

Food-derived Bioactive Peptides as Potential Therapeutics and Nutraceuticals

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Background Information

Diet & Disease Prevention

- Inflammation is associated with numerous chronic age-related diseases.
- A plant-based diet may reduce inflammation, as fruits, vegetables, pulses and nuts are rich sources of biologically active substances.
- Inadequate fruit and vegetable intake has been recognized as a risk factor for almost all non-communicable diseases (NCD).

Phytochemicals Bioactive peptides from plant sources and phytonutrients

- Fruits and vegetables are rich sources of beneficial immune protective compounds, including vitamins carotenoids and flavonoids, which affect cellular growth and differentiation and are needed for the optimal functioning of the immune system.
- Recently, peptides from plant sources have been recognized as having bioactivity

Peptides as therapeutics & nutraceuticals

- Increasing the utilization of plant proteins supports the production of protein-rich foods that could replace animal proteins in the human diet and reduce the strain that intensive animal husbandry poses to the environment.
- Bioactive peptides can exert health beneficial properties and have potential as nutraceuticals.

Peptide databases available

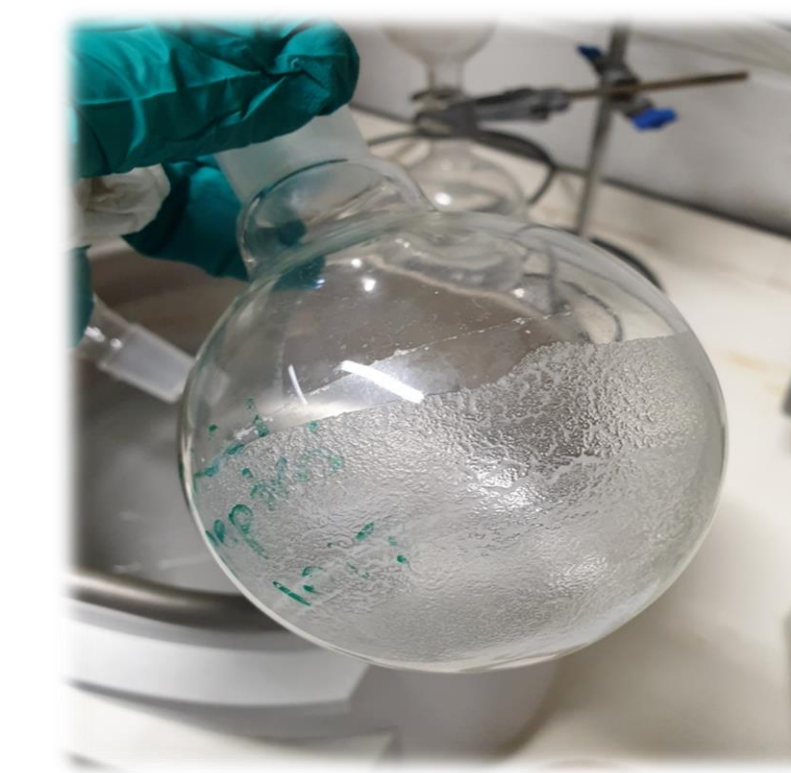
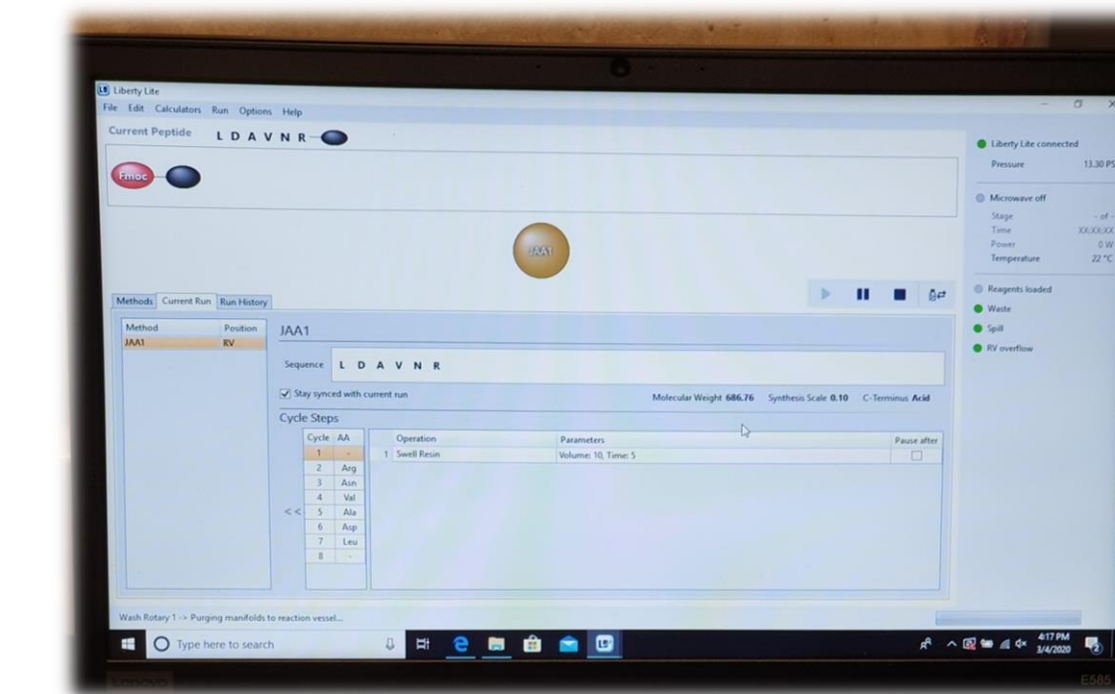
- PlantPepDB (<http://223.31.159.8/PlantPepDB/index.php>)
- PeptideDB: (<http://www4g.biotech.or.th/PeptideDB/>)
- BIOPEP-UWM Database of Bioactive Peptides (<http://www.uwm.edu.pl/biochemia/index.php/en/biopep>)
- StraPep: a structure database of bioactive peptides (<http://isyslab.info/StraPep/>)

Aim & Methods

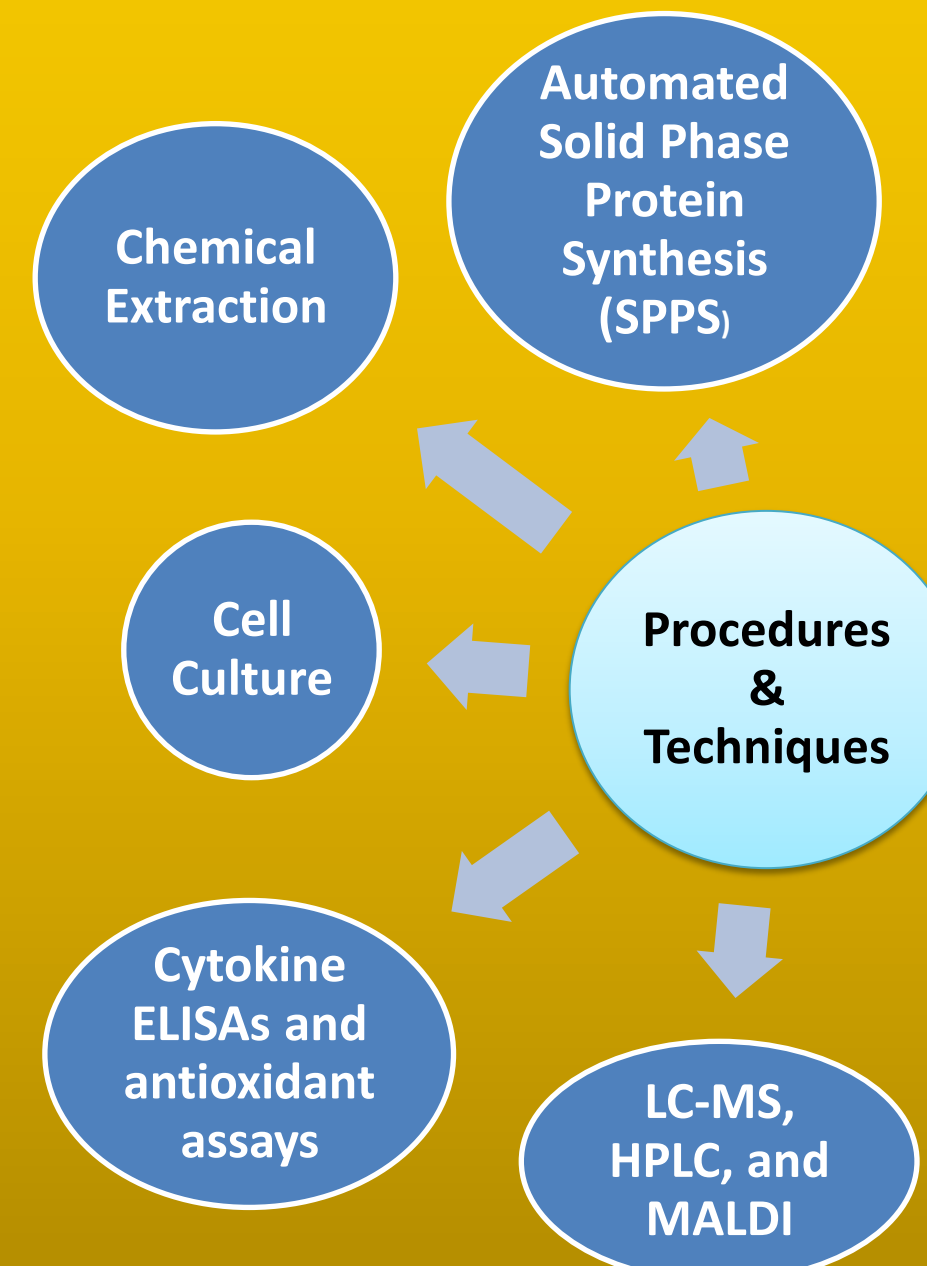
- Review the literature to compile a database of plant food-derived bioactive peptides with anti-inflammatory, antioxidant, and cytoprotective effects.
- Synthesize and extract the bioactive peptides from the food sources to investigate their activity and potential role in disease prevention.



The synthesis of the peptide (LDAVNR) using automated solid phase protein synthesis (SPPS)

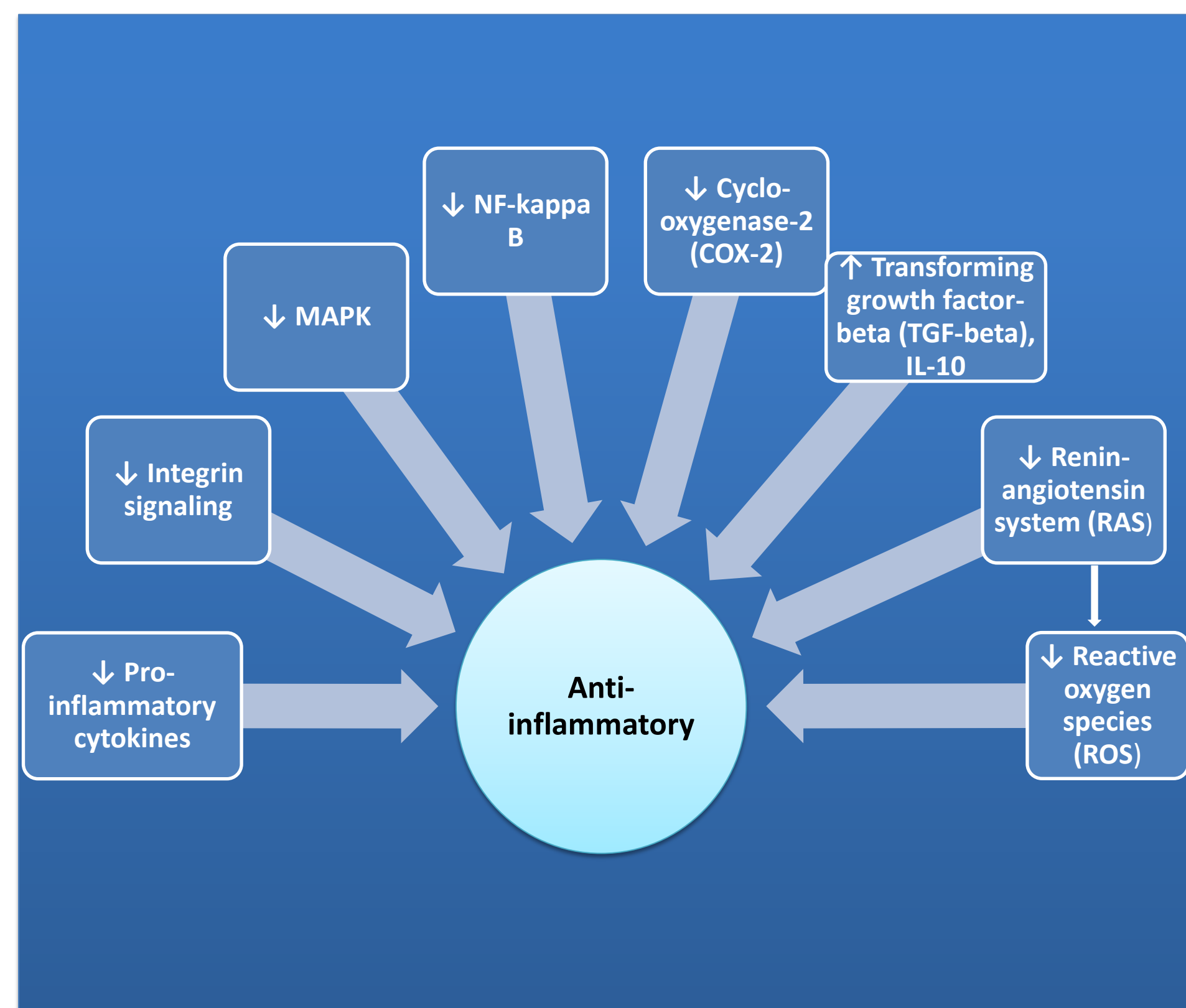


Methods

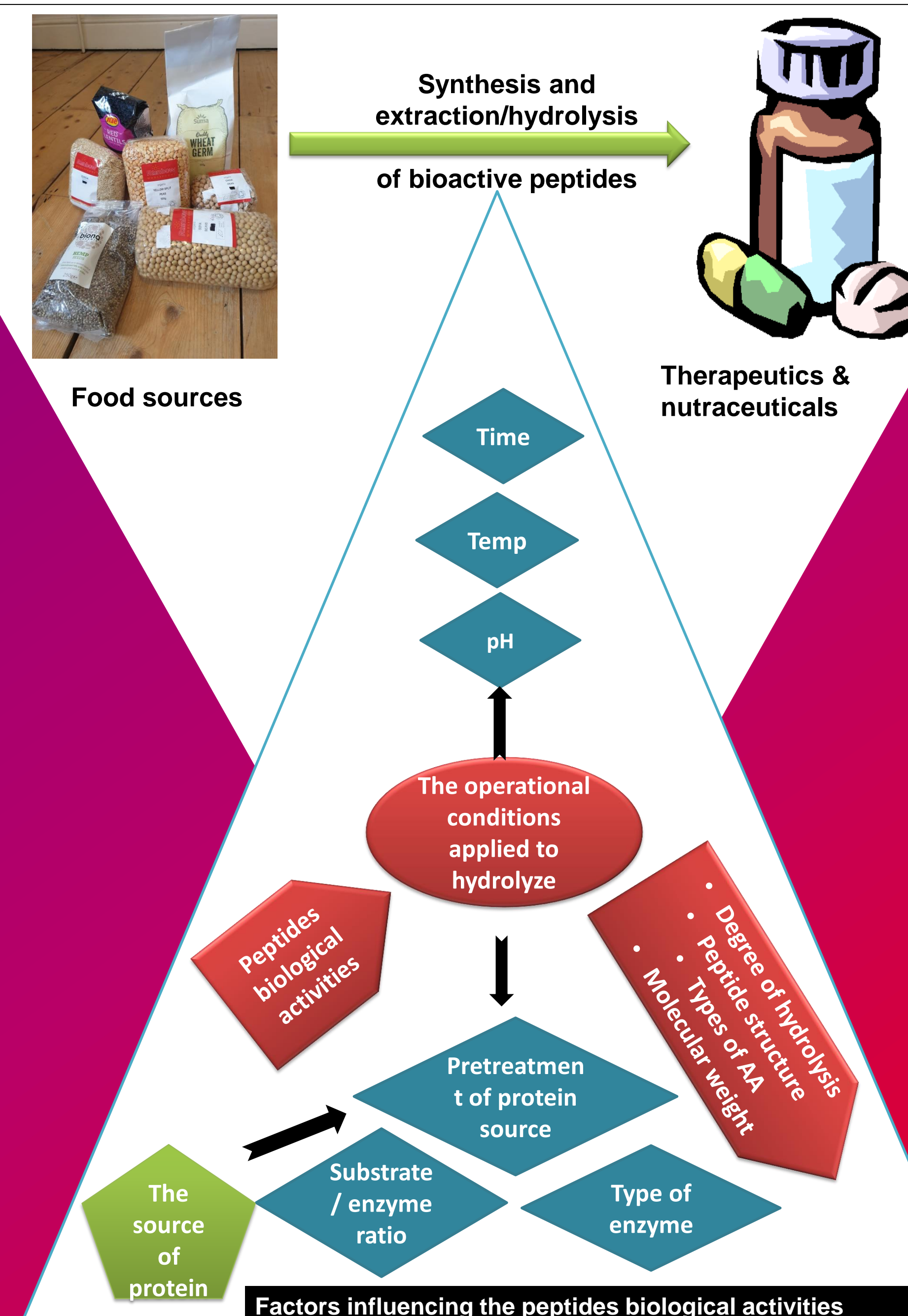


Anti-inflammatory activity

- Inflammation is a complex multisystem process affecting a wide range of cells, tissues, and organs.
- Numerous pro-inflammatory mediators, including pro-inflammatory cytokines (eg TNF- α , IL-1,6,8), chemokines (eg MCP-1), growth factors (eg TGF β) and reactive oxygen species (eg superoxide and peroxynitrite) are involved in both the generation and propagation of the inflammatory response. Several intracellular signaling pathways regulate inflammation, including NF- κ B, mitogen activated protein (MAP) kinases and activator protein-1 (AP-1).
- Bioactive peptides may inhibit these pro-inflammatory mediators and intracellular signaling pathways.



Food source	Sequence/ name of peptide	Bioactivity
Amaranth	Low molecular mass peptides less than 2064 Da	Reduced proliferation of NO, TNF-alpha, PGE2 and COX2 in in LPS stimulated THP-1 and RAW 264.7 cells
Edible microalgae (Spirulina maxima)	<ul style="list-style-type: none"> Leu-Asp-Ala-Val-Asn-Arg (686 Da) Met-Met-Leu-Asp-Phe (655 Da) 	Inhibition on the production of IL-8 in histamine stimulated endothelial cells
Rice	AAGALPS	Inhibition of TNF- α -induced inflammation & oxidative stress in vascular endothelial cells



Amino Acid sequences & structural features

- Activities of the bioactive peptides (2-20 AA) may be related to the amino acid composition, sequence and length.
- All proteinogenic amino acids have amino and carboxyl groups, enabling them to form peptide bonds.

Anti-inflammatory activity & structural requirements

- The presence of **positively** charged and **hydrophobic** AA in the peptide sequence, especially in the N & C terminal.
- Peptides having **low molecular weight** => easily crosses the intestinal barrier and avoids proteolytic digestion
- Being rich in **hydrophobic AA** and mainly clustered towards the **N-terminal** such as VH, VPP, FLV, LDAVNR, and MMLDF.
- The presence of hydrophobic AA enhances the interaction between the peptide and cell membrane => modulating the downstream signaling pathways and exhibiting the anti-inflammatory effect.



LDAVNR 686.77 Da (Spirulina Maxima)

- N-terminal:** Nonpolar side chains & Hydrophobicity: ++++
- Suppressed** L-histidine decarboxylase (HDC) expression

Anti-oxidant activity & structural requirements

- Hydrolysates exert higher AOX activity than purified peptides.
- AOX peptides have a molecular mass **lower** than 1 kDa = 1000 Da
- AA with **aromatic residues** improve the radical-scavenging properties of the peptides since they can donate protons to electron deficient radicals.
- The presence of **hydrophobic** AA and **negatively** charged residues that quench free radicals due to the excess electrons.
- Hydrophobicity leads to a high interactions between the peptide and the fatty acids, concluding in protection against oxidation.



Hemp seed protein (Hydrolysis with pepsin)

At 0.5 mg/mL, *Trp-Val-Tyr-Tyr* (WVYY) and *Pro-Ser-Leu-Pro-Ala* (PSLPA) were the most active antioxidant peptides with 67% and 58% DPPH scavenging and metal chelation activity of 94% and 96%, respectively.