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## Effects of cranberry (poly)phenols on mental health in university students: the CRANMOOD randomized controlled trial

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Increasing evidence indicates that (poly)phenol consumption can have beneficial effects in human brain function<sup>(1)</sup>. The overall aim of this project is to investigate whether consumption of a (poly)phenol rich cranberry drink improve mental health and cognitive function in university students via the gut-brain axis.

A parallel randomised controlled trial was conducted in 72 young healthy final year university students assigned to consume 236 mL cranberry drink (442 mg polyphenols) or nutrient matched placebo, daily for 12 weeks. The primary outcome was mood, measured as Total Mood Disturbance (TMD), using the Profile of Mood States (POMS) questionnaire. Secondary outcomes included stress, anxiety and depression levels, measured using the Perceived Stress Scale (PSS), and the Hospital Anxiety Depression Scale (HADS) questionnaire, salivary cortisol levels and cognitive function measured using the Online General Cognitive Assessment Battery (CogniFit). All of these questionnaires were measured every 4 weeks. Blood and urine samples were collected to measure inflammatory markers, gut-brain-axis metabolites, short chain fatty acids (SCFA), and cranberry polyphenols metabolites. Faecal samples were also collected for measuring gut microbiome diversity and composition and faecal metabolomics. Diet was assessed using food frequency questionnaires (FFQ), 7-day food diaries (EPIC) and 24 h online dietary recalls (intake 24) during the study. Linear mixed-effect model (LMM) and ANCOVA were used to investigate the relationship between the 2 trial arms.

No significant differences were found between treatments for mood, stress levels, anxiety, depression, circulating short chain fatty acids or inflammatory markers, however a significantly lower diurnal area under the curve of salivary cortisol (p = 0.010) and significantly higher short-term memory (Z-score: p = 0.024; Raw-score: p = 0.034) was found at 12 weeks in the cranberry group compared with the placebo. Besides, significant differences between interventions were found in plasma gut-brain axis metabolites, including the kynurenine and bile acids pathway which were kynurenine (p = 0.023), kynurenic (p = 0.032), quinolinic (p = 0.018), and glycolithocholic acid (p = 0.04) as well as several plasma and urinary cranberry (poly)phenol metabolites were modulated by cranberry consumption.

In conclusion, daily cranberry (poly)phenol supplementation for 12 week did not improve mood, stress, anxiety, and depression symptoms in healthy university students, however it may modulate cortisol levels and some aspects of cognitive function via the gutbrain axis.

## References

1. Carregosa D, Mota S, Ferreira S et al. (2021) Nutr 13(9), 2940.