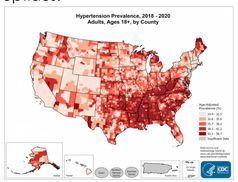
Understanding the role of the gastrointestinal microbiota in modulating the anti-hypertensive effect of egg white hydrolysate

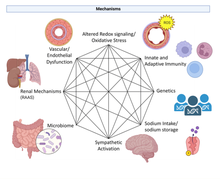
Emerson Nolasco[1], Devin Rose[1], Kaustav Majumder[1]
[1] Food Science and Technology, University of Nebraska-Lincoln, Lincoln, NE 68588-6205, United States

Contact Information:
enolasco2@huskers.unl.edu; kaustav.majumder@unl.edu

INTRODUCTION

- Cardiovascular diseases (CVDs) represent a leading cause of mortality worldwide whose prevalence comprised 48% in adults ≥20 yrs in which **hypertension** is a main risk factor.
- Hypertension is a multifactorial disease which treatments are often single target drugs, leading to adverse events as acute kidney injury or hypotension.
- Egg white hydrolysate (EWH) has arisen as a promising natural alternative since it represents a good source of anti-hypertensive peptides.





CHALLENGES AND APPROACH

CHALLENGE

- Hypertension mechanisms, besides renin-aldosterone-angiotensin system (RAAS), simultaneously modulated by EWH are unclear. Moreover, protein fermentation by the gut microbiome is expected to produce negative metabolites.

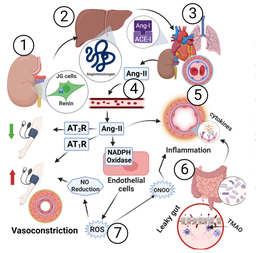


Figure 1. RAAS (1-4), vascular inflammation (5), gut microbiome (6), and oxidative stress (7) hypertension mechanisms and their interaction.

APPROACH

- Anti-hypertensive, antioxidant, and anti-inflammatory activity activity of EWH along with the gut microbiome fermentation metabolites will be elucidated.

HYPOTHESIS AND AIM

Hypothesis: food hydrolysate reduces hypertension progression through the modulation of hypertension mechanisms and the gut microbiome metabolites

Aim: determine EWH capacity to modulate diverse hypertension mechanisms and characterize the metabolites from its gut microbiome fermentation.

METHODS AND RESULTS

1. Egg white hydrolysate (EWH) process.

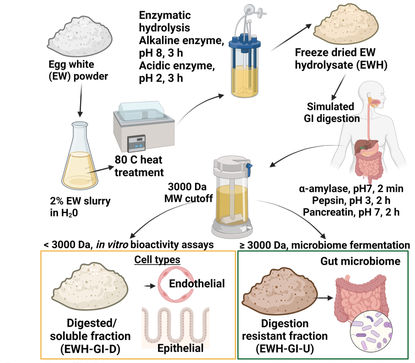


Fig. 2. EWH production and subjected to *in vitro* gastrointestinal (GI) digestion and fractionation (3000 Da).

2. Antioxidant activity by superoxide quenching in epithelial cells

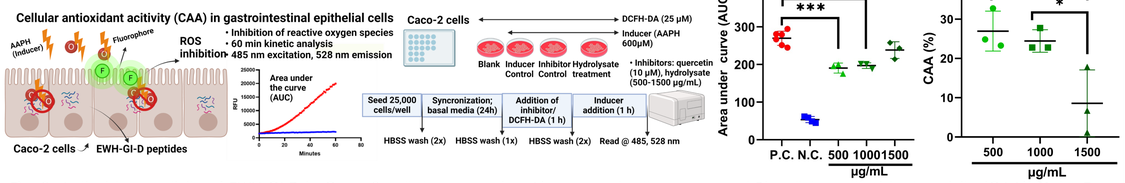


Fig. 3. Antioxidant activity of EWH-GI-D in Caco-2 cells by measuring A) area under the curve and B) cellular antioxidant activity (CAA). **Note**: Error bars: SD. AAPH: 2,2'-azobis (2-amidinopropane) dihydrochloride.

3. Anti-inflammatory activity in endothelial cells markers

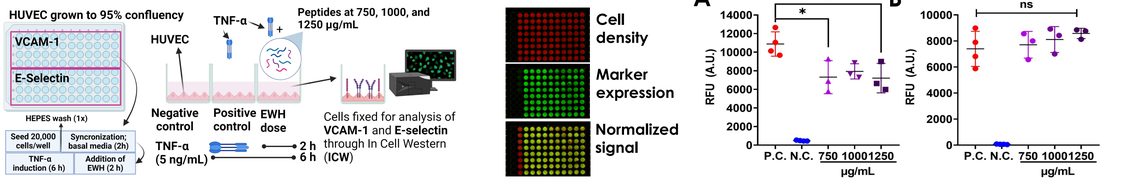


Fig. 4. Anti-inflammatory activity of EWH-GI-D in human umbilical vein endothelial cells (HUVEC) by measuring A) vascular cell adhesion molecule-1 (VCAM-1) and B) E-selectin expression through in cell western (ICW). **Note:** Error bars: SD.

4. Metabolite production of EWH-GI-U by the gut microbiome

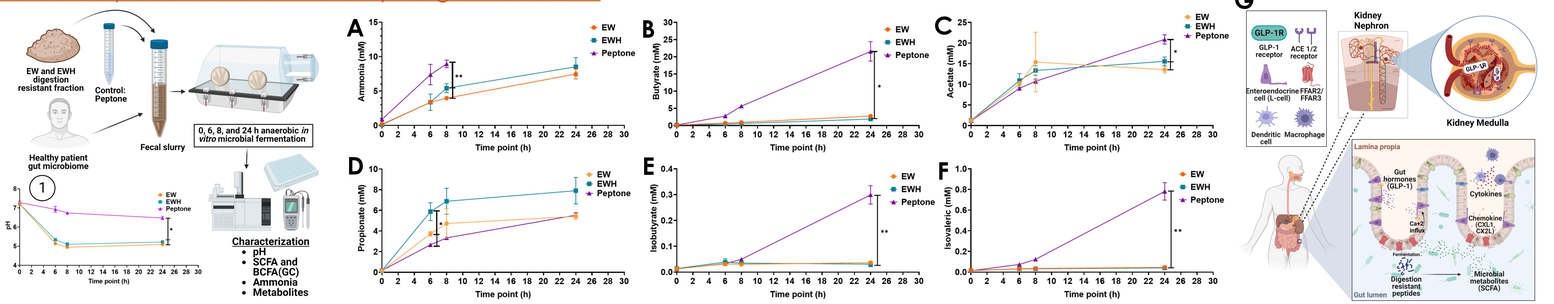


Fig. 5. EWH-GI-U gut microbiome fermentation and metabolite production of A) ammonia, B) butyrate, C) acetate, D) propionate, E) isobutyrate, and F) isovaleric at different time points. G) Proposed modulation of EWH anti-hypertensive activity through short chain fatty acid (SCFA) production by the gut microbiome **Note:** Error bars: SD. BCFA: branched chain fatty acid, ACE: Angiotensin converting enzyme, GLP: glucagon-like peptide-1, FFAR: Free fatty acid receptor 1/2.

5. Antihypertensive activity of EWH on a hypertension model

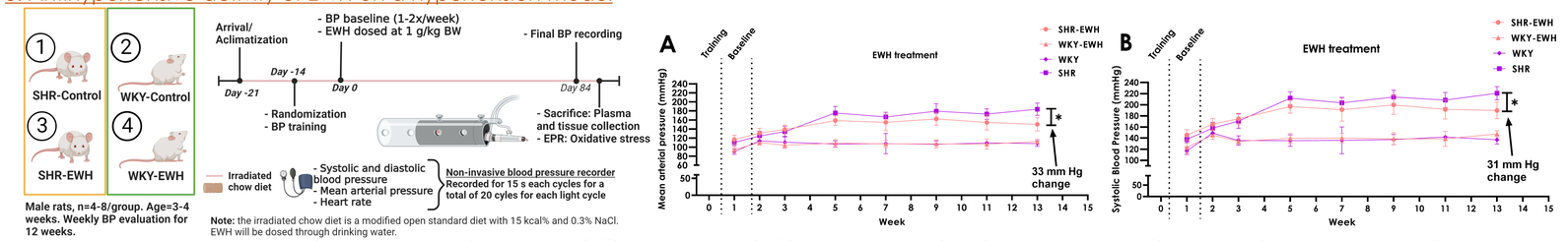


Fig. 6. *In vivo* anti-hypertensive activity of EWH in spontaneously hypertensive (SHR) and Wistar Kyoto (WKY) rats measured on A) systolic blood pressure and B) mean arterial pressure through the plethysmography. **Note:** Error bars: SD.

CONCLUSIONS

1. EWH digested fraction was able to modulate alternative hypertension mechanism by reducing oxidative stress and inflammation *in vitro*.
2. Fermentation of EWH digestion resistant fraction was conditioned by its low pH, in which at a pH below 6.5, Clostridia dominates the fermentation. Influencing the metabolites being produced such as SCFA.
3. A high concentration of propionate and low concentration of ammonia and BCFA suggest potential health benefits.
4. EWH reduced SBP (31 mm Hg) and MAP (33 mm Hg) *in vivo* in SHR after 12 weeks of treatment.
5. EWH represents a promising dietary alternative against single target drugs in a multifactor disease as hypertension.

REFERENCES

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SYSTEM SCIENCE
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