ISRCTN83028296 https://doi.org/10.1186/ISRCTN83028296

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?
Dr Zeyad Alehaideb
alehaidebze1@ngha.med.sa

Contact information

Type(s)
Scientific

Contact name
Dr Zeyad Alehaideb

ORCID ID
http://orcid.org/0000-0002-7185-2820

Contact details
3690
Al Yasmin
Riyadh
13325 8348
Riyadh
Saudi Arabia
11111
0566188111
alehaidebze1@ngha.med.sa

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
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

Secondary study design
Non randomised study

Study setting(s)
Home

Study type(s)
Prevention

Participant information sheet
See additional files

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 measure
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

Secondary outcome measures
Caffeine concentrations in urine collected 4 - 8 hours post-dosing

Overall study start date
26/06/2011

Completion date
29/06/2017

Eligibility

Key inclusion criteria
Aged 20-35 years

Participant type(s)
Healthy volunteer

Age group
Adult

Sex
Both

Target number of participants

8

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

Sponsor details
Department of Biological Sciences
Burnaby
Canada
V5A 1S6
+966566188111
zehaideb@gmail.com

Sponsor type
University/education

Website
http://www.sfu.ca

ROR
https://ror.org/0213rcc28

Organisation
King Abdullah International Medical Research center

Sponsor details
Department of Medical Genomics
King Abdullah International Medical Research Center
P.O. Box 3660
Riyadh
Saudi Arabia
11111
+966566188111
zehaideb@gmail.com

Sponsor type
Research organisation

Website
http://www.kaimec.med.sa

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

Publication and dissemination plan
To be published in thesis and journals.

Intention to publish date
01/07/2019

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?
Participant information sheet		20/09/2012	11/06/2019	No	Yes
Results article	results	01/10/2019	16/01/2020	Yes	No
Results article		29/04/2021	28/04/2021	Yes	No
Other publications		22/07/2021	15/10/2021	Yes	No
Results article		01/03/2023	19/07/2023	Yes	No