INFORMATION SHEET

An examination into the effects of a saffron extract (affron®) on mood and general wellbeing in adults experiencing low mood: a randomised, double-blind, placebo-controlled trial

Investigator (s)	**Dr Adrian Lopresti and Dr Stephen Smith**
Principal Investigator:	**Dr Adrian Lopresti**
Address	**38 Arnisdale Rd, Duncraig WA 6023**
Telephone No.	**(08) 9448 7376**

You are invited to participate in this study.

Background

Saffron is a dietary spice that has been shown in several studies to improve mood, overall wellbeing, and sleep quality. In this study, we are interested in examining the effects of saffron on mood and general wellbeing in adults experiencing a low mood.

This study will be conducted by Dr Adrian Lopresti and Dr Stephen Smith (Clinical Research Australia).

Information about funding source and declaration of interests

This study is funded by Pharmactive Biotech, the company that produces the patented saffron extract (affron®) that will be used in this study. However, this study is being independently managed by Clinical Research Australia (CRA) without external influence from Pharmactive.

Aim of the study

We would like to know whether taking saffron tablets, twice daily for 12 weeks can improve mood, sleep, and general wellbeing in adults experiencing a low mood.

What does participation involve? **(see study flow chart on page 3)**

This study will comprise several steps as outlined below:

Step 1: Complete an online initial screening

This questionnaire consists of approximately 30 questions and takes approximately 10 minutes to complete. It provides us with information relating to the eligibility criteria. If, based on the results of the screening questionnaire, you are assessed as 'likely' eligible you will be contacted for a phone interview. Ineligible volunteers will be informed by email that they do not fulfil the eligibility criteria.

Step 2: Phone Interview for an initial assessment of eligibility

If you are potentially eligible to participate in the study, you will be interviewed by a researcher. The interview will be conducted over the phone (approx. 20 minutes). The purpose of this interview is to obtain relevant background information (e.g., age, sex, illnesses, medication use, etc.), provide you with further details about the study and what the next step is in the qualification process, and assess other relevant eligibility criteria. This includes obtaining further details about your mood and confirmation of your current medication and supplement intake.

Step 3: Complete a consent form

If, after the phone interview, you are eligible and willing to participate in this study, you will be sent a follow-up email to complete a consent form. This consent form must be signed electronically before you proceed further in the study. This ensures that you agree to participate in the study and are aware of all the requirements in this study.

Step 4: Post your study tablets

After you have completed your consent form, we will then post out your study tablets. You should receive your tablets within 1 to 5 working days.

In this study, we will be using a randomised, double-blind, placebo-controlled design. This means that half of the participants will be placed on saffron tablets, and the other half will be placed on placebo (dummy) tablets.

Neither you nor the investigator will be aware of which group you have been placed in. This random, placebo allocation is important for us to assess the true effects of saffron on mood, sleep, and recovery.

** Placebo involves providing a substance with no known treatment effects. In this case, the placebo will contain cellulose powder (a fibre).*

Step 5: Complete questionnaires after you receive your tablets

When you receive your tablets, you will need to notify us immediately. We will then send you an email to complete further online questionnaires. This will take approximately 15 minutes.

Step 6: Next day, start taking your tablets for 12 weeks

The day after you complete your first questionnaires, you will start taking your tablets

You will be required to take 1 tablet, twice daily (morning and evening) with or without food.

Step 7: Complete a brief questionnaire every 2 days

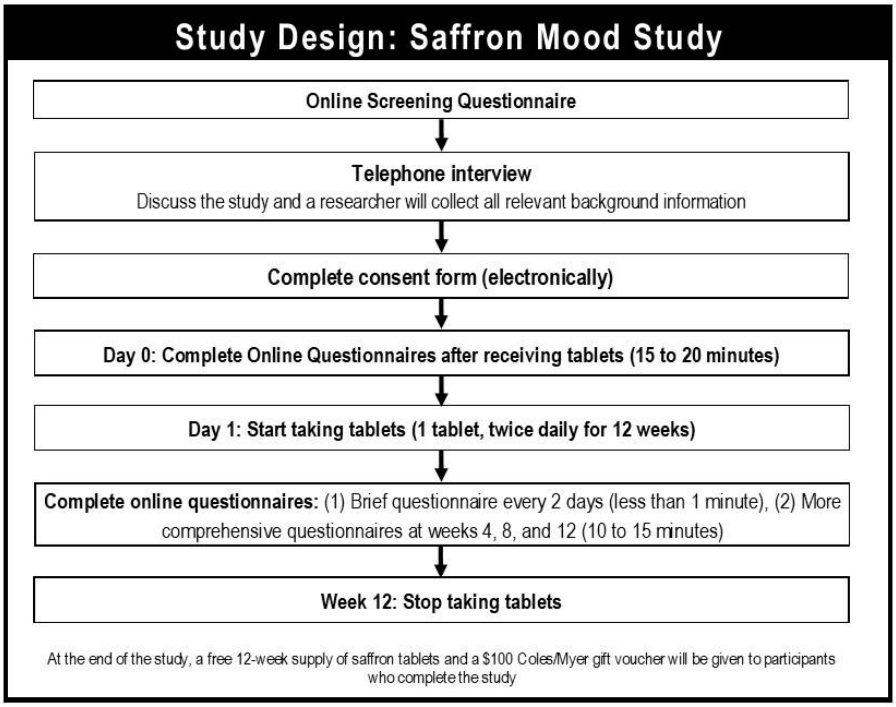
Every second day at approximately 7pm, you will receive an SMS to complete a brief questionnaire about your mood over the day. This questionnaire will take less than 1 minute to complete. For us to have accurate records of your progress, it is important that you promptly complete these questionnaires.

Step 8: Complete online questionnaires at weeks 4, 8, and 12

At weeks 4, 8, and 12, you will be required to complete some online questionnaires about your mood and sleep. You will receive an email notification to complete these questionnaires, which will take approximately 15 minutes.

Step 9: Stop taking your tablets at week 12

After 12 weeks of taking your tablets, you will now stop, and the study is now completed.



Compensation for participating in this study

1. To compensate you for the time associated with participating in this study, we will give you a $100 Coles Group voucher when you complete the study.
2. At the end of the study, all volunteers will be offered a free supply of saffron tablets to try for 12 weeks.

Criteria for inclusion/ exclusion in this study

To be included in the study, the following inclusion criteria must be met:

1. You are aged between 18 to 70 years
2. You have mild-to-moderate severity depressive symptoms as assessed by a validated questionnaire
3. You are a non-smoker
4. You have a body mass index (BMI) between 18 and 35 kg/m^2
5. You have no plan to commence any new treatments over the study period
6. You are willing to provide a personally signed and dated informed consent form detailing all pertinent aspects of the trial.

If any of the exclusion criteria below are met, you will <u>not</u> be suitable for participation in this study:

1. In the last 12 months you have received a diagnosis of a psychiatric disorder by a health professional
2. You are currently receiving regular psychological therapy/ counselling
3. You are currently experiencing a severe life stressor (e.g., work, finances, relationship, health) that significantly impacts on your daily function and activity
4. You suffer from a recently diagnosed or unmanaged medical condition including but not limited to: diabetes, hyper/hypotension, cardiovascular disease, gallbladder disease, autoimmune disease, endocrine disease, or cancer/ malignancy
5. You have a neurological condition/ disease including but not limited to Parkinson's or Alzheimer's disease
6. You regularly take medications such as anticonvulsants, benzodiazepines, opioids, corticosteroids, or immunosuppressants.
7. You have changed your medication (dose or type) in the last 3 months or you expect to change it during the study
8. In the last 3 months, you have commenced or changed your dose of nutritional and/or herbal supplements that may impact on treatment outcome
9. You currently take supplements containing saffron
10. You drink more than 14 standard servings of alcohol per week
11. You currently (or in the last 12 months) have a problem with the use of illicit drugs
12. You plan on making major lifestyle change in the next 3 months
13. You are pregnant, breastfeeding, or intend to fall pregnant in the next 3 months
14. You have had a major surgery in the last 12 months
15. You have participated in another clinical trial in the last 3 months

Voluntary participation and withdrawal from the study

It is important that you understand that your involvement in this study is voluntary. While we are grateful to have you participate, we respect your right to decline. There will be no consequences to you if you decide not to participate, and this will not affect any future treatment/service. If you decide to discontinue participation at any time, you may do so without providing an explanation. If you withdraw, any assessments already conducted may continue to be used for analysis.

Please note that if you choose to commence a treatment to improve your mental health, or you require medical treatment for any other condition during the study, this may result in withdrawal from the study. Daily saffron supplementation is not recommended during pregnancy, therefore, if you fall pregnant during the study, you must immediately stop taking your tablets and inform us as soon as possible. Falling pregnant during the study will result in your immediate withdrawal from the study. Your health is the utmost priority, and your choice/need to commence new treatment before completing this study is respected and supported.

Your privacy

Your privacy is very important to us. Your participation in this study and any information will be treated in a confidential manner. Your name and identifying details will not be used in any publication arising out of the research. Following the

study, the data will be kept in a de-identified format in a locked cabinet in the office of the Investigator and will be held for statistical analysis for future publication. Re-identifying codes will be retained for 6 months in case this is needed and will then be destroyed.

Possible benefits

Like many spices, saffron is a natural antioxidant and anti-inflammatory and is reported to be associated with several health benefits. If saffron is found to be effective, it will provide us with options to help improve mood, sleep, and general wellbeing in adults experiencing a low mood.

Possible risks

Participation in this study carries little risk and many measures will be in place to decrease the likelihood of potential risks. Below is a list of possible risks associated with participating in this study:

- Saffron intake - daily doses of up to 1500mg of saffron are considered safe, and dosages of 30mg have been used in several clinical studies. In this study, we will be using a dose of 28mg a day of saffron. Saffron has been shown to have very few side effects, although there have been infrequent reports of mild nausea and headaches.
- Daily saffron supplementation is not recommended during pregnancy; therefore, if you fall pregnant during the study, you must immediately stop taking your tablets and inform us as soon as possible. Falling pregnant during the study will result in your immediate withdrawal from the study.
- Further details about saffron and its intake are included in the 'Saffron Information Sheet'.

What to do if you experience significant side effects

If you experience any significant illness, injury, or side effects from taking your supplements, please contact Dr Adrian Lopresti or Dr Stephen Smith immediately (contact details are below). You may be asked to cease participating in the study and to seek medical advice

Dr Stephen Smith: Ph: 9448 7376 | Mob: 0412 813 518 | Email: steve@clinicalresearch.com.au

Dr Adrian Lopresti: Ph: 9448 7376 | Mob: 0411 969 797 | Email: adrian@clinicalresearch.com.au

Feedback on study results

It is estimated the results of this study will be finalised in late 2024. A summary of the results obtained from all participants in this study will be emailed to you when they have been published in a peer-reviewed journal.

Questions

If you would like to discuss any aspect of this study, please feel free to contact Dr Adrian Lopresti on 08 9448 7376.

We would like to thank you in advance for your assistance with this research project. We look forward to hearing from you soon.

If you are interested in participating in this study, please contact Dr Adrian Lopresti on 9448 7376 or email adrian@clinicalresearch.com.au

This study has been approved by the National Institute of Integrative Medicine (NIIM) Human Research Ethics Committee (HREC) (Trial Reference Number: 0134E_2023). If you have any reservation or complaint about the ethical conduct of this research, and wish to talk with an independent person, you may contact the NIIM Research Ethics Office (Tel. 03 9804 0646) or e-mail hrec@niim.com.au). Any issues you raise will be treated in confidence and investigated fully, and you will be informed of the outcome.