Steinert R.E. and Beglinger  
C. (2011) *Physiol Behav*



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## A grape seed extract increases active glucagon-like peptide-1 levels after an oral glucose load in rats†

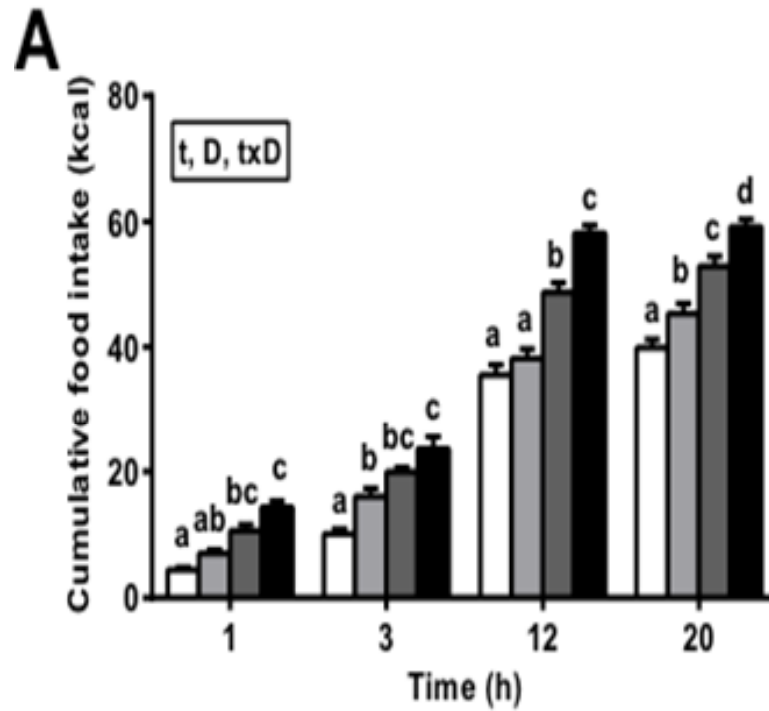
Noemi González-Abuin,<sup>a</sup> Neus Martínez-Micaelo,<sup>a</sup> Maria Margalef,<sup>a</sup> Mayte Blay,<sup>a</sup> Anna Arola-Arnal,<sup>a</sup> Begoña Muguerza,<sup>ab</sup> Anna Ardévol<sup>\*a</sup> and Montserrat Pinent<sup>a</sup>

Could grape-seed derived proanthocyanidin  
extract be useful in limiting food intake?

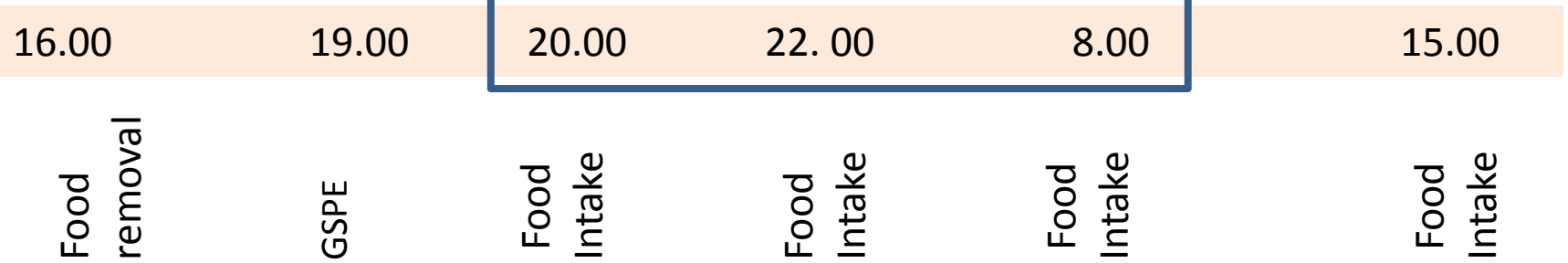
Rat model for food intake measurement:



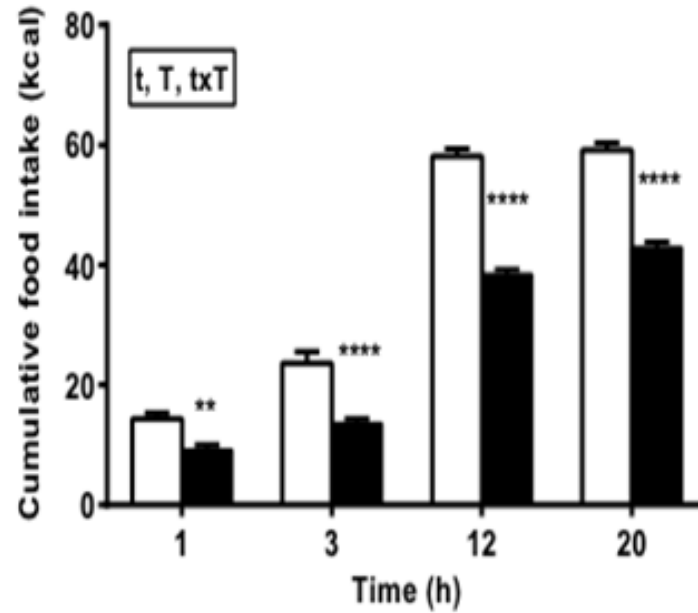
Chow   
Tasty diet 







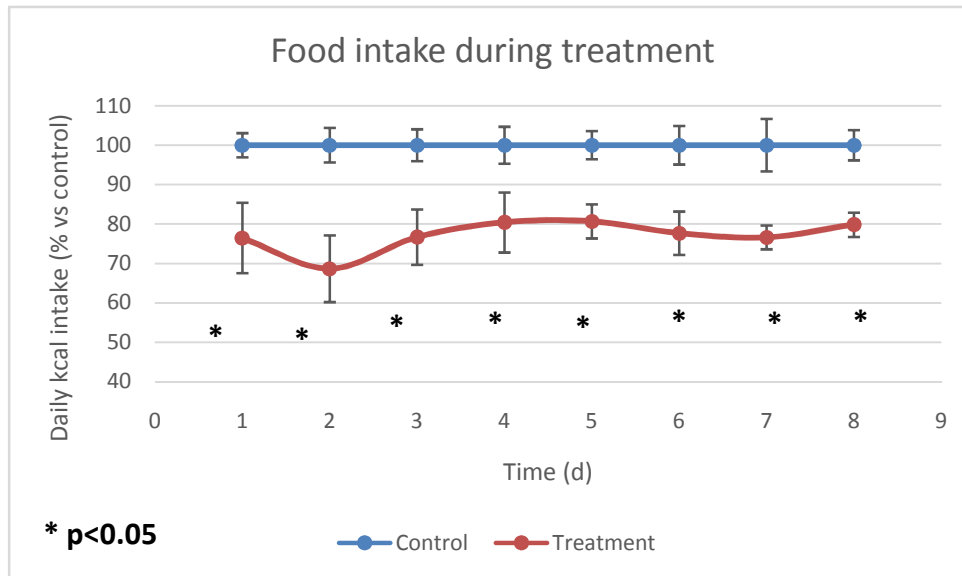
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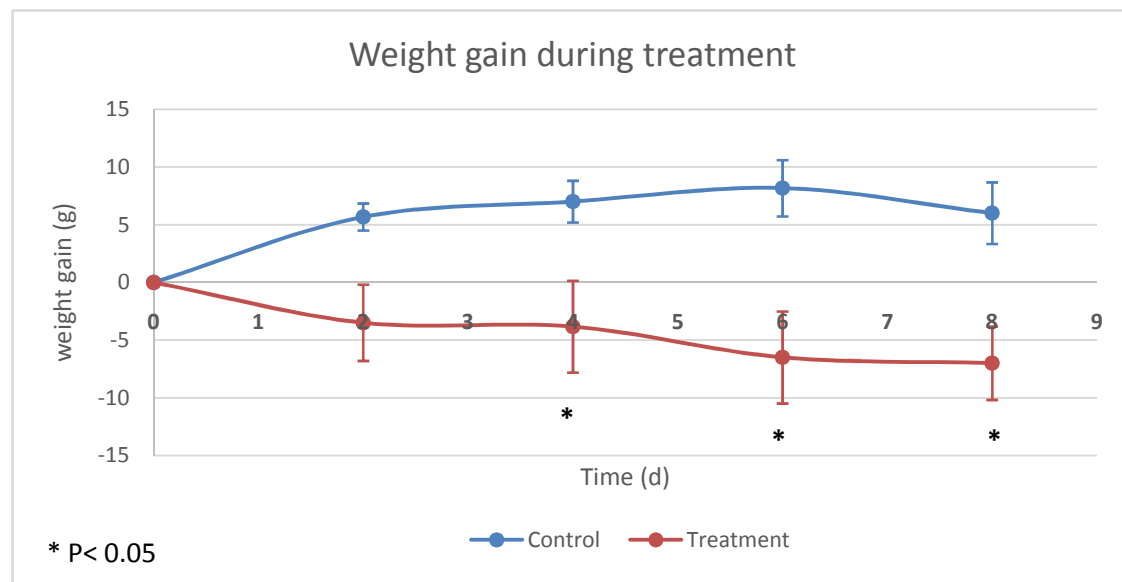
Tasty diet  
+ GSPE



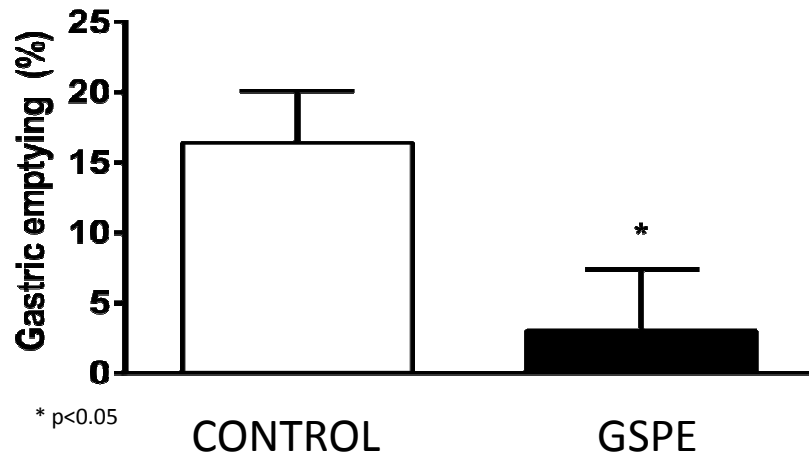
Food intake inhibitory activity of proanthocyanidin extracts under different conditions						
Sex	BW (g)	Diet	H dose	Extract	Dose	12h food intake inhibition (%)
♀	207	Chow	-1	GSPE	A	22.2 ± 3.8 **
♀	223	Chow	-1	GSPE	A/2	18.7 ± 3.4***
♀	217	Chow + 11ml HS	-1	GSPE	A/2	15.9 ± 3.1*
♀	219	Chow + 11ml HS	-1	GSPE	A/10	1.4 ± 5.0
♀	204	Chow	0	GSPE	A	27.7 ± 9.0*
♂	542	Chow	-1	GSPE	A	25.0 ± 4.5**
♂	543	Chow	1	GSPE	A	16.2 ± 7.1



Treatment:  
one dose/day for 8 days

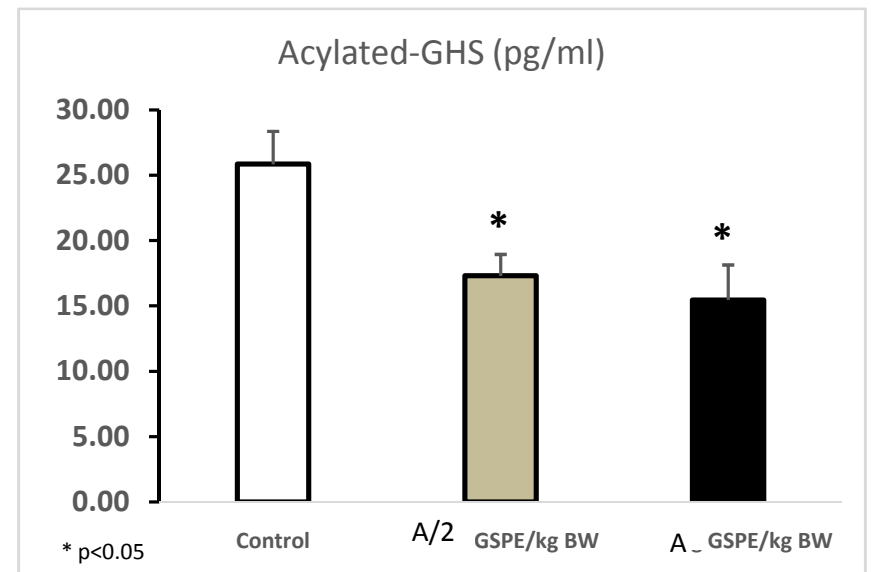
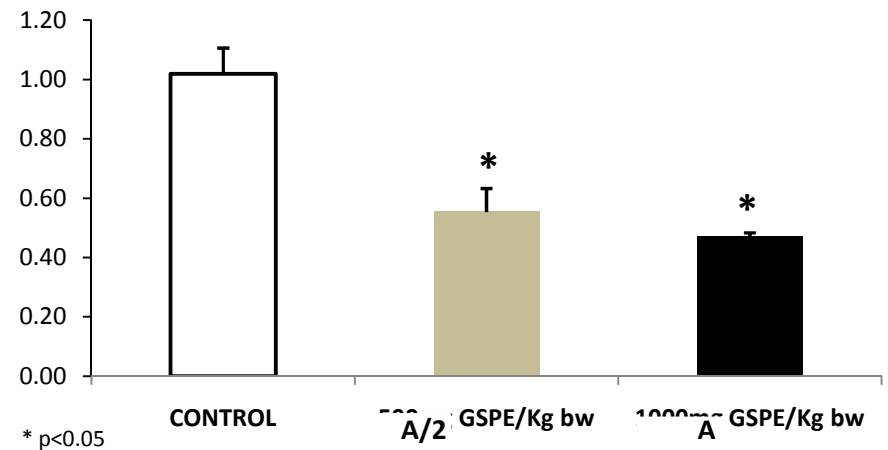


How it works?



Portal levels of GLP-1 and insulin		
Hormone	Treatment	80min
GLP-1	Control	3.84 ± 0.35
	GSPE	8.64 ± 1.00***
Insulin	Control	1.76 ± 0.31
	GSPE	3.29 ± 0.72*

## Stomach ghrelin expression



→ What we know:

- How much GSPE is needed to limit food intake and how to administer it to produce this effect
- To a certain extent, how it works
- That it is a safe product for human health
- That the extract can be repeatedly obtained

## Is this an innovative approach?

- There are several products derived from grape seed extracts on the market.
  - Most of them emphasize the **antioxidant** properties of these extracts.
  - In some cases they are also offered as an **immune stimulator** and/or a product with **anticancer** properties.
  - The suggested doses for these properties are a **maximum of 20 g/** dose.
  - Their antioxidant effect is scientifically proved; there is also overwhelming evidence of their anti-inflammatory activity and anticancer effect.
  - **There are no products on the market that propose using this extract as a satiating agent because, prior to our work, there was no evidence of it.**
- Some products offer a satiating effect, mainly based on fibre composition.
  - There is **scarce scientific support** for this effect. Additionally, **EFSA is not approving applications for it** due to the lack of effect and the difficulty in determining the composition of the product.
- We propose using the satiating effects of a by-product of the huge winery industry: grape seed extract
  - It could be **easily developed** from a **natural extract** that is **already available** on the market.
  - To date, we have found compelling evidence in animal studies, with a statistically significant effect (**20% reduction in energy ingested**).
  - We need **to run a human trial to** adjust the best dose, to reproduce the optimal effects we have achieved in rats.



→ What we need before going to market:

Before going to market as a nutraceutical	Expected time	Expected €
Safety and reproducibility of production	0	√
Clinical trial	10 months	40 000
Better understanding of the effect	10 months	AGL2014-55347-R
Intellectual property and legal aspects	Patent application on October 2014	10 000
Technological aspects for industrial development	6 months	50 000
Market and marketing analysis	3 months	10 000
Total amount	≈ 2 years	≈ 200 000




Thank you very much!

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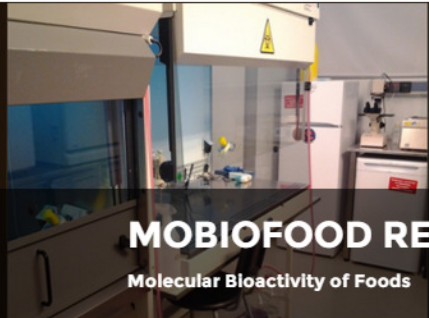
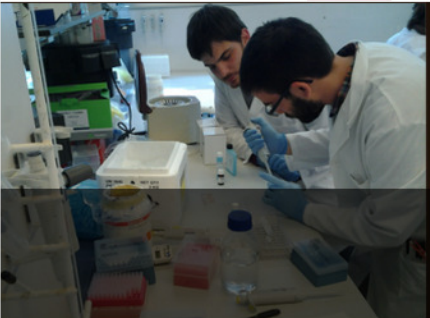
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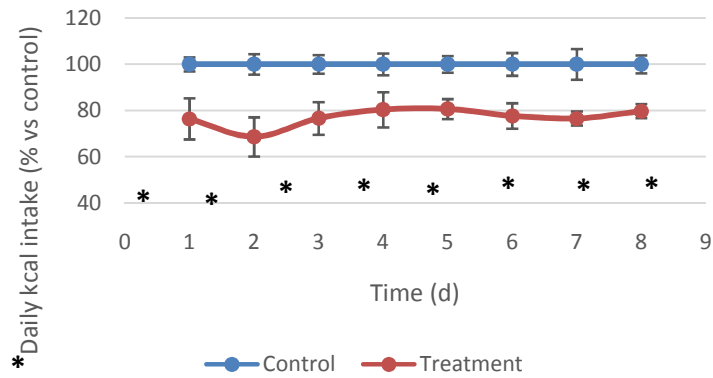
COVER WHO PUBLICATIONS FUNDING EXPERTISE THESIS CONTACT



**MOBIOFOOD RESEARCH GROUP**  
Molecular Bioactivity of Foods

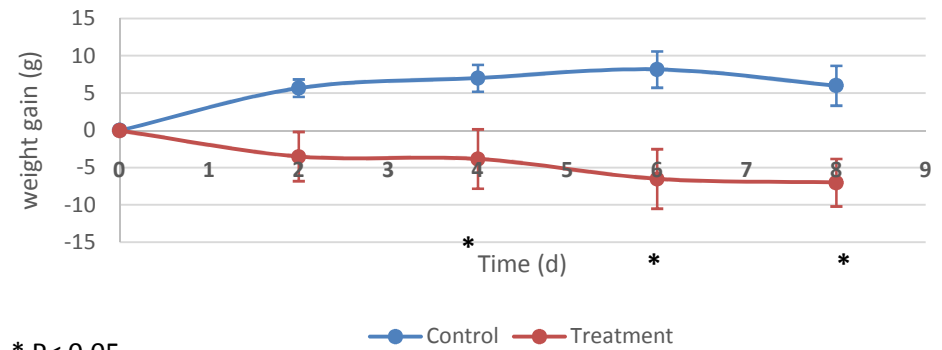
The expertise of this group is in the area of flavonoids. We have described the bioactivity of procyanidins on glucose homeostasis; we have a high expertise describing how they act as anti-inflammatory agents, mainly at the adipose tissue. At present, we are focused on **the study of**

### Food intake during treatment



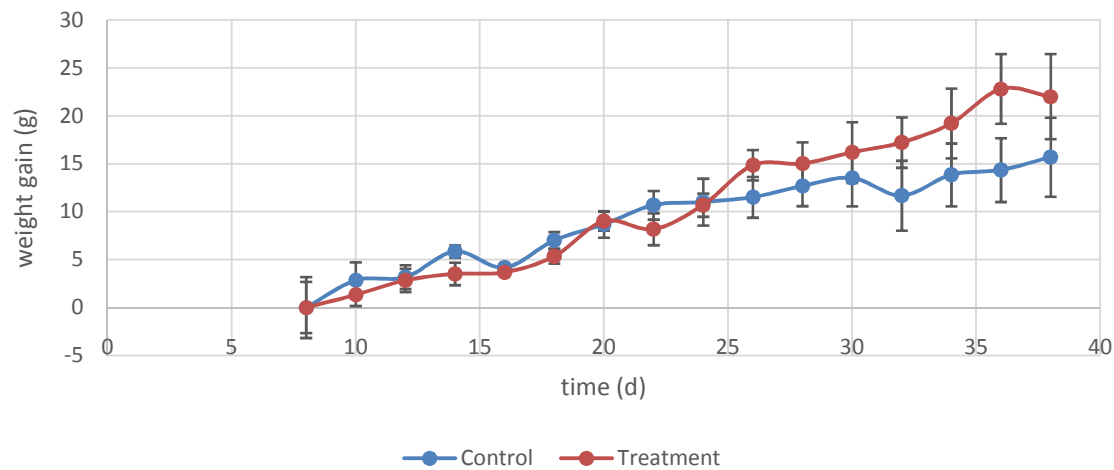
**p<0.05**

### Weight gain during treatment



**\* P<0.05**

### Weight gain after treatment



## As a nutraceutical (one of the possibilities):

