PARTICIPANT INFORMATION AND CONSENT FORM

SWINBURNE UNIVERSITY OF TECHNOLOGY

The Kava Anxiety-Lowering Medication (KALM) Study

(Kava in the Treatment of Generalised Anxiety Disorder)

Principle Investigators: Professor Con Stough[1], Dr Jerome Sarris[1, 2]
Associate Investigators: Professor Isaac Schweitzer[2], Ms Marni Kras[1]
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1. Introduction

You are invited to take part in this research project. This Participant Information and Consent Form informs you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research. Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor. Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether you take part or not.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:
• Understand what you have read;
• Consent to take part in the research project;
• Consent to have the tests and treatments that are described;
• Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2. What is the purpose of this research?

The aim of the study is to evaluate the effects and potential benefits of an anti-anxiety herbal medicine (Kava) tablets (3.2 grams twice per day) versus placebo (dummy tablets). Kava has traditional uses in the South Pacific as a medicine and a ceremonial drink, which commonly elicits dose-dependent psychological and physiological relaxation. Kava is currently used as an alternative treatment for anxiety compared to standard medications such as benzodiazepines or antidepressants. The data collected from the trial will be used for Postdoctoral research by Dr Jerome Sarris. Co-investigators include Professor Con Stough, Professor Isaac Schweitzer, and Ms Marni Kras. This project is being financially sponsored by Integria (a company based in New Zealand which owns MediHerb, a natural products company providing the herbal tablets).

3. What does participation in this research involve?

To be eligible to participate in this project you must:

- Be aged between 18 and 65 years.
- Be currently experiencing chronic anxiety (or have a current diagnosis of Generalised Anxiety Disorder).
- Be fluent in written and spoken English.
- Never have had a diagnosis of a Psychotic disorder or currently be diagnosed with Bipolar Disorder or Major Depressive Disorder.

- Not currently be taking Antidepressants, Mood Stabilizers (e.g., Lithium), Antipsychotics, Opioid-based Analgesics (e.g., panadeine, codeine, or morphine), St John's Wort, HIV medications, Anti-Tumoral/Cancer medications, Warfarin, Parkinson's Disease medications, Epilepsy medications, or medications for Thyroid problems.
- Not have commenced psychotherapy in the last 1 month or be receiving intensive psychotherapy (>1 session per week).
- Have no diagnosed hepato-biliary (liver) disease/inflammation.
- Be free from substance abuse or dependency disorder (including alcohol) in the previous 6 months.
- Have had no previous adverse reaction to kava.
- Have not used kava or benzodiazepines regularly in the previous 12 months.
    - If have used either, then you must not have had more than one occasion of kava or benzodiazepine use each week over the past month (alternatively, you can participate if you have not used kava or benzodiazepines in the past 2 weeks).
- Not be currently pregnant or lactating, or trying to conceive.

Participation in the study will involve attending Swinburne University's Brain and Psychological Sciences Research Centre (BPsyC) on 6 separate occasions.

The BPsyC is located at:
Swinburne University of Technology
Brain Sciences Institute
427-451 Burwood Rd, Hawthorn

Participation in the study involves three components:

1) Having your physical and psychological health, including mood and anxiety assessed via a brief interview and questionnaires, and by filling out assessment forms.

2) Being randomly assigned during the study to take 1 tablet twice a day of either 3.2 gm of kava: 120mg of kavalactones ~ the active natural chemical) or a placebo version (dummy non-active tablet). This dosage may be increased to 2 tablets twice a day during the study (of kava or placebo).

3) Undergoing 3 blood tests to assess your liver and thyroid function, and to take genetic material (cytochrome P450 2D6 and 3A4, and brain chemical DNA (GABA receptors and transporters, noradrenaline and serotonin transporters, Val158Met), and liver enzymes (to assess liver function). The genetic material will not personally identify you. The purpose of collecting this DNA is to see if any differences in your DNA may be affecting how you respond to the medication given.

The following outlines what you will be required to do each visit:

<u>Visit 1 (1-1.5 hours):</u>

At the first visit the study will be explained to you in detail and you may ask the researchers any questions or raise any concerns that you may have about the study. If consenting to take part in the study, during the first session you will be asked to participate in a brief clinical interview as well as to complete some screening assessments. If you meet the criteria to participate in the study you will be asked to give your written consent. You will be given oral tablets to take daily (1 tablet twice a day) for one week. Finally, you will be given a referral slip and asked to attend an appointment at your local Healthscope pathology lab to give a blood sample (liver function and thyroid function test) at a time of your convenience no cost to you. A qualified venepuncture technician will be collecting the blood sample. They will extract approximately 10ml of blood from a vein in your arm using a syringe. The blood sample will be kept securely at the pathology lab for analysis as described in section 4.

Visit 2 (30 – 45 minutes):

One week later, you are asked to return to the BPsyC. In this session you will be asked to complete some of the same psychological questionnaires as you were given in your first visit, as well as some further screening assessments. You will be given another supply of tablets to take daily for the following 3 weeks. In addition, you will be given a referral slip to visit your local Healthscope pathology lab for another blood test (liver function test and collection of genetic material: see below for more detail) at a time of your convenience during that week at no cost to you. A qualified venepuncture technician will be collecting the blood sample. They will extract approximately 6ml of blood from a vein in your arm using a syringe. The blood sample will be kept securely at the pathology lab for analysis as described in section 4.

Visit 3 (30 - 45 minutes):

In this session, the same assessments will be conducted as Visit 2. No blood tests are required during this week.

Visit 4 (45 minutes):

In this session you will complete the same assessments as the previous two visits. You may be assigned to a group that will be required to take an additional daily tablet for the following 3 weeks of the trial.

Visit 5 (45 minutes):

In this session you will be asked to complete the same questionnaires as the previous visit, and be given a final referral slip to visit your local Healthscope pathology lab to undergo the last blood test (liver function test) at a time of your convenience during that week at no cost to you. A qualified venepuncture technician will be collecting the blood sample. They will extract approximately 6ml of blood from a vein in your arm using a syringe. The blood sample will be kept securely at the pathology lab for analysis as described in section 4. You will be given a final one week supply of tablets to take daily.

Visit 6 (1 - 1.5 hours):

The final visit requires you to complete the same brief interview and questionnaires as in previous visits. An additional questionnaire will be given to you where you will have the opportunity to describe your personal experience of taking the tablets throughout the trial.

You will be compensated $100 for you participation at the end of the trial and offered the opportunity to be given 2 free bottles of kava (not compulsory).

4. What will happen to my test samples?

A blood sample will be taken on 3 occasions as part of this study. The blood sample will be taken at a Healthscope pathology lab where it will be stored in a secure room until it is analysed in order to assess liver and thyroid function, and DNA: liver enzyme and brain chemical genes. The results of the DNA analysis will be stored securely and will be available for

you if wish to know the results. After the samples have been analysed, they will be destroyed appropriately (before 12 months) and therefore not used for any other research other than the current study.

You will be able to contact the pathology lab for the results of your genetics and blood tests. The results of this test will remain confidential. You can decide whether or not you would like to view the results of this test. If you choose you would like the results, they will not be given directly to you. They will be given to your nominated GP or health care professional who will be able to communicate the results to you. We will also provide your GP with the contact details of a qualified genetic counselor. If you have any concerns about the meaning of these results we will provide you with the contact details of a genetic counselor who can further explain the meaning of the results to you.

It should be noted that the genetic tests we are using will not provide any results that would indicate you have a particular disease, that could be of concern e.g. Alzheimers disease.

5. What are the possible benefits?

We cannot guarantee or promise that you will receive any benefits from this research however, it is possible that you may experience reduced symptoms of anxiety.

6. What are the possible risks?

Although Kava is a relatively safe drug, medications have the potential to produce negative reactions in some people (see the consumer information sheet).

Potential reactions to kava that may infrequently occur are:
Skin complaints e.g. rashes, itching, scaling, discolouration
Digestive symptoms e.g. stomach upsets, bloating, reflux, change in stools, nausea
Headaches, Dizziness
Mental changes e.g. drowsiness, irritability, hyperactivity, insomnia
Cardiovascular changes e.g. heart rate or blood pressure changes
Respiratory symptoms e.g. asthma, hayfever

Potential reactions to kava that may very rarely occur:
Liver problems e.g. liver- inflammation, toxicity, failure
Psychiatric disturbances e.g. heavy sedation
Movement and speech changes (e.g. slow speech)

While the assessments are conducted with your care in mind, talking, reading or writing about aspects of health may cause in some people distress. If so we are available to provide support, advice and appropriate referral if needed.

Having blood taken may cause some discomfort or bruising. Sometimes, the blood vessel may swell, or blood may clot in the blood vessel. Rarely, there could be a minor infection or bleeding. If this happens, please inform the research nurse or your local health care professional.

All staff members are trained in first-aid, and in the unlikely event you do experience any discomfort or symptoms immediately contact our research Nurse, Rosamund on 9214 5758 or your local health care professional.

7. What if new information arises during this research project?

During the research project, new information about the risks and benefits of the project may become known to the researchers. If this occurs, you will be told about this new information and decide if it affects you.

8. Can I have other treatments during this research project?

It is important to tell your doctor and the research staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments.

9. Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part you don't have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

10. What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team before you withdraw.

11. How will I be informed of the results of this research project?

The results of the study will be published in a peer reviewed journal. All data will be approved by the sponsor before being published.

12. What else do I need to know?

- **What will happen to information about me?**

Any information obtained in connection with this research project that can identify you will remain confidential and will only be used for the purpose of this research project. Investigators in possession or control of participant data that may contain personal information shall not disclose that information to anyone other than the individual concerned. Names of participants will only feature on consent forms and will not be attached to any other data on which names will be replaced by codes. Integria Healthcare own all information collected during this study. All information sent to Integria Healthcare will remain confidential and will only be used for the purpose of this study. During the study, the data will be kept in the possession of the investigator(s) when needed as reference, but otherwise kept locked in a secure filing cabinet at Swinburne University. Data and records relating to the study will be stored at Swinburne University for 15 years. In any publication and/or presentation, information will be provided in such a way that you cannot be identified.

- **How can I access my information?**

In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to access the information collected and stored by the researchers about you. You also have the right to request that any information with which you disagree be corrected. Please contact one of the researchers named at the end of this document if you would like to access your information.

- **What happens if I am injured as a result of participating in this research project?**

If you suffer an injury as a result of participating in this research project, hospital care and treatment will be provided by the public health service at no extra cost to you if you elect to be treated as a public patient.

- **Is this research project approved?**

The ethical aspects of this research project have been approved by the Human Research Ethics Committee of Swinburne University

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research* (2007) produced by the National Health and Medical Research Council of Australia. This statement has been developed to protect the interests of people who agree to participate in human research studies.

13. Consent

I have read this document and I understand the purposes, procedures and risks of this research project as described within it.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I have read and understood the consumer information sheet on kava.

I understand that I have a 50% chance of receiving kava and a 50% chance of receiving placebo (dummy pill); and that this is by random assignment.

I freely agree to participate in this research project as described.

I understand that I will be given a signed copy of this document to keep.

I understand that information collected during this study could lead to commercial products or patents, and understand and agree not to disclose information regarding the study that is revealed to me throughout my participation in the study.

I consent to the collection, storage and use of blood samples containing genetic material taken from me for use in this specific research project which will be destroyed no longer than 12 months after collection.

I consent to the storage and use of blood samples taken from me for use in this specific research project only as described in Section 4 of this document.

Participant's name (printed) ……

Signature Date

Researcher's name (printed) ……

Signature Date

Participant's name (printed)……

Signature Date

Researcher's name……

Signature Date

Note: All parties signing the consent section must date their own signature.

14. Who can I contact?

The person you may need to contact will depend on the nature of your query. Therefore, please note the following:

For further information or appointments:

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal researcher (Professor Con Stough) on 9214 8167 or any of the following people:

Name: *Dr Jerome Sarris*

Role: Principal Investigator

Telephone: 0404 083 393

Name: *Tasha Wahid*

Role: Chronic Kava Study Research Co-ordinator

Telephone: 9214 4924 or 0413502068

For complaints:

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Research Ethics Officer, Swinburne Research (H68),
Swinburne University of Technology, P O Box 218, HAWTHORN VIC 3122.
Tel (03) 9214 5218 or +61 3 9214 5218 or resethics@swin.edu.au

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Revocation of Consent Form

Full Project Title: The Kava Anxiety-Lowering Medication (KALM) Chronic Study (Kava in the Treatment of Generalised Anxiety Disorder).

I hereby WITHDRAW my consent to participate in the research proposal described above and understand that such withdrawal WILL NOT jeopardise any treatment or my relationship with Swinburne University of Technology or the researchers involved in this study.

Participant's Name
(printed)

_____

Signature: Date:

Name of Witness
(printed)

_____

Signature: Date: