LUNASIN AND PEPTIDES RELEASED DURING ITS GASTROINTESTINAL DIGESTION, NOVEL NUTRITIONAL ALLIES AGAINST CHRONIC DISEASES

P. Indiano-Romacho[1], S. Fernández-Tomé[2], L. Amigo[1], B. Hernández-Ledesma[1]

[1] *Instituto de Investigación en Ciencias de la Alimentación, CIAL (CSIC-UAM), Nicolás Cabrera, 9, 28049 Madrid, Spain*

[2] *Instituto de Investigación Sanitaria del Hospital Universitario de La Princesa (IIS-IP), Diego de León, 62, 28006, Madrid, Spain*

*pedro.indiano@csic.es

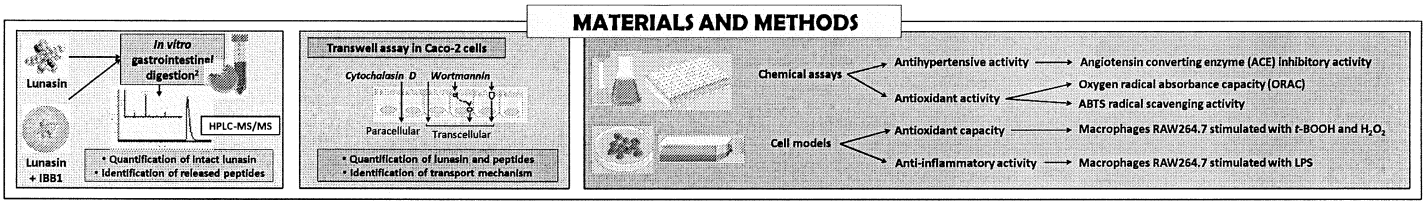
INTRODUCTION

- Chronic diseases have been associated to multiple altered states such as inflammation, oxidative stress, hypertension and/or hyperglycemia. These states can be modulated by the diet.
- Lunasin is a 43 amino acid soy-derived peptide with multiple health benefits.
- Different animal and human models have demonstrated lunasin's bioavailability[1], suggesting that the protective role exerted by soybean protease inhibitors against digestion was the principal responsible factor.

OBJECTIVES

1. STUDY LUNASIN'S BIOAVAILABILITY UNDER GASTROINTESTINAL DIGESTION AND ABSORPTION CONDITIONS
2. EVALUATE THE CONTRIBUTION OF NEW PEPTIDES RELEASED DURING DIGESTION ON LUNASIN'S MULTIFUNCTIONALITY

MATERIALS AND METHODS



RESULTS

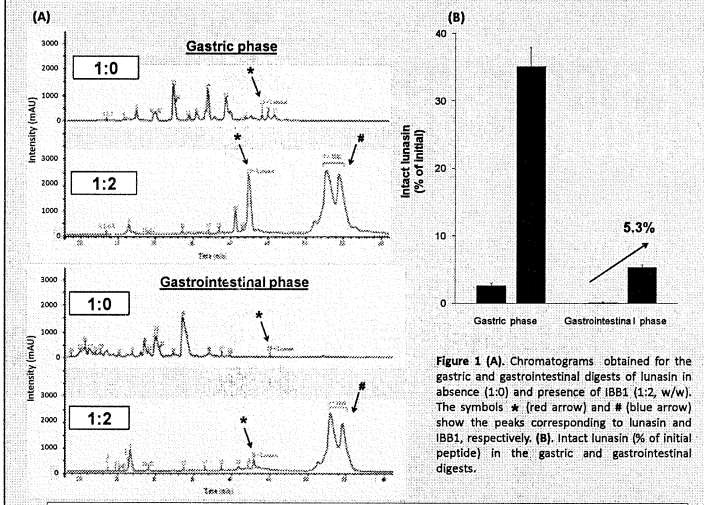


Figure 1 (A). Chromatograms obtained for the gastric and gastrointestinal digests of lunasin in absence (1:0) and presence of IBB1 (1:2, w/w). The symbols ★ (red arrow) and # (blue arrow) show the peaks corresponding to lunasin and IBB1, respectively. **(B).** Intact lunasin (% of initial peptide) in the gastric and gastrointestinal digests.

After simulated gastrointestinal digestion of lunasin:IBB1 mixtures, 5.3% of lunasin remained intact, confirming the protective role exerted by IBB1 against the action of digestive enzymes on lunasin

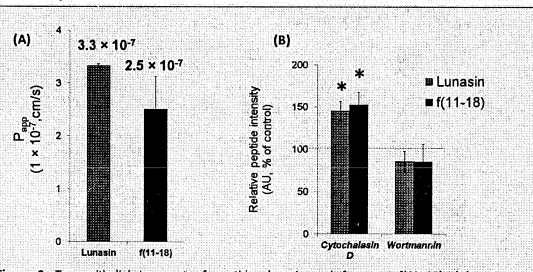
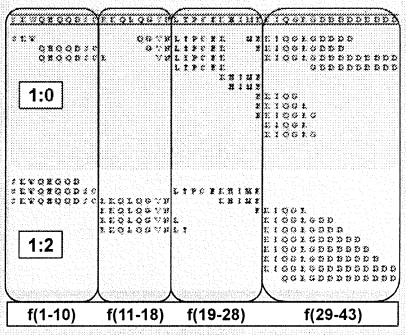


Figure 3. Transepithelial transport of peptides lunasin and fragment f(11–18). **(A)** Apparent permeability coefficient (Papp). **(B)** Effects of cytochalasin D and wortmannin on the transepithelial transport of peptides.

Lunasin and f(11-18) are bioavailable through a paracellular transport mechanism



Seventeen peptides resistant to the action of digestive enzymes were identified in gastrointestinal digests of lunasin:IBB1 mixtures

Figure 2. Lunasin-derived fragments identified in the gastrointestinal digests of lunasin in absence (1:0) and presence of IBB1 (1:2, w/w). Resistant regions to the action of digestive enzymes are shown.

Table 1. *In vitro* ACE-inhibitory and antioxidant activity of lunasin (SKWQHQQDSCRKQLQGVNLTPCEKHIMEKIQGRGDDDDDDDD) and derived-fragments identified in the gastrointestinal digest of mixture lunasin:IBB1 (1:2, w/w). n.d.: not detected. TE: Trolox equivalents

Peptide	Sequence	ACE inhibitory activity (IC_{50}, μM)	Antioxidant activity	
			ORAC (μmol TE/μmol peptide)	ABTS (μmol TE/μmol peptide)
Lunasin	Lunasin	<15	3,44 ± 0,07	3,47 ± 0,07
f(1-10)	SKWQHQQDSC	200,3 ± 9,56	1,94 ± 0,17	1,71 ± 0,03
f(11-18)	RKQLQGVN	n.d.	n.d.	n.d.
f(17-28)	VNLTPCEKHIME	41,1 ± 2,69	1,02 ± 0,03	0,96 ± 0,02
f(19-28)	LTPCEKHIME	17,64 ± 2,52	0,83 ± 0,07	0,86 ± 0,01
f(29-41)	KIQGRGDDDDDDD	n.d.	n.d.	n.d.
f(29-43)	KIQGRGDDDDDDDDD	n.d.	n.d.	n.d.
f(30-43)	IQGRGDDDDDDDDD	n.d.	n.d.	n.d.
f(34-43)	GDDDDDDDDD	n.d.	n.d.	n.d.

Lunasin is the most potent ACE-inhibitory and antioxidant peptide. Central and N-terminal regions contribute to the *in vitro* activities

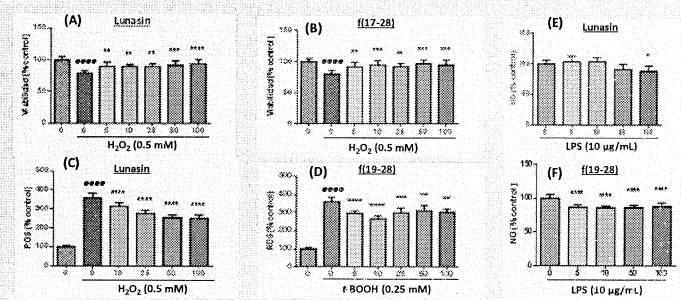


Figure 4. (A-B) Cell viability (% of control), (C-D) reactive oxygen species (ROS) levels (% of control) and (E-F) nitric oxide (NO) levels (% of control) of lunasin and derived-fragments f(17-28) and f(19-28) corresponding to central region of lunasin. The assays were performed in macrophages RAW264.7 stressed with H_2O_2 and/or **t-BOOH** (antioxidant activity) and with **LPS** (anti-inflammatory activity). Data are presented as mean ± SEM. Statistical analysis was based on one-way ANOVA and Dunnett post hoc test; *p<0.05,**p<0.01, ***p<0.001, ****p<0.0001 *vs.* stressed group; @@@@p<0.0001 *vs.* non-stressed group.

Lunasin exerts antioxidant and anti-inflammatory activities in stimulated macrophages RAW264.7 cells. Peptides found in the lunasin's central region are the main contributors on the observed effects

CONCLUSIONS

REFERENCES

(1) Hsieh, C.-C., et al. J. Sci. Food Agric. 2018, 98, 2070-2079.

(2) Minekus, M., et al. *Food & Funct.*, 2014, 5, 1113-1124.

ACKNOWLEDGEMENTS

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