FOOD ANTIHYPERTENSIVE PEPTIDES

Guillem Pascual Fabregat

Universitat Autònoma de Barcelona

FOOD SCIENCE & TECNOLOGY

INTRODUCTION

Bioactive peptides are encrypted within the primary of **food proteins** where they remain inactive until realise by hydrolysis. **Antihypertensive peptides** are those peptides which have the ability to modulate the activity of the enzymes and receptors that regulate human **blood pressure**. They could modulate the **renin-angiotensin system (RAS)** and other pathways like **arginine-nitric oxide system**.

This project focuses on describing the main peptides and protein hydrolisates **production methods** and their subsequent *in vitro* and *in vivo* **activity essays**. Also, it describes which **molecular targets** such **ACE** inhibits and how. And, finally, it classifies hypotensive peptides according to their **protein source**.

METHODOLOGY

- Bibliographic search of reviews and research articles in databases.
- Reading and abstracting the collected literature in order to elaborate the written review.

Keywords: antihypertensive peptides, ACE –inhibitor peptides, food proteins, protein hydrosilates

HYPERTENSION PHISIOPHATOLGY & PEPTIDES ACTION MECHANISMS

THE RENIN-ANGIOTENSINE SYSTEM & ARGINE-NITRIC OXIDE SYSTEM PAHTWAYS

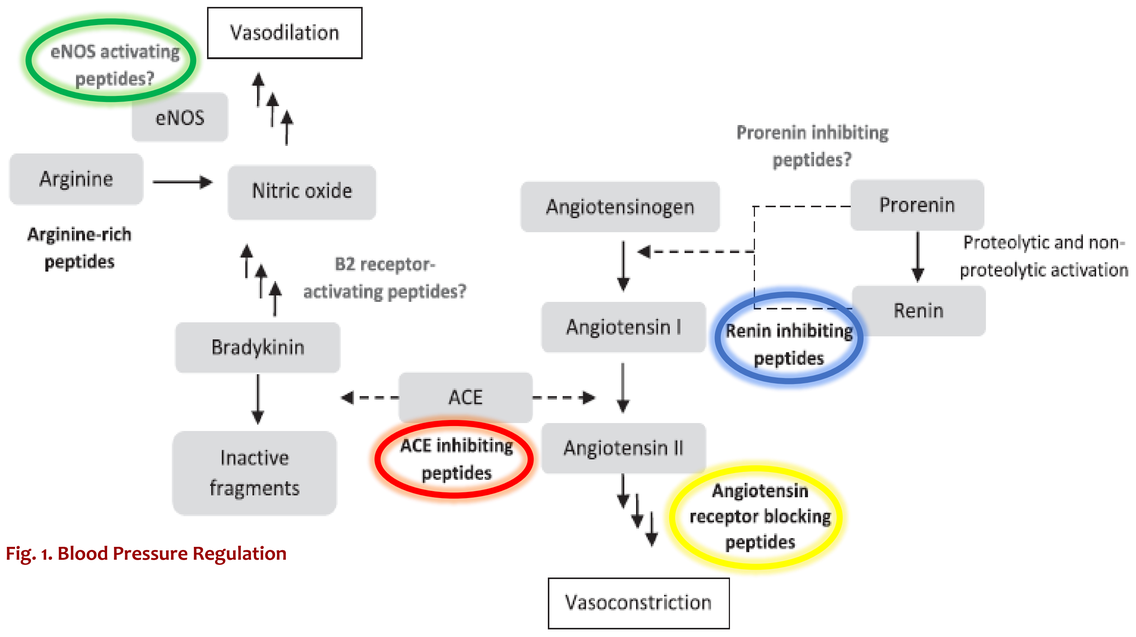

Fig. 1. Blood Pressure Regulation

ACE INHIBITION

The **primary structure** of peptides is a relevant factor to search potentially ACE inhibitors. **Statistical modelling** plus ***in vitro* essays** are used to identify the active peptides sequence with **peptides databases** help.
The results obtained for ACE-inhibitors are:

- **BBCAAs** like Valine & Isoleucine
- **AAAs** like Phenylalanine, Tryptophan
- **C-terminal Proline**

* *Wu et al.*, & *Sagardia et al.* reveal the importance of **C-terminal sequence**.

- **C2 (aa +)**
- **C4 (Trp)**

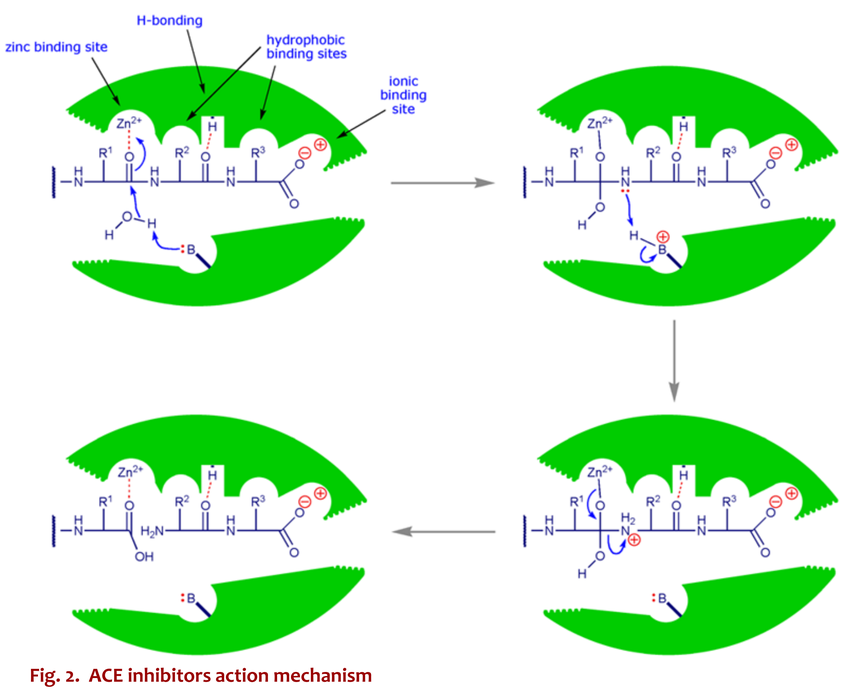

Fig. 2. ACE inhibitors action mechanism

Examples of antihypertensive peptides depending on molecular targets

-Collagen hydrosilate inhibits competitively. (1)
-Egg albumen peptides from lysozyme inhibits no competitively. (2)

→ Egg peptide (Arg-Val-Pro-Ser-Leu) reduce renal AT-II renal RNAm expression. (4)
Lactoferrin milk peptide block AT-II. (5)

Pea protein hydrosilate studied with SHR model and human. (3)
Egg pentapeptide (RVPSL) reduce mRNA expression. (4)

→ Amarant glutenin digested by tripsin induce NO production. (6)

FROM PROTEIN SUBSTRATE TO COMERCIAL PRODUCTS

PROTEIN SOURCE

The population ingest an average of **50-70 g of protein per day.** Some of antihypertensive peptides had been found intrinsically in natural products, such as fermented food like tofu or cured meats. The most studied food groups are **milk** and **eggs**, but recently scientists have been studying another kind of animal and vegetable proteins.

PROTEIN HYDROLIS

- **Chemic hydrolysis**: Use of **acid** and **alkali** solutions. Bad specificity.
- **Enzymatic hydrolysis:** Use of **proteases** and **peptidases** (optimal Tª& pH). **Enzyme cleavage** is very important to originate bioactive peptides.
- **Microbial fermentation:** During the fermentation, some **bacteria** and **yeast** secrete **exoproteases** that digest food proteins.
- **Recombinant DNA technology:** Genetic recombination is used to achieved DNA which will express a novel mRNA, translating a novel protein. Emerging methodology.

ASSAY TESTING

In vitro
The reduced or potentiated activity of a enzyme involved in blood pressure modulation could be estimated by different methods, like **spectrophotometry**, **HPLC** or **fluorometry.**

In vivo
Consist on proving the antihypertensive peptides effects, like the measure of systolic and diastolic blood pressure, in **spontaneous hypertensive rats** modelling (SHR).

COMERCIAL PRODUCT

Name	Product type	Active sequence(s)
Calpis®	Fermented milk product	VPP, IPP
Vasotensin®	Bonito protein hydrolyzate	LKPNM, LKP
Peptide C12®	Casein hydrolyzate	FFVAPFPEVFGK
Evolus®	Fermented milk product	VPP, IPP
Tensiocontrol®	Egg protein hydrolyzate	RADHPFL, YAEERYPIL, IVF
Biozate®	Whey protein hydrolyzate	Whey peptides
Lowpept®	Casein hydrolyzate	RYLGY, AYFYPEL

Before commercialisation of novel products is necessary exhaustive investigations to prove the antihypertensive effects in **humans** and the **minimum doses needed.**

CONCLUSIONS

There are multitude of different antihypertensive peptides. Those hypotensive peptides could be classified according to their **natural source** (e.g. milk), their **production method** (e.g. enzymatic hydrolysis), **the molecular targets** that they modulate (e.g. ACE) or the correspondent **activity assays** to evaluate their antihypertensive potential (e.g. SHR).
Also, one key is their **bioavailability**. Some of they are not available to be absorbed by intestinal epithelium, or they could be digested by endogens enzymes and become inactive.

FUTURE PRESPECTIVES

Anyway, antihypertensive peptides are a suitable tool **to reduce the blood pressure.** In the near future they could **substituted synthetics drugs**. For now, more research, concerning the **structural requirements** for modulating the biological targets is needed. As well as **humans essays** that demonstrate the healthy properties of peptides r**educing** the incidence of **hypertension**.

REFERENCES

1. Banerjee P, Shanthi C. 2012. Isolation of novel bioactive regions from bovine Achilles tendon collagen having angiotensin I-converting enzyme inhibitory properties. *Process Biochem.* 47:2335–46
2.Memarpoor-Yazdi M, Asoodeh A, Chamani JK. 2012. Structure and ACE-inhibitory activity of peptides derived from hen egg white lysozyme. *Int. J. Pept. Res. Ther.* 18:353–60
3.Li H, Prairie N, Udenigwe CC, Adebiyi AP, Tappia P, et al. 2011. Blood pressure lowering effect of a pea protein hydrolysate in hypertensive rats and humans. J. Agric. Food Chem. 59:9854–60
4.Yu Z, Yin Y, Zhao W, Chen F, Liu J. 2014. Antihypertensive effect of angiotensin-converting enzyme inhibitory peptide RVPSL on spontaneously hypertensive rats by regulating gene expression of the reninangiotensin system. J. Agric. Food Chem. 62:912–17
5. Yu Z, Yin Y, Zhao W, Chen F, Liu J. 2014. Antihypertensive effect of angiotensin-converting enzyme inhibitory peptide RVPSL on spontaneously hypertensive rats by regulating gene expression of the reninangiotensin system. J. Agric. Food Chem. 62:912–17
6. Maldonado-Cervantes E, Jeong HJ, León-Galván F, Barrera-Pacheco A, De León-Rodríguez A, González De Mejia E, De Lumen BO, Barba De La Rosa AP. 2010. Amaranth lunasin-like peptide internalizes into the cell nucleus and inhibits chemical carcinogen-induced transformation of NIH-3T3 cells. Peptides. doi:10.1016/j.peptides.2010.06.014