ISRCTN14506218 https://doi.org/10.1186/ISRCTN14506218

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

Submission date
01/01/2022

Recruitment status
No longer recruiting

Registration date
04/01/2022

Overall study status
Completed

Last Edited
17/05/2024

Condition category
Other

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
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

Secondary study design
Randomised cross over trial

Study setting(s)
Other

Study type(s)
Other

Participant information sheet
No participant information sheet available

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 measure
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 (PVTT) at baseline, 1 hour after initial ingestion and after the completion of a 10-kilometer run.

Secondary outcome measures
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 runing.

Overall study start date
01/07/2019

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

Age group
Adult

Sex
Both

Target number of participants
13

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
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Sponsor information

Organisation
Ingenious Ingredients L.P.

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Sponsor type
Industry

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Funder(s)

Funder type
Industry

Funder Name
Ingenious Ingredients, L.P.

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed scientific journal.

Intention to publish date
30/06/2022

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		09/05/2024	17/05/2024	Yes	No