

## PhD Project Advertisement

**Project title:** Understanding the mechanism of cardiovascular disease reduction and cognitive enhancement by dietary flavanols: the impact of flavanols on blood rheology and erythrocyte deformability

**Project No:** FBS2023-55-Spencer-rs

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### Project description:

Over 7.5 million people in UK are living with a cardiovascular disease (CVD). Treating morbidity places a huge burden on the NHS and the wider UK economy with additional costs to the individual of reduced quality of life. Dietary-based approaches for primary and secondary prevention of CVD are becoming widely accepted and could reap multifaceted benefits. Plant bioactives, such as polyphenols, reduce the risk of CVD but there is little understanding of their underlying mechanisms.

Flavanols, a sub-class of polyphenol have been specifically noted for their ability to reduce non-communicative disease risk and morbidity; namely by inducing improvements in the circulatory system and exhibiting improvements in cognition. These findings have recently been confirmed in the seminal COSMOS trial; a randomised controlled trial (RCT) with ~22k participants treated with cocoa flavanols ~4 ½ years; 500 mg/d of flavanol supplement reduced total cardiovascular events (including heart attacks, strokes, cardiovascular surgery and deaths) by up to 40%. However, the mechanism by which these dietary flavanols exert these protective effects remain unknown.

### Central research question

How do dietary flavanols reduce stroke, and other CVD risk and what is their mode of action. This proposal will investigate the mechanisms by which these dietary compounds exert their physiological function using existing blood samples collected on the COSMOS trial and by conducting a clinical trial to investigate their efficacy in stroke rehabilitation patients.

### Hypothesis

Dietary flavanols reduce the risk of stroke and induce improvements in cognition through modulation of blood rheology (haemorheology), notably the viscosity of blood plasma and the potential of red blood cells to flow freely in the circulatory system.

### Objectives:

1. To explore the impact of long-term flavanol intake on haemorheology markers in blood samples from the COSMOS trial. In the COSMOS trial there were 237 incidences of stroke; 194 were ischemic, 29 were haemorrhagic and 14 were not classified. By analysing blood samples from these participants, as well as participants without stroke, for haemorheology markers, including blood viscosity, plasma viscosity, haematocrit, and mechanical properties of red blood cells, such as red blood cell deformability and aggregation, we hope to shed significant light on the mechanism by which flavanols protect against stroke and other forms of cardiovascular disease.
2. To assess the efficacy of cocoa flavanol intervention in stroke treatment and secondary prevention. A randomised controlled trial will be performed in patients attending the stroke rehabilitation clinic. The trial will investigate the impact of cocoa flavanol intervention (identical to the COSMOS trial) on markers of stroke risk, (blood pressure, arterial stiffness, vascular function, and biochemical parameters), on blood haemorheology, and on cognitive performance.

### Key methods:

Both laboratory and clinical methodology will be employed in the project. Briefly, these will include basic biochemical assays as well as more advanced analytical techniques such as LCMS to assess flavanol-related metabolites. COSMOS

blood samples will undergo full haemorheology assessment (both flavanol and control group) and will include measures of 1) plasma viscosity, blood viscosity and blood viscoelasticity; 2) red blood cell aggregation; 3) red blood cell deformability; and 4) white cell rheology. The randomised controlled trial will use basic haemodynamic assessment (e.g., blood pressure) as well as more novel techniques such as carotid-femoral pulse wave velocity (by tonometry) to measure arterial stiffness and flow mediated dilatation (using ultrasound) for endothelial function in combination with relevant cognitive test batteries focused on stroke and cerebrovascular disease (i.e., to test episodic and working memory, executive function, and processing speed).

#### **Training opportunities:**

The student would be supported to attend international conferences to present findings of the project, e.g., International Conference on Polyphenols and Health and Plant Bioactives and Health. They would also be encouraged to apply to training programmes such as the Food and Nutrition Summer School hosted by University of Parma and the prestigious ENLP (European Nutritional Leadership Programme).

#### **Student profile:**

The student should have undertaken a BSc in a biological sciences subject, including Biochemistry, Physiology, Biomedical Science, Nutrition. We are looking for someone that looks beyond the human clinical outcome to ask why and how a molecule induces the medical outcome. Those with enquiring minds who are motivated by the precise mechanism by which foods, nutrients and non-nutrient components of foods exert biological function.

#### **Stipend (Salary):**

FoodBioSystems DTP students receive an annual tax free stipend (salary) that is paid in instalments throughout the year. For 2022/23 this will be £17,668 and this will increase slightly each year at rate set by UKRI.

#### **Equality Diversity and Inclusion:**

The FoodBioSystems DTP is committed to equality, diversity and inclusion (EDI), to building a doctoral researcher(DR) and staff body that reflects the diversity of society, and to encourage applications from under-represented and disadvantaged groups. Our actions to promote diversity and inclusion are detailed on the [FoodBioSystems DTP website](#).

In accordance with UKRI guidelines, our studentships are offered on a part time basis in addition to full time registration. The minimum registration is 50% FT and the studentship end date will be extended to reflect the part-time registration.

**For up to date information on funding eligibility, studentship rates and part time registration, please visit the [FoodBioSystems website](#).**