## Dose-ranging study of paraxanthine ingestion on cognition, executive function, and psychomotor vigilance

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## Background

Acute ingestion of 200mg of paraxanthine (PX) affects measures of short-term memory, reasoning, response time to cognitive challenges, and as well as help sustain attention. The optimal and minimal effective dose of PX is currently unknown. The purpose of this study was to assess the efficacy and safety of different doses of PX on markers of cognition, executive function and psychomotor vigilance to one week of continued supplementation.

## **Materials and Methods**

In a randomized, double blind, placebo-controlled, crossover, and counterbalanced manner, 12 healthy male and female subjects (22.7±4 years, 165±7 cm, 66.5±11 kg, 24.4±3 kg/m<sup>2</sup>) were assigned to ingest 200 mg of a placebo (PLA), 50 mg of PX (ENFINITY<sup>™</sup>, Ingenious Ingredients, L.P.) + 150 mg PLA, 100 mg PX + 100 mg PLA, or 200 mg of PX. Participants completed stimulant sensitivity and side effect questionnaires and donated a fasting blood sample. Participants then performed the Berg- Card Sorting task test (BCST) that is an executive function test that assesses long thought, including reasoning, learning, executive control, and attention shifting; the Go/No-Go test (GNG) that assesses sustained attention and response control through reaction time and accuracy to visual stimuli; the Sternberg task test (STT) that assesses short-term/working memory involving cognitive control processes using reaction time and accuracy; and, the Psychomotor Vigilance Task Test (PVTT) that assesses sustained attention reaction times through responses to visual stimuli. Participants then ingested on capsule of PLA or PX treatments with 8 ounces of water. Participants completed side effects and cognitive function tests after 1, 2, 3, 4, 5, and 6 hours of after ingestion of the supplement. Participants continued ingesting one dose a day of the assigned supplement and then returned to the lab to donate a fasting blood sample. After a 7-day washout period, participants returned to the lab to repeat the experiment. Participants this protocol two additional times until all fore treatments were assessed. Data were analyzed by a General Linear Model (GLM) univariate analyses with repeated measures using weight as a covariate and assessing mean and percent changes from baseline with 95% Confidence Intervals (Cl's).

#### Results

STT 4-Letter Length Present Reaction Time tended to differ among groups (p-0.06). Assessment of mean changes from baseline with 95% Cl's revealed several significant differences among treatments in BCST Correct Responses, Preservative Errors (PEBL), and Preservative Errors (PAR Rules) providing some evidence that PX at varying doses enhanced thought, reasoning, learning, executive control, and attention shifting. There was also evidence of significant differences among treatments in GNG Tasks in Mean Accuracy and response time markers under various conditions assessed providing some evidence that PX influences helps sustain attention. Likewise, there were significant differences among treatments at several timepoints of increasing complexity among STT variables assessed suggesting that PX enhanced the ability to store and retrieve random information from short-term memory of increasing complexity to a greater degree. Finally, there was evidence from the PVTT assessment that response time improved over the series of 20 trials assessed as well as over the course of the 6-hour experiment in the PX treatment suggesting that PX helped sustain attention. Benefit compared to PLA were seen with each dose studied but more consistent effects appeared to be at 100m and 200mg doses. No significant differences were observed in side effects or standard clinical chemistry panels.

#### Conclusions

Results provide some evidence that acute ingestion of 100 mg and 200 mg of PX may affect some measures of short-term memory, reasoning, response time to cognitive challenges, and as well as help sustain attention and that 7-days of PX ingestion is not associated with any clinically significant side effect.

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