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# Does an extract of the plant Cosmos caudatus affect cognitive function and other health markers in older adults in Malaysia with mild cognitive impairment?

**Submission date**
14/11/2019

**Registration date**
20/12/2019

**Last Edited**
17/01/2023

**Recruitment status**
No longer recruiting

**Overall study status**
Completed

**Condition category**
Mental and Behavioural Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

## Plain English summary of protocol

Background and study aims
Mild cognitive impairment (MCI) is where people start to become forgetful but can still cope with most of the activities of daily life. It can be considered the stage between aging and dementia. Cosmos caudatus is an annual plant in the genus Cosmos. It is widely grown and eaten in Malaysia and is locally known as ulam raja. It is used in traditional medicine and may have effects in preventing aging-related diseases. If these effects can be proven, people could be encouraged to eat this plant as a cheap and easy way to improve their health. This study will compare Cosmos caudatus extract with a sugar pill in older adults who have MCI to see if there is any effect on their MCI.

Who can participate?
Adults aged 60-75 with MCI

What does the study involve?
Participants will be randomly allocated to one of two groups. Both groups will take two capsules each day for 12 weeks. The capsules will contain Cosmos caudatus extract or an inactive sugar substance depending on the group. The capsules look exactly the same and participants and the researchers will not know which group has received which capsule. Participants will have tests to examine their cognitive function and will be asked about their diet before starting the study and at 6 and 12 weeks after starting the trial. They will be asked to provide a blood sample before starting the study and at 6 and 12 weeks after starting the trial. Some of the participants will be asked to undergo a brain scan to investigate brain activity.

What are the possible benefits and risks of participating?
This study will provide evidence on the importance and benefits of using plants as a natural source in preventing disease and improving health. The effects of Cosmos caudatus on brain activity, especially cognitive function, will be determined. The extract has been tested on animals and the dose given is considered to be at a safe level in humans. If there are any

abnormal results obtained from the brain scan, the subject may be referred directly to a specialist so that any problems with the brain can be identified. No risks are known as the procedures involved are part of standard procedures. The results of the data obtained will be reported in a collective manner with no reference to any specific individual. The data from each individual will remain confidential. Participants will be told their results only.

Where is the study run from?
The National University of Malaysia

When is the study starting and how long is it expected to run for?
January 2019 to December 2019

Who is funding the study?
Ministry of Education (Malaysia)

Who is the main contact?
1. Mr Yee Xing You, yeexing@gmail.com
2. Professor Suzana Shahar, suzana.shahar@ukm.edu.my

# Contact information

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Scientific

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# Additional identifiers

### Protocol serial number
NN-2019-137

# Study information

### Scientific Title
The effects of Cosmos caudatus (ulam raja) extract in improving cognitive function, brain activity, mood state and health parameters among older adults with mild cognitive impairment

### Study objectives
Cosmos caudatus extract supplementation can improve cognitive function, brain activation, mood state and health parameters among older adults with mild cognitive impairment (MCI).

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Approved 15/08/2019, Sekretariat Penyelidikan Dan Inovasi [National University of Malaysia Medical Research and Ethics Committee] (Aras 2, Pejabat Dekan, Fakulti Perubatan, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur Malaysia; +603-9145 9480/9481; sppi@ppukm.ukm.edu.my), ref: UKM.FSK.TDPI.800-1/1/5(NN-2019-137), UKM.PPl.800-1/1/5/JEP-2019-480

### Primary study design
Interventional

### Study design
Double-blind placebo-controlled randomized trial

### Study type(s)
Treatment

### Health condition(s) or problem(s) studied
Mild cognitive impairment

### Interventions

Name of treatment: Cosmos caudatus extract, Placebo (maltodextrin)
The powder form extract was packed into capsules by the repacker from Universiti Teknologi Malaysia, then they packaged the capsules into the bottles which were labelled either A or B.

The study aims to conduct a randomized, double-blind, placebo-controlled study for 12 weeks to determine the effects of Cosmos caudatus extract supplementation on cognitive function and brain activation among older adults with MCI. Blinding procedure will be ensured by labelling the Cosmos caudatus aqueous extract and placebo capsules as either A or B. Only the manufacturer and repacker will know the coding for both A and B labelled capsules. The randomization we used is block randomization.

Cosmos caudatus extract is considered as a nutraceutical product. The Cosmos caudatus extract was manufactured by Institute of Bioproduct Development (IBD), Universiti Teknologi Malaysia. IBD is a fine specialty chemical Research and Bioproduct Development centre which is a certified International Organization for Standardisation (MS ISO/IEC 17025) under Department of Standard Malaysia and the Herbal Extraction Centre was awarded MESTI and HALAL accrediation. All the eligible subjects will be randomized to consume two capsules daily for 12 weeks, each containing either mixture of maltodextrin (250 mg) and Cosmos caudatus extract (250 mg) or maltodextrin placebo (500 mg). The dosage of the Cosmos caudatus extract capsule is below the toxicity level which has been tested in Wistar rats for acute oral toxicity by Mohamed et al. (2013). 20 ml of blood will be taken for biomarkers (BDNF, MDA, INOS, COX-2, SOD) and basic health profiles (full blood count, fasting blood sugar, lipid profile, liver function test and renal function) analysis at pre- and post-intervention.

Eligible subjects who are willing to participate in this research will be required to attend three visits including baseline, 6th week and 12th week follow up. Subjects will be given two bottles of supplements with each containing 90 capsules during baseline and 6th week. During the three visits, their cognitive functions and mood state, as well as dietary intake will be assessed by using a series of questionnaire assessments. Basic health blood profile, selected biomarkers including BDNF, oxidative stress and inflammatory markers, and metabolites will only be measured at baseline and 12th week follow up. 10 participants from each groups will also be randomly chosen to undergo fMRI scan to determine their brain activity at baseline and 12th week follow up. Adverse events reported by the subjects will be based on the latest National Cancer Institute Common Toxicity Criteria (NCI CTC Version 5). The Cosmos caudatus extract and placebo groups will receive capsules supply at baseline and 6th week of the study. Compliance will be assessed by performing a capsule count at the end of the 6th week and the 12th week. The researcher will remind the subjects to take the capsule regularly as instructed previously through phone calls and texts daily. Subjects will be able to know their health status, through blood analysis, cognitive status, anthropometry and dietary intake assessment.

## Intervention Type
Supplement

## Primary outcome(s)
1. Cognitive impairment assessed using Mini-Mental State Examination (MMSE) at baseline, week 6 and week 12
2. Short-term memory assessed using Digit Span at baseline, week 6 and week 12
3. Verbal memory assessed using validated Malay version of Rey Auditory Verbal Learning Test (RAVLT) at baseline, week 6 and week 12
4. Processing speed assessed using the validated Digit Symbol Substitution Test (DSST) at baseline, week 6 and week 12

5. Visual memory assessed using validated Visual Reproduction at baseline, week 6 and week 12
6. Mood state assessed using using validated Profile of Mood state questionnaire at baseline, week 6 and week 12
7. Brain activity assessed using functional magnetic resonance imaging at baseline and 12 weeks

### Key secondary outcome(s)
1. Body weight measured using digital weighing scale Tanita HD-309 (Tanita Corporation, Tokyo, Japan) at baseline, week 6 and week 12
2. Standing height measured by using SECA Leicester Portable Height Measure (SECA, Germany) at baseline, week 6 and week 12
3. Waist circumference measured using a flexible, non-extensible Lufkin tape to the nearest 0.1 cm at baseline, week 6 and week 12
4. Hip circumference measured using a flexible, non-extensible Lufkin tape to the nearest 0.1 cm at baseline, week 6 and week 12
5. Body composition measured using bio-electric impedance (BIA) meter (model Inbody S10®) at baseline, week 6 and week 12
6. Blood level of brain-derived neurotrophic factor (BDNF) measured using BDNF Elisa kits at baseline and week 12
7. Blood level of malondialdehyde (MDA), a marker of oxidative stress, measured using MDA Elisa kits at baseline and week 12
8. Blood level of inducible nitric oxide synthase (iNOS) measured using iNOS Elisa kits at baseline and week 12
9. Blood level of cyclooxygenase 2 (COX-2) measured using COX-2 Elisa kits at baseline and week 12
10. Blood level of superoxide dismutase (SOD) measured using SOD Elisa kits at baseline and week 12
11. Full blood count provided by PathLab-Pathology and Clinical Laboratory (M), Sdn Bhd, Klang Valley branch, at baseline and week 12
12. Fasting blood glucose provided by PathLab-Pathology and Clinical Laboratory (M), Sdn Bhd, Klang Valley branch, at baseline and week 12
13. Lipid profile provided by PathLab-Pathology and Clinical Laboratory (M), Sdn Bhd, Klang Valley branch, at baseline and week 12
14. Liver function provided by PathLab-Pathology and Clinical Laboratory (M), Sdn Bhd, Klang Valley branch, at baseline and week 12
15. Renal function provided by PathLab-Pathology and Clinical Laboratory (M), Sdn Bhd, Klang Valley branch, at baseline and week 12
16. Dietary nutrient intake using researcher's validated dietary questionnaires (Shahar et al, 2000) at baseline, week 6 and week 12

### Completion date
21/12/2019

## Eligibility

### Key inclusion criteria
1. Malaysian older adults aged 60-75 years at the time of informed consent
2. Mild cognitive impairment based on Petersen’s criteria:
2.1. No clinical judgment of dementia
2.2. No or very minimal limitations in Instrumental Activities of Daily Living (IADL) with a score of ≤1.5 SD from mean norm
2.3. Essentially preserved general cognitive functioning, with a score ≥19 in Mini Mental State

Examination (MMSE)
2.4. Objective memory impairment, with a score of at least 1.5 SD below the mean average in one or more cognitive tests (Rey Auditory Verbal Learning Test [RAVLT] or Digit Span)
3. Able to communicate in Malay or English language
4. Body mass index (BMI) of 20-30 kg/m2

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Senior

### Sex
All

### Total final enrolment
48

### Key exclusion criteria
1. Alcohol and/or substance dependence
2. Smoker
3. Any type of neurodegenerative diseases (i.e. Parkinson disease, dementia, etc)
4. Diagnosis of a depressive disorder, schizophrenia or score >5 in Geriatric Depression Scale (GDS)
5. Any medical conditions that might interfere with the subject's participation in the trial (i.e. uncontrolled diabetes, chronic heart disease, cancer and kidney, liver or renal failure)
6. Attention Deficit Hyperactivity Disorder (ADHD) or other conditions that might interfere with the outcomes, such as cognition function and psychosocial status
7. Regular consumer of traditional herbs, vitamin and mineral supplementation for the past 6 months, since this might jeopardize the effects of the supplement used in the study
8. Females receiving Hormone Replacement Therapy (HRT)
9. Taking medications which might be interfered with by the product (i.e. warfarin etc.)

### Date of first enrolment
01/05/2019

### Date of final enrolment
01/09/2019

## Locations

### Countries of recruitment
Malaysia

### Study participating centre

**Center of Ageing and Wellness (H-CARE)**
Faculty of Health Sciences
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**Study participating centre**
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# Sponsor information

**Organisation**
Universiti Kebangsaan Malaysia [National University of Malaysia]

# Funder(s)

**Funder type**
Government

**Funder Name**
Ministry of Education Malaysia and Fundamental Research Grant Scheme (FRGS)

# Results and Publications

**Individual participant data (IPD) sharing plan**
The datasets generated during and/or analysed during the current study will be available upon request from Suzana Shahar (suzana.shahar.ukm.edu.my). Only statistical data will be provided after obtaining the consent from subjects.

## IPD sharing plan summary

Available on request

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | | 29/01/2021 | 17/01/2023 | Yes | No |
| Basic results | | 06/04/2020 | 07/04/2020 | No | No |