

**CARDIOVASCULAR AND MENTAL HEALTH BENEFITS OF SOY CONSUMPTION:  
ROLE OF SOY ISOFLAVONES**

**Alicia A Thorp**

**B Med Pharm Biotech (Hons)**

**A thesis submitted for the degree of Doctor of Philosophy**

**Discipline of Physiology**

**University of Adelaide**

**South Australia**

**May 2008**

**APPENDIX 5- Recruitment Material for Isoflavone Supplement Intervention**



## ***Can Soy make a person smarter?***

The Nutritional Physiology Research Centre needs healthy male volunteers for a 12-week diet study to see whether soy isoflavones, by improving blood flow, can help to improve cognition (memory, planning, information processing).

Volunteers will take soy isoflavone supplements twice daily for six weeks and a matching placebo for a further six weeks. Circulatory and cognitive functions will be tested before and after each six week phase.

To be eligible, you should not eat soy more than twice a week or take any medications or natural supplements that can affect your heart or mental health.

For further information or to enrol, please contact Ms Alicia Thorp (Project Co-ordinator)  
Phone: (08) 8302 1822 or email: [alicia.thorp@unisa.edu.au](mailto:alicia.thorp@unisa.edu.au)



# Can Soy make a person smarter?

The Nutritional Physiology Research Group needs

## Healthy male volunteers who don't regularly consume soy

to participate in a 12-week diet study to see whether soy isoflavones, by improving blood flow, can help to improve cognition (memory, planning, information processing).

The study commences in March 2007. Volunteers will take soy isoflavone supplements twice daily for six weeks and a matching placebo for a further six weeks. Circulatory and cognitive function will be tested at the beginning and end of each six week phase.

To participate, you should not eat soy more than twice a week or take any medications or natural supplements that can affect your heart or mental health.

For further information or to enrol in the study, please contact Ms Alicia Thorp: Phone: (08) 8302 1822 (9-4pm Monday-Friday or leave a message any time) or email: [alicia.thorp@unisa.edu.au](mailto:alicia.thorp@unisa.edu.au)

This project has been approved by the University of Adelaide's Human Research Ethics Committee.

<p><b>SOY SMART STUDY 2007</b></p> <p>Contact: Ms Alicia Thorp</p> <p>Ph: 8302 1822 (9-4 pm weekdays)</p> <p>Email: <a href="mailto:alicia.thorp@unisa.edu.au">alicia.thorp@unisa.edu.au</a></p>	<p><b>SOY SMART STUDY 2007</b></p> <p>Contact: Ms Alicia Thorp</p> <p>Ph: 8302 1822 (9-4 pm weekdays)</p> <p>Email: <a href="mailto:alicia.thorp@unisa.edu.au">alicia.thorp@unisa.edu.au</a></p>	<p><b>SOY SMART STUDY 2007</b></p> <p>Contact: Ms Alicia Thorp</p> <p>Ph: 8302 1822 (9-4 pm weekdays)</p> <p>Email: <a href="mailto:alicia.thorp@unisa.edu.au">alicia.thorp@unisa.edu.au</a></p>	<p><b>SOY SMART STUDY 2007</b></p> <p>Contact: Ms Alicia Thorp</p> <p>Ph: 8302 1822 (9-4 pm weekdays)</p> <p>Email: <a href="mailto:alicia.thorp@unisa.edu.au">alicia.thorp@unisa.edu.au</a></p>	<p><b>SOY SMART STUDY 2007</b></p> <p>Contact: Ms Alicia Thorp</p> <p>Ph: 8302 1822 (9-4 pm weekdays)</p> <p>Email: <a href="mailto:alicia.thorp@unisa.edu.au">alicia.thorp@unisa.edu.au</a></p>
--	--	--	--	--

### **Background on Soy Isoflavones**

- Component in soy
- Two major types: daidzein and genistein
- Has a similar chemical structure to estrogen which the body naturally produces
- Bind exclusively to estrogen  $\beta$  receptors in the body which are located predominately in the lining of arteries.
- Can potentially increase blood flow through arteries in cerebral and peripheral circulation

### **Misconceptions/Controversy regarding Isoflavones:**

- Isoflavones do not have the same potency as estrogen supplements or oestradiol which the body naturally produces. (Potency is  $\sim 100,000x <$  estrogen)
- Isoflavone supplementation has not been shown to affect hormonal levels of males.

### **What is known from Previous Studies**

- Increased blood flow to the brain improves cognitive function
- Soy isoflavone supplementation has been shown in healthy adults and post menopausal women to improve aspects of cognitive function.
- Soy Isoflavone supplementation has been shown in post menopausal women to enhance peripheral blood flow.

### **Importance of Study**

- First to date to look exclusively at the effect soy isoflavone supplementation has on cognitive function in healthy males.
- Traditionally soy isoflavone supplementation has only been looked at in post menopausal women to improve cognition.
- Suspect improvements in cognition will be due to increased cerebral blood flow
- Hope to show an improvement in blood flow is not restricted to just the brain but improves throughout the entire body from soy isoflavone supplementation.
- Will assess this hypothesis by looking non-invasively at blood flow through peripheral arteries and correlating changes in blood flow with improvements in cognition.

### **What the study involves:**

- Require 40 healthy males to participate in a 12 week study.
- Participants will take each day take four capsules, two in the morning and two at night. For six weeks the capsules will contain soy isoflavones (equivalent to 120 mg/per day) and for remaining time they will be a placebo.
- Participants will not be told if when they are taking the active or the placebo capsules.
- Will need to come to the clinic three times over the 12 weeks.
- At each visit will have a non invasive ultrasound test looking at blood flow through the artery in the upper arm (brachial) and perform a range of simple cognitive tests (verbal/ listening and written assessment based exercises)

### **Characteristics of Study Participants:**

- **Male**
- **Healthy**
- **Don't eat soy products more than twice a week**
- **Don't smoke**
- **Not on any medication**
- **Not diagnosed with cardiovascular disease or diabetes mellitus**



## VOLUNTEER INFORMATION SHEET

### Effects of soy isoflavones on vascular and cognitive function

#### Background

Foods containing soy have long been thought to offer a wide range of health benefits. While the major component of soy is protein, it also contains a group of bioactive nutrients called isoflavones. Isoflavones are classified as "phytoestrogens" because they have a similar structure to the hormone oestrogen which the body naturally produces, but come from a non-human source (phyto= plant). There are several types of isoflavones in soy, with the most common being genistein and daidzein and they have been shown to bind to oestrogen receptors that are located in the part of the brain that we use for short and long term memory recall, to process information and maintain attention/alertness. Isoflavones have also been shown to bind to oestrogen receptors found on the inside lining of blood vessels (endothelium) which control their ability to dilate/expand in the body. Appropriate dilatation of arteries in the brain and body is very important for maintaining normal blood flow and an inability to do so has also been linked to the early onset of cardiovascular disease.

Previous studies in post menopausal women have shown taking soy isoflavones can enhance these oestrogen- dependent mechanisms and improve mental function, dilation of arteries and reduce blood pressure. However to date, little is known if such positive effects on the cardiovascular system and cognitive function occur in males who already have normal levels of oestrogen and what impact taking isoflavones may have.

In the study we will be asking subjects to take 120mg of isoflavones each day for six weeks which will be given in four x 30mg isoflavone capsules, and to take a placebo containing dietary fibre for another six weeks. Supplements will be provided by Soy Health Pty Ltd who manufacture a range of soy products for commercial use.

#### Purpose of the Study

The purpose of this study is to assess whether regular consumption of isoflavones found in soy can significantly improve the ability of arteries to dilate and enhance mental function in healthy males.

#### Research Plan

We require 40 healthy males to take part in our 12 week study which will be conducted at the Nutritional Physiology Research Centre located at the University of South Australia (City East Campus) on Frome Road.

You will be assessed for your suitability to take part by completing a diet, health and lifestyle questionnaire and attending a brief screening visit where you will have your height, weight and blood pressure taken.

Once you have given your signed consent to participate and it has been established that you meet all the inclusion criteria you will be invited to attend our clinic where we will ask you to provide us with a small specimen of urine that you would have collected over night (from the time you went to bed the night before till the first time you went to the toilet that morning).

We will then perform a non-invasive ultrasound assessment which will determine the ability of an artery in your arm to dilate in response to increased blood flow. To assess arterial dilatation, you will be asked to lie on your back while an ultrasound probe takes an image of the large artery in your upper right arm (brachial artery). A blood pressure cuff will be placed around the right forearm and inflated to a high pressure for five minutes. It will then be released and a second image of the artery will be taken to measure the change in the artery's diameter in response to the increased flow of blood to the forearm.

This test will take approximately 30 minutes to complete. It is important that you come to this visit having fasted (no food or drink) and avoided any stimulants (ie caffeine, cocoa, cigarettes) for a minimum of six hours as this can affect the results of the test.

You will then be offered a small snack (glass of juice and a biscuit) and participate in an approximately 60 minute long session where we will get you to do a series of tests that assess your cognitive function. These tests are non-threatening, routinely used by psychologists and meant to be enjoyable yet slightly challenging to perform. They are generally word and numbers based and require you to use basic mental applications like recalling and processing information, maintaining concentration for set periods of time and using planning strategies to workout basic problems.

After these baseline assessments have been performed, which will take between one and one and a half hours to complete, you will then be allocated at random (by chance) to receive either the isoflavone or the placebo supplements each day for the six weeks.

Each day you will take a total of four capsules. We will ask to you to take two of the capsules (containing either 30mg isoflavone or placebo) in the morning and then another two of the same capsules (containing either 30mg isoflavone or placebo) at night.

At the end of the six weeks you will need to again attend the clinic fasted and having avoided any stimulants (ie caffeine, cocoa, cigarettes) for a minimum of six hours. We will then repeat the non-invasive ultrasound assessment as performed at your first visit as well as the same set of cognitive tests.

You will then start taking four of the other type of capsule each day for another 6 weeks. At the end of this period of time, you will again come back to the clinic and undertake the same set of assessments a final time.

We will supply all of the active isoflavone capsules and matching placebo capsules that you will need for the study.

Please be aware that you will not be told which tablets you are taking during your two 6 week supplement periods.

We will also ask you throughout the study to keep a record of how many capsules you take a day over each six week period and give you a list of foods that contain soy which you should avoid having over the entire 12 weeks.

The study is scheduled to commence in late March and will be completed in June 2007.

#### **Confidentiality**

All information collected as part of the study will remain confidential and no information that could lead to identification of any individual will be released. The information collected in this study will be stored on a CD-ROM in a secure data store for a period of 15 years at the Nutritional Physiology Research Centre located within the University of South Australia City East Campus. Participants in the study may withdraw at any stage without prejudice. Participants will be provided with a letter within 6 months of completing the study outlining the results of the entire group as well as a brief summary of the major research findings.

#### **In summary, you would be asked to:**

- Attend our research clinic at the University on four occasions lasting approximately 60- 90 minutes ( one of the visits will be a brief screening/information visit of approximately 30 minutes duration)
- Take four capsules (containing either soy isoflavones or a placebo) each day (two in the morning and two at night) for six weeks then swap over to the other type of capsule and take them for another six weeks.
- Perform a series of tests which assess cognitive function on three occasions (Week 0, 6 and 12 of trial)
- Provide 24 hour urine collections on three separate occasions (Week 0,6 and 12 of trial)
- Undergo ultrasound assessments to measure arterial dilatation on three occasions (Week 0, 6 and 12 of trial).

Your participation in the study is entirely voluntary and you would be free to refuse to participate or withdraw at any time.

If you would like to participate or have any enquiries about the research, please contact Principle Supervisor of Study Professor Peter Howe on 8302 1200 or PhD Candidate and study co-ordinator Ms. Alicia Thorp on 8302 1822

This project has been approved by the University of Adelaide and the University of South Australia's Human Research Ethics Committees. If you have any ethical concerns about the project or questions about your rights as a participant please contact the Executive Officer of the University of South Australia's Human Ethics Committee, Ms Vicki Allen Tel: +61 8 8302 3118; Email: [Vicki.allen@unisa.edu.au](mailto:Vicki.allen@unisa.edu.au).



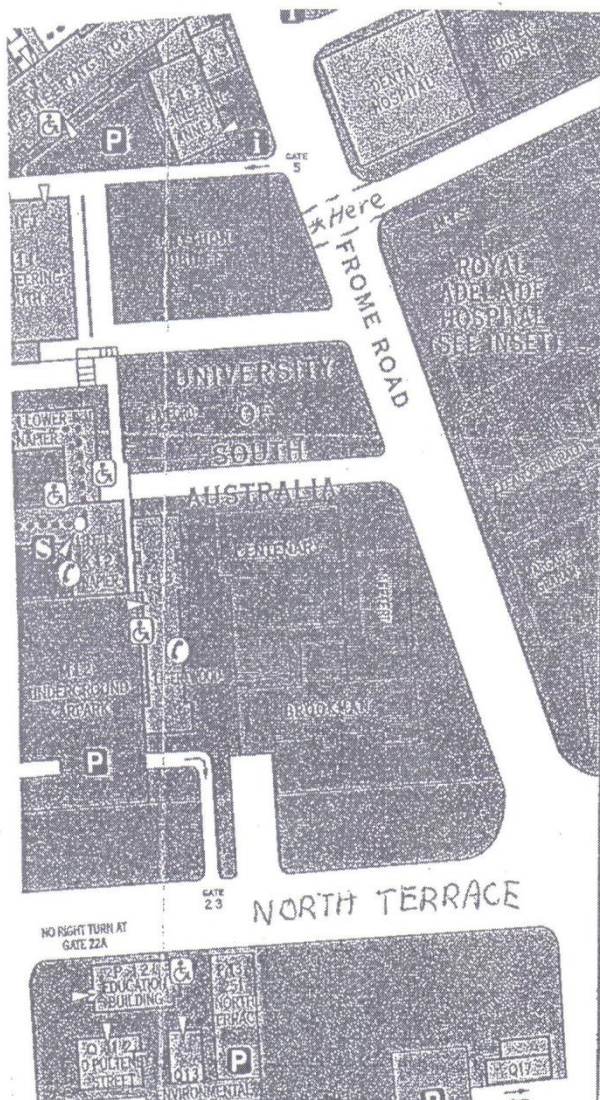
Dear Participant

Thank you for volunteering for the 2007 Soy Smart Study. The clinic you will attend for your screening visit (and all other study visits) is located in the Bonython Jubilee Building at the University of South Australia, City East Campus. The entrance to the building is situated directly opposite the IMVS building and Dental Hospital on Frome Rd. A set of pedestrian lights on Frome Rd leads to the front of the building. Attached to the entrance doors is a sign for 'Breast screen SA'

Once you have entered the building, walk down a small flight of stairs and at the bottom, turn right. You will see a sign to your right on the wall saying 'Nutritional Physiology Research Facility'. Please enter the first door on your right and wait in the reception area for me.

Kind regards,

Alicia Thorp



Ticket parking is available behind the zoo and botanic gardens, along Queen Victoria Drive or Frome Road.

Alternatively, there are 30 minute loading zones that would be suitable for parking during your screening visit located next to the Bonython Jubilee Building. You can access these parks by entering the university at Gate 5 when driving north down Frome Rd. (entrance is directly after set of pedestrian lights).



Room BJ1-61, Bonython-Jubilee Building  
School of Health Sciences, University of South Australia  
Adelaide, SA 5000  
Ph: 8302 2097

## DIET, HEALTH & LIFESTYLE QUESTIONNAIRE

### Soy Smart Study 2007

In this questionnaire general questions are asked about your health, diet and some background information about yourself. All information will be kept strictly confidential. If you have any concerns about the questions in this form or have difficulty in answering any questions please do not hesitate to contact PhD Candidate Ms. Alicia Thorp (8302 1822) or Principle Supervisor Professor Peter Howe (8302 1200)

Today's Date: \_\_\_\_\_

First name: \_\_\_\_\_ Last name: \_\_\_\_\_

Postal Address:

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

Telephone Nos: Home: \_\_\_\_\_ (Please tick best number to contact you on)

Work: \_\_\_\_\_

Mobile: \_\_\_\_\_

Email: \_\_\_\_\_

Date of birth: \_\_\_\_\_ day \_\_\_\_\_ month \_\_\_\_\_ year

Age: \_\_\_\_\_

PLEASE COMPLETE IF KNOWN:

Weight: \_\_\_\_\_ kg

Height: \_\_\_\_\_ cm

BMI: \_\_\_\_\_

Blood Pressure: Systolic \_\_\_\_\_ Diastolic: \_\_\_\_\_

PLEASE COMPLETE THE FOLLOWING DETAILS :

Doctors Name: \_\_\_\_\_

Name of Practice: \_\_\_\_\_

Address: \_\_\_\_\_

Post Code: \_\_\_\_\_ Telephone: \_\_\_\_\_

Would you be happy for us to notify your doctor of your involvement in this study and if necessary contact them:

Yes

No

**1. Have you had, or do you have :**

	Yes	No	Not sure
High blood pressure	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Heart condition	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
High cholesterol (>6mmol/L)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
High triglycerides (>2mmol/L)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Type 1 or 2 Diabetes Mellitus (diagnosed)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Peripheral vascular disease	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Sleep apnoea	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Psychological disorder	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Any other medical condition (Please describe) \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

Are you undergoing treatment for any of the above conditions? Yes  No

If yes please give details (and medication , if any):  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

**2. Do you have a family history of :**

	Yes	No	Not Sure
Obesity	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Heart disease	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
High blood pressure	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Diabetes mellitus (Type 1 or 2)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Hyperlipidemia (high cholesterol)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Psychological disorder	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

**3. Have you ever been a smoker ?**

Yes  No  (Go to Q 4)

If yes, how long ago did you give up : \_\_\_\_\_

OR

If you **currently still smoke** how many cigarettes approx. would you smoke in a day: \_\_\_\_\_

How many years have you been a smoker? \_\_\_\_\_

**4. Do you take any medication regularly?**

Eg: do you regularly use lipid and/or blood pressure lowering drugs, drugs for depression, pain or inflammation condition?

Yes

No  (Go to Q5)

If yes, please give details:

---

---

**5. Do you regularly take vitamin, mineral or other dietary supplements?**

Eg. fish oil capsules, vitamin C etc.

Yes

No  (Go to Q 6)

If yes, please give details of dose and frequency of consumption: \_\_\_\_\_

---

**6. Do you eat soy products regularly?**

Yes

No  (Go to Q 7)

If yes, what type and approx. amount (eg, tofu, soy milk, soy powder, soy yoghurt, soybeans)

---

---

How often?

Daily

A few days a week

Once a week

Occasionally or never

**7. Would you be prepared to not consume any soy containing products throughout the study period?**

Yes

No



University of  
South Australia

# Nutritional Physiology Research Centre

## SOY SMART STUDY 2007 SCREENING INTERVIEW

SCREENING ID: Sc \_\_\_\_\_ APPOINTMENT DATE & TIME \_\_\_\_\_

FIRST NAME \_\_\_\_\_ SURNAME \_\_\_\_\_

Height : \_\_\_\_\_ cm      Weight: \_\_\_\_\_ kg      BMI: \_\_\_\_\_

DOB \_\_\_\_/\_\_\_\_/\_\_\_\_      Age: \_\_\_\_\_

### STUDY CRITERIA:

#### Exclusion Criteria

- شا Diagnosed with peripheral vascular disease, cardiovascular disease or mental condition/disorder
- شا Known presence of Type 1 or 2 diabetes
- شا Eat soy products > 2 times/week
- شا Take anti-hypertensive, lipid lowering or mood altering medication
- شا Take >1000 mg fish oil capsules p/day
- شا Smoke

**BLOOD PRESSURE** (3 measurements recorded, 1 min apart, seated, not talking):

Cuff size:      M / L      Bladder voided   Y / N      Legs uncrossed  

Any stimulants consumed in past 2 hours   Y / N    If yes, what time: \_\_\_\_\_

	SYSTOLIC BP	DIASTOLIC BP	PULSE
1			
2			
3			
<b>AVERAGE</b>			

### VISITS:

What day and time would best suit you for a 1.5 hr testing session.

Monday     Tuesday     Wednesday     Thursday     Friday

7- 8.30am     8.45-10.15am     11-12.30pm     1- 2.30pm     2.45- 4.15pm     4.30- 6 pm

Other time: \_\_\_\_\_    Week starting Mon April 2<sup>nd</sup>     Week starting Tuesday April 10<sup>th</sup>

Attending Info Night 26/3/07 @ 6-7pm:   Y     N     Screening Code: \_\_\_\_\_



University of  
South Australia

# Nutritional Physiology Research Centre

## PROJECT CONSENT FORM

**PROJECT TITLE:**      **Effect of soy isoflavones on cognition and vascular function in healthy males**

**INVESTIGATORS:**

Ms Alicia Thorp  
Professor Peter Howe  
Associate Professor Jon Buckley  
Dr Alison Coates

1. I have read the Information Sheet, and the nature and the purpose of the research project and the risks inherent in my participation have been explained to me. I understand and agree to take part.
2. I understand that I may not directly benefit from taking part in the study.
3. I understand that while information gained during the study may be published, I will not be identified and my personal results will remain confidential.
4. I understand that I can withdraw from the study at any stage and that this will not affect my rights or the responsibilities of the researchers in any respect.
5. I have had the opportunity to discuss taking part in this study with a family member or friend or a GP.
6. I understand that I will receive not receive payment for my assistance in this research project.
7. I confirm that I am over 18 years of age.

Name of Subject .....

Signed .....Date .....

I have explained the study to the subject and consider that he/she understands what is involved.

Signed .....Date .....



University of  
South Australia

# Nutritional Physiology Research Centre

Tuesday 17<sup>th</sup> April , 2007

Dear

Thank you for expressing an interest in participating in the **2007 Soy Smart Study**. Unfortunately based on information you provided in your Diet and Lifestyle Questionnaire, it appears that you do not meet our strict inclusion criteria for this particular study. Although you are not eligible to participate in this study, we have similar studies running from time to time and we will notify you of any future studies that may be of interest to you.

If you have any questions about why you were not eligible to participate in this study please feel free to contact me on 8302 1822 or email me at [alicia.thorp@unisa.edu.au](mailto:alicia.thorp@unisa.edu.au).

We at the Nutritional Physiology Group appreciate that the ongoing success of our studies relies heavily on people like yourself, who are willing to volunteer their time and efforts for scientific research, and we would like to thank you very much for your interest in our study.

Yours sincerely

Ms Alicia Thorp  
*for* Prof Peter Howe  
Head, Nutritional Physiology Research Group