# Interaction between herbal remedies (danshen and baizhi) and caffeine

Submission date	Recruitment status No longer recruiting Overall study status	<ul><li>Prospectively registered</li></ul>		
10/06/2019		☐ Protocol		
Registration date		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

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## Additional identifiers

#### Clinical Trials Information System (CTIS)

Nil known

#### ClinicalTrials.gov (NCT)

Nil known

#### 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 furanocoumarincontaining 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

Αll

#### 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
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes