Plasma Metabolomic Changes After Red Wine Consumption

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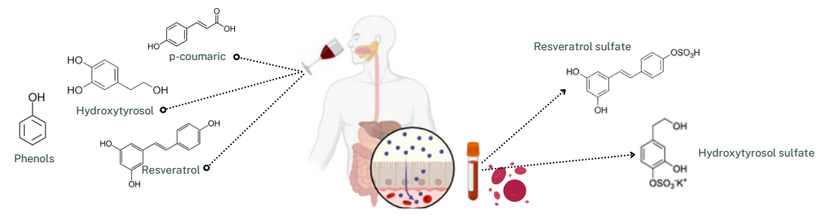
INTRODUCTION

Wine is a chemically complex beverage composed of ethanol and a wide array of bioactive constituents, most notably **phenolic compounds such as flavonoids, phenolic acids, and stilbenes**, known for their potential **health-promoting effects**. These compounds are absorbed and extensively metabolized after ingestion, resulting in a wide array of **phase I and II metabolites** detectable in plasma, urine, and feces. **Red and white wines differ** significantly in both phenolic concentration and composition, potentially eliciting **distinct metabolic responses in humans**. Understanding these differential effects is essential for elucidating the specific contribution of wine phenolics to health-related outcomes.

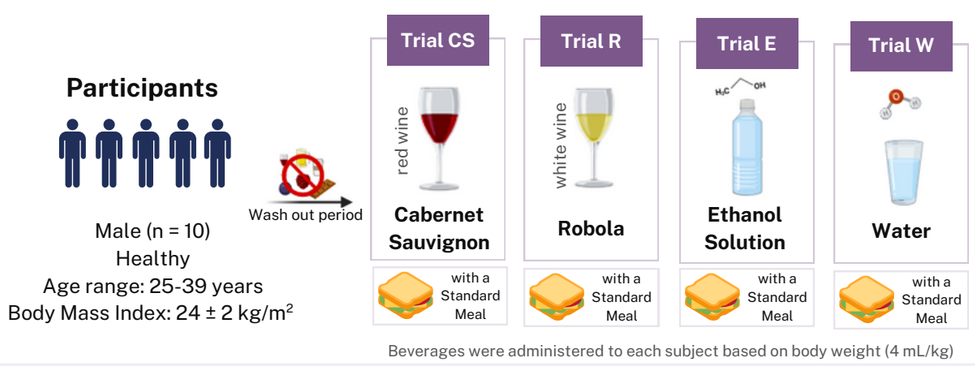
Aim of the study

To explore how **acute intake of red and white wine** influences **phenolic metabolite changes** in human **plasma.**

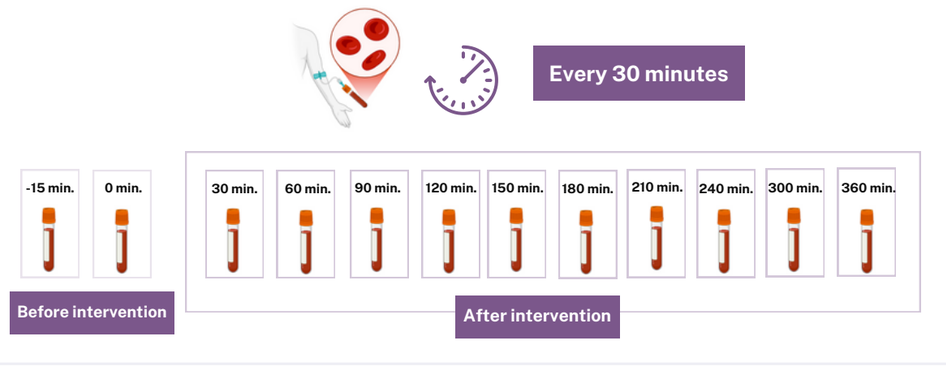


EXPERIMENTAL FLOW CHART

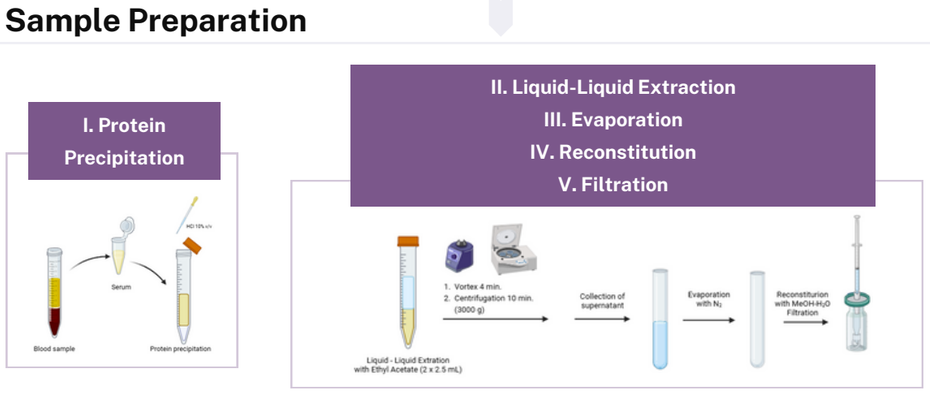
1. Clinical Trial



2. Sample Collection



3. Sample Preparation



4. Analysis

Liquid Chromatography

Reverse Phase (RP) (-)
C18 column (2.1 m × 100 mm, 2.2 µm)
Mobile phase mixures:
(A) Mili-Q H_2O: MeOH (90:10)
(B) MeOH,
with both A and B containing 5mM ammonium acetate

High Resolution Mass Spectrometry

Electrospay ionization (ESI)
Capillary voltage: 3500 V
m/z range: 50 - 1000
(with a scan rate of 2 Hz)
Collision energies: 4 eV and 25 eV
in **Data Independent Acquisition (DIA) mode**

Data Processing

Suspect screening was performed using a curated list of **124 wine-related phenolic compounds**, compiled from 51 human intervention studies reporting significant alterations in plasma, serum, urine or feces following wine intake. The resulting dataset was preprocessed through **feature filtering**, followed by **Pareto scaling** and **log transformation**.

RESULTS

- **Differences between interventions**

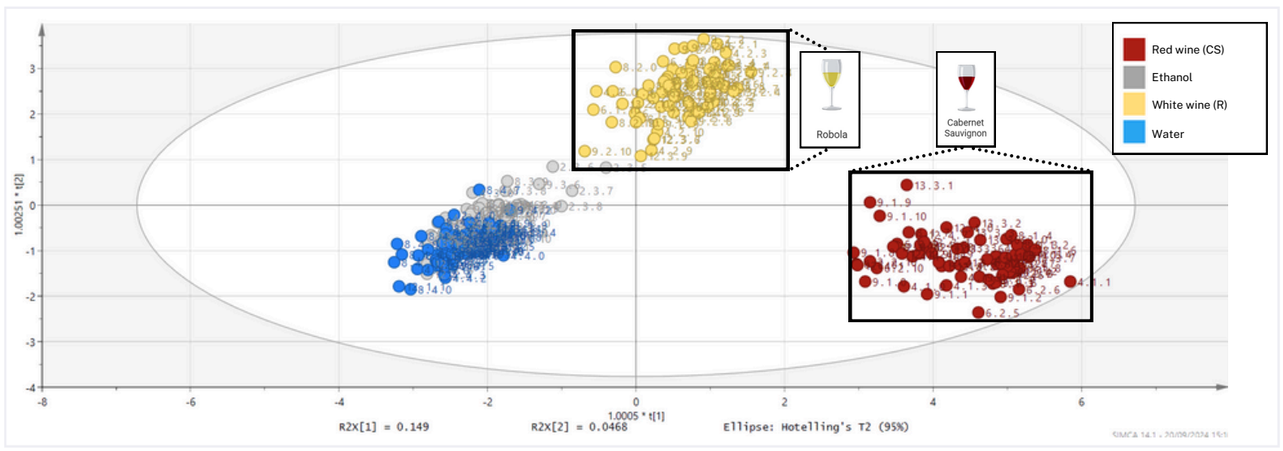


Figure 1. OPLS-DA of Phenolic Metabolites in Human Plasma after Red (CS) and White (R) wine, Ethanol (E), Water (W)

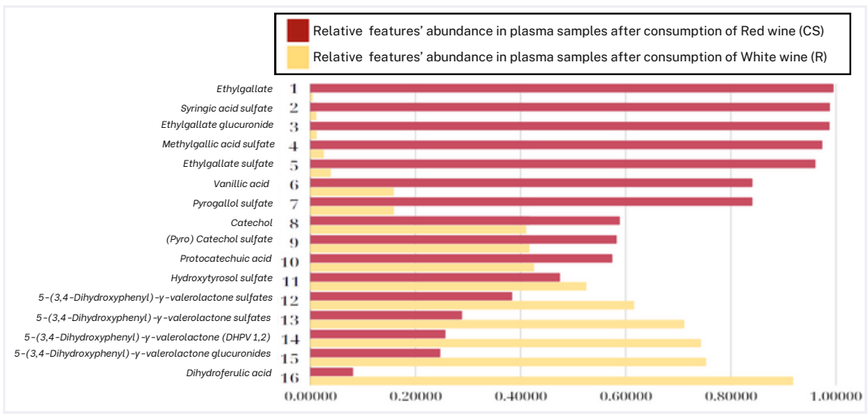


Figure 2. Relative metabolic features' abundance in plasma samples after consumption of Red (CS) and White (R) wines highlighting the differential metabolic impact of red and white wine

- **Time points after Red (CS) and White (R) wine consumption**

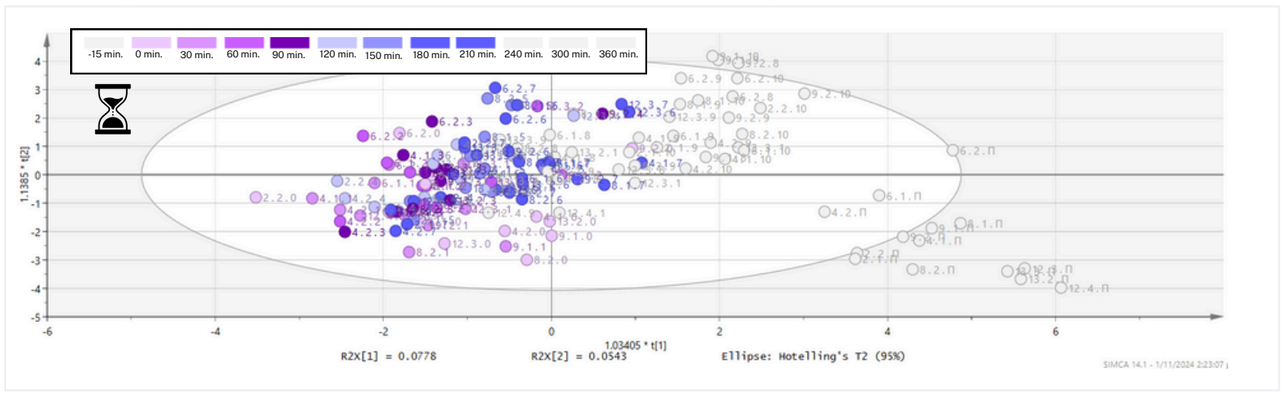


Figure 3. OPLS-DA analysis of the metabolomics fingerprint of the plasma samples after Red (CS) and White (R) wine

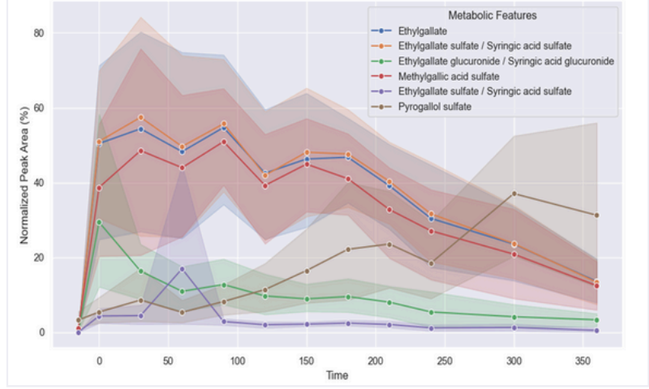


Figure 4. Time-Dependent Metabolic Trends of distinctive phenolic metabolic features attributed to red wine consumption after Peak Area Normalisation

CONCLUSIONS

1. **Red and white wine consumption led to distinct phenolic metabolite profiles,** including compounds such as ethyl gallate, syringic acid sulfate, syringic acid glucuronide and ethyl gallate glucuronide.
2. **Ethanol and water trials** led to different phenolic profiles, suggesting effects beyond baseline variability.
3. Participants showed **inter-individual differences**, allowing classification into **high and low phenolic metabolizers**.
4. **Most phenolic metabolites peaked at 30 minutes** post-consumption.

Related Literature

[1] J. M. **Guilford** and J. M. **Pezzuto**, "Wine and Health: A Review," **2011**
[2] M. **Lombardo**, A. Feraco, E. Camajani, M. Caprio, and A. Armani, "Health Effects of Red Wine Consumption: A Narrative Review of an Issue That Still Deserves Debate," **2023**
[3] I. **Buljeta**, A. Pichler, J. Šimunović, and M. Kopjar, "Beneficial Effects of Red Wine Polyphenols on Human Health: Comprehensive Review," **2023**
[4] E. **Fragopoulou**, M. Choleva, S. Antonopoulou, and C. A. Demopoulos, "Wine and its metabolic effects. A comprehensive review of clinical trials," **2018**
[5] P. **Lekka**, E. Fragopoulou, A. Terpou, and M. Dasenaki, "Exploring Human Metabolome after Wine Intake — A Review," **2023**

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