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Dose-response of paraxanthine on brain function

Submission date	Recruitment status	[_] Prospectively registered
23/09/2021	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
24/09/2021	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
05/01/2022	Other	

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 in humans and is less toxic than caffeine. One-time ingestion of 200 mg PX has been shown to improve cognition, short-term memory and helps to sustain attention. However, the minimal effective and optimal dose of acute paraxanthine ingestion, and if continued daily ingestion of PX increases or decreases effectiveness, is currently unknown. The aim of this study is to measure the dose-response of paraxanthine on brain function.

Who can participate?
Healthy males and females between the ages of 18 to 59 years

What does the study involve?
Participants will be randomly allocated to receive PX or placebo (dummy) capsules, and then perform four cognitive function tests that assess a range of cognitive and executive function aspects.

What are the possible benefits and risks of participating?
The potential benefit of participating is an increase in executive functioning. The ingestion of a maximum of 200 mg of paraxanthine would be less than that obtained from consuming a premium cup of coffee or energy drink.

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?
April 2019 to October 2021

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

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
0454D

Study information

Scientific Title
A dose-ranging study of paraxanthine ingestion on cognition, executive function, and psychomotor vigilance

Acronym
PXDR

Study objectives
One-time ingestion of 200 mg paraxanthine has been shown to improve cognition, short-term memory and helps to sustain attention. However, the minimal effective and optimal dose of acute paraxanthine ingestion, and if continued daily ingestion of paraxanthine will result in increased or diminished efficacy is currently unknown.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 28/10/2019, 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: IRB2019-0807F

Primary study design
Interventional

Study design
Interventional double-blinded randomized crossover controlled trial

Study type(s)
Other

Health condition(s) or problem(s) studied
Executive functioning in healthy individuals

Interventions
Subjects consume capsules containing 50, 100 or 200 mg of paraxanthine (ENFINITY™, Ingenious Ingredients L.P., Lewisville, TX, USA) or capsules containing wheat flour placebo (placebo) once they have completed baseline testing. One capsule of the PLA or PX is taken with 8 ounces of water daily for 7 days. A computer-generated randomization to treatment is used. Once subjects are randomized to start, they follow the counterbalance progression.

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, 2, 3, 4, 5 and 6 hours after initial ingestion and 1 hour after daily ingestion for 7 days
2. The Go/No-Go test (GNG) at baseline, 1, 2, 3, 4, 5 and 6 hours after initial ingestion and 1 hour after daily ingestion for 7 days
3. Sternberg Task Test (STT) at baseline, 1, 2, 3, 4, 5 and 6 hours after initial ingestion and 1 hour after daily ingestion for 7 days
4. Psychomotor Vigilance Task Test (PVTT) at baseline, 1, 2, 3, 4, 5 and 6 hours after initial ingestion and 1 hour after daily ingestion for 7 days

Key secondary outcome(s)
Safety measured using:
1. Side Effect Questionnaire: participants will rank the frequency of dizziness, headache, tachycardia, heart skipping/palpitations, shortness of breath, nervousness, blurred vision, and any other adverse effects) using a scale where 0 = none; 1 = 1-2/week, 2 = 3-4/week, 3 = 5-6 /week, 4 = 7-8/week, and 5 = ≥9/week. They will also rate the severity of these side effects where 0 = none, 1 = minimal, 2 = slight, 3 = moderate, 4 = severe, and 5 = very severe at baseline, 6 hours after the first ingestion, and 1 hour after daily ingestion on day 7
2. Changes in blood clinical chemistries at baseline, 6 hours after the first ingestion, and 1 hour after daily ingestion on day 7

Completion date

06/10/2021

Eligibility

Key inclusion criteria
All subjects were healthy and free from known:
1. Cognitive deficit conditions
2. Wheat flour allergies
3. Sleep disorders
4. Cardiovascular, metabolic, or pulmonary diseases
5. History of hypertension, migraine headaches, cardiac arrhythmias, or anxiety
6. Gastrointestinal reflux disease or ulcers

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
15

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 caffeine and/or stimulant intake

Date of first enrolment
01/11/2019

Date of final enrolment
21/07/2020

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) with any requests.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		15/12/2021	05/01/2022	Yes	No