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Interaction between herbal remedies (danshen and baizhi) and caffeine

Submission date	Recruitment status	[_] Prospectively registered
10/06/2019	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
11/06/2019	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
19/07/2023	Other	

Plain English summary of protocol

Background and study aims
Chemicals known as furanocoumarins (8-methoxypsoralen [8-MOP] and 5-methoxypsoralen [5-MOP]) are known to inhibit the breakdown (metabolism) of caffeine. However, it is not known if ingestion of herbs containing these chemicals will have the same effect. The aim of this study is to determine if a single meal of furanocoumarin-containing herb (or vegetable) would cause inhibition of caffeine metabolism after co-administration.

Who can participate?
Healthy volunteers aged 20 - 35 years (non-smoker, not pregnant or breastfeeding).

What does the study involve?
Collection of timed saliva and urine samples from you after ingesting caffeine tablets (200 mg) alone and caffeine tablets (200 mg) with an herb (or vegetable) together (total caffeine consumption by you is 400 mg for the whole study).

What are the possible benefits and risks of participating?
BENEFITS:
You will not benefit directly from this study. No information or results obtained by this study will be made available to you. However, there is the potential to benefit other people in the future if the study leads to the development of an effective method for predicting caffeine/herb interaction using in vitro data.
RISKS:
There will be no risk to your health because the amount of caffeine ingested is equivalent that in a cup of coffee. Moreover, the herbs (or foods) selected for the study are found in our daily diets. Please note that caffeine overdose only occurs when large amount of caffeine (more than the recommended dose by Health Canada) is ingested. Caffeine overdose may result in adverse health effects including nausea, vomiting, irritability, nervousness, anxiety, panic attacks, dehydration, and sleep disorders in sensitive individuals (Health Canada, 2012).

Where is the study run from?
Department of Biological Sciences, Simon Fraser University, BC, Canada

When is the study starting and how long is it expected to run for?
June 2012 to June 2016

Who is funding the study?
1. Simon Fraser University, Canada
2. Global Collaborative Research, King Abdullah University of Science and Technology

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
KAIMRC ZE-001

Study information

Scientific Title
Caffeine/Angelica dahurica and caffeine/Salvia miltiorrhiza metabolic inhibition in humans: In vitro and in vivo studies.

Study objectives
Caffeine metabolism (CYP1A2-Mediated) can be modulated by pre-consumption of two Chinese medicines of Danshen (Salvia miltiorrhiza) and Baizhi (Angelica dahurica).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/09/2012, Simon Fraser University Office of Research Ethics Committee (Discovery 2 building, 8900 Nelson Way, Burnaby BC V5A 4W9; +1 778-782-6593dore@sfu.ca), ref: 2012s0565

Study design
Interventional (cross-over) single center

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
N/A

Interventions
Participants are asked to refrain from ingesting caffeine, caffeinated drinks and furanocoumarin-containing foods for 3 days before and after participating in the first pharmacokinetic study (without co-treatment with an herb) and until the end of the second pharmacokinetic study (with co-treatment of an herb). Participants are provided with a study kit consisting of caffeine tablets (400 mg), an herbal extract, and several coded containers for saliva and urine sample collection. Participants conduct the studies in the home:
First pharmacokinetic study:
Time course of caffeine and metabolite concentrations in the saliva of humans without herb /food extract co-treatment. On the day of the experiment, ingest 200 mg caffeine tablets (equivalent to the amount of caffeine in a cup of coffee or in a can of energy drink). A saliva sample (about 3 ml) will be collected in a coded, siliconized glass tube just before dosing. Serial saliva samples also will be collected at 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8 and 12 hr post-dosing. A 30 ml urine sample will be collected at 4-8 hr post caffeine administration since the half-life of caffeine clearance in the human is about 4-4.5 hr.
Second pharmacokinetic study:
Time course of caffeine and metabolite concentrations in the saliva of humans co-treated with an herb/food extract. After a 3-day wash-out period, ingest 4.5 g (or 9 g) of a dehydrated herb (or food) in the form of an aqueous extract 3 hr before ingesting the caffeine tablets. One of the following herbs or vegetables: parsnip, celery, dill, parsley, angelica, false bishop’s weed, common rue, lovage, khella, dong quai, and baizhi. A saliva sample (about 3 ml) will be collected in a coded, siliconized glass tube just before dosing. Serial saliva samples also will be collected immediately after dosing with an herb extract at 0.5, 1, 1.5, 2.5, 3.0 hr and after dosing with 200 mg caffeine at 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8 and 12 hr. 30 ml urine samples will be collected before dosing and at 4-8 hr post-caffeine ingestion.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)

Caffeine; herbal whole aqueous extract of either Danshen (Salvia miltiorrhiza) and Baizhi (Angelica dahurica).

Primary outcome(s)
Caffeine concentrations in human saliva collected at 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8 and 12 hr post-dosing using liquid chromatography

Key secondary outcome(s))
Caffeine concentrations in urine collected 4 - 8 hours post-dosing

Completion date
29/06/2017

Eligibility

Key inclusion criteria
Aged 20-35 years

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
4

Key exclusion criteria
1. Smoker
2. On medication
3. Pregnant or breast feeding
3. Any health issue(s) that would affect the results of the study

Date of first enrolment
20/06/2012

Date of final enrolment
01/06/2016

Locations

Countries of recruitment
Canada

Study participating centre
Simon Fraser University
Department of Biological Sciences
Simon Fraser University
Burnaby
Canada
V5AIS6

Sponsor information

Organisation
Simon Fraser University

ROR
https://ror.org/0213rcc28

Organisation
King Abdullah International Medical Research center

Funder(s)

Funder type
University/education

Funder Name
Simon Fraser University

Alternative Name(s)
SFU

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Canada

Funder Name
Global Collaborative Research, King Abdullah University of Science and Technology

Alternative Name(s)
GCR, KAUST

Funding Body Type
Private sector organisation

Funding Body Subtype
Research institutes and centers

Location
Saudi Arabia

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to the raw data not being available.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2019	16/01/2020	Yes	No
Results article		29/04/2021	28/04/2021	Yes	No
Results article		01/03/2023	19/07/2023	Yes	No
Other publications		22/07/2021	15/10/2021	Yes	No
Participant information sheet		20/09/2012	11/06/2019	No	Yes