

# Does paraxanthine provide greater improvement in cognitive function than caffeine or in combination with caffeine prior to and following running?

<b>Submission date</b> 01/01/2022	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 04/01/2022	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 17/05/2024	<b>Condition category</b> Other	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study arms

Paraxanthine (PX) is a natural dietary component that can be found in different parts of *Theobroma cacao* (cocoa tree) fruits, in *Coffea arabica* (coffee plant), in *Sinomenium actum* (a traditional Chinese herbal medicine), and in citrus flowers. PX is the major metabolite (breakdown product) of caffeine (CA) in humans and is less toxic than caffeine. One-time ingestion of as little as 50 mg PX has been shown to improve cognition, short-term memory and helps to sustain attention. However, if paraxanthine is more effective than CA, or has synergistic effects when combined with CA, is currently unknown. The aim of this study is to measure the effects of paraxanthine with and without caffeine and compared to CA on brain function.

### Who can participate?

Healthy males and females between the ages of 18 to 40 years

### What does the study involve?

Participants will perform two cognitive function tests that assess a range of cognitive and executive function aspects. Then participants will be randomly allocated to receive PX, CA, PX+CA or placebo (dummy) capsules, and then perform the same cognitive function tests. Following a 10-kilometer run, participants will perform the same cognitive function tests a third time.

### What are the possible benefits and risks of participating?

The potential benefit of participating is an increase in executive functioning. Paraxanthine is self-affirmed GRAS (generally recognized as safe) and studies have shown PX is less toxic than CA.

### Where is the study run from?

Texas A&M University (USA)

When is the study starting and how long is it expected to run for?  
July 2019 to May 2021

Who is funding the study?  
Ingenious Ingredients L.P. (USA)

Who is the main contact?  
Richard B. Kreider  
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## Contact information

**Type(s)**  
Scientific

**Contact name**  
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## Additional identifiers

**Clinical Trials Information System (CTIS)**  
Nil known

**ClinicalTrials.gov (NCT)**  
Nil known

**Protocol serial number**  
0454E

## Study information

**Scientific Title**  
Effects of ParaXanthine supplementation with and without CAffeine on executive Function (PXCAF)

**Acronym**

PXCAF

### **Study objectives**

Paraxanthine, the main metabolite of caffeine in humans, is an effective nootropic agent at doses as low as 50 mg. However, if paraxanthine shows greater beneficial effects on cognition compared to caffeine, or synergistic effects when combined with caffeine is currently unknown.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Approved 04/12/2019, Texas A&M University Institutional Review Board (517 Blocker Building, 155 Ireland Street, Texas A&M University, College Station, TX 778431, USA; +1 (0)979 458 4067; irb@tamu.edu), ref: IRB2019-0928

### **Study design**

Interventional double-blind randomized crossover controlled trial

### **Primary study design**

Interventional

### **Study type(s)**

Other

### **Health condition(s) or problem(s) studied**

Executive functioning in healthy individuals

### **Interventions**

Subjects consume capsules containing 400 mg of placebo (PL); or 200 mg of PL + 200 mg of caffeine (CA); or 200 mg of PL+ 200 mg of PX (ENFINITY™, Ingenious Ingredients, Lewisville, TX, USA); or 200 mg CA + 200 mg of PX (CA+PX) with a 7 – 14 day washout between treatments. Capsules are taken with 8 ounces of water. A computer-generated randomization to treatment is used. Once subjects are randomized to start, they follow the counterbalance progression.

Procedure for each treatment period:

Upon arriving at the lab, participants had weight, resting heart rate, and blood pressure determined. Participants then completed a side effects questionnaire, performed cognitive function tests, donated a fasting blood sample, and then ingested 1 of 4 randomly assigned oral supplements (PRE). Participants then rested for 15-minutes and repeated these tests. Volunteers then performed a 10-km run time-trial at their self-determined pace.

### **Intervention Type**

Supplement

### **Primary outcome(s)**

The Psychology Experiment Building Language (PEBL) software program (Version 2.1, <http://pebl.sourceforge.net>) was used to administer four cognitive function tests that assessed a range of cognitive and executive function aspects:

1. Berg-Wisconsin Card Sorting Task test (BCST) at baseline, 1 hour after initial ingestion and

after the completion of a 10-kilometer run.

2. Psychomotor Vigilance Task Test (PVT) at baseline, 1 hour after initial ingestion and after the completion of a 10-kilometer run.

### **Key secondary outcome(s)**

Safety measured using:

1. Side Effect Questionnaire at baseline, 1 hour after initial ingestion and after the completion of a 10-kilometer run.

2. Changes in blood clinical chemistries at baseline, 1 hour after initial ingestion and after the completion of a 10-kilometer run.

3. Changes in heart rate after initial ingestion and after each kilometer running.

### **Completion date**

01/05/2021

## **Eligibility**

### **Key inclusion criteria**

All subjects were healthy and free from known: (1) a medical condition which hinders performance in a standard exercise program; (2) a history of cognitive dysfunction; (3) been currently taking prescription medications; (4) a known allergy to wheat flour; (5) a sleep disorder; (6) been/were pregnant or breastfeeding; or (7) a physician's order to abstain/restrict caffeine or stimulant intake

### **Participant type(s)**

Healthy volunteer

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Sex**

All

### **Total final enrolment**

13

### **Key exclusion criteria**

Subjects who were taking prescription medications in the month prior to the initiation of the study and/or were told by a physician to abstain or restrict physical exercise, caffeine and/or stimulant intake

### **Date of first enrolment**

01/01/2020

### **Date of final enrolment**

28/02/2021

# Locations

## Countries of recruitment

United States of America

## Study participating centre

### Texas A&M University

675 Kimbrough Blvd. Building #1542

College Station

United States of America

77843-4253

# Sponsor information

## Organisation

Ingenious Ingredients L.P.

# Funder(s)

## Funder type

Industry

## Funder Name

Ingenious Ingredients, L.P.

# Results and Publications

## Individual participant data (IPD) sharing plan

All data generated or analysed during this study will be included in the subsequent results publication. Please contact Prof. Dr Richard Kreider ([rbkreider@tamu.edu](mailto:rbkreider@tamu.edu)) with any requests.

## IPD sharing plan summary

Available on request, Published as a supplement to the results publication

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		09/05/2024	17/05/2024	Yes	No