INFORMATION SHEET

The effects of a saffron extract on mood, sleep, and physical appearance attributes in women aged 50 to 70 years experiencing low mood and poor sleep: a randomised, double-blind, placebo-controlled trial

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

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 further examining its effects on mood and sleep in women aged 50 to 70 years experiencing depressive symptoms and poor sleep. Furthermore, we are interested in examining its effects on self-esteem, self-perception of physical appearance, and facial skin age.

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

Information about the 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.

What does participation involve? **(see study flow chart on page 2)**

This study will comprise several steps as outlined below:

Step 1: Completion of initial online 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 screening questionnaire results, 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 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. 5 minutes). The purpose of this interview is to obtain relevant background information (e.g., medication use, current treatments, sleep and depressive symptoms, etc.), and assess other relevant eligibility criteria. We will also provide you with further details about the study. If you meet our eligibility criteria and agree to participate in the study, you will proceed to the next step.

Step 3: VISIT 1 (day 0): Face-to-face assessment (approx. 45 mins)

During this visit, the following tasks will be completed:

1. Have your weight, height, and blood pressure measured
2. Have your photo taken by a researcher
    a. This photo will be taken using a dedicated phone used for this clinical trial. Your photo will be used to estimate your facial skin age. Your anonymised photo will be uploaded on a secure password-protected application for this analysis. This photo can only be accessed by the

company responsible for the facial analysis (Topazium) and will be deleted when the study is completed.

b. You will be asked to attend the visit without make-up or to remove any make-up before the photo is taken. This provides a better estimate of your skin age.

3. Complete questionnaires about your mood, sleep, self-esteem, and general wellbeing
4. Receive a 12-week supply of tablets containing saffron or a placebo

Step 4: Take your tablets

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

Neither you nor the investigator will know which group you have been placed in. This random placebo allocation is important for us to assess the true effects of saffron.

You will be required to take ONE tablet, TWICE daily with or without food.

* Placebo involves providing a substance with no known treatment effects. In this case, the placebo will contain magnesium stearate.

It is extremely important that you take these tablets every day. We will send you reminders.

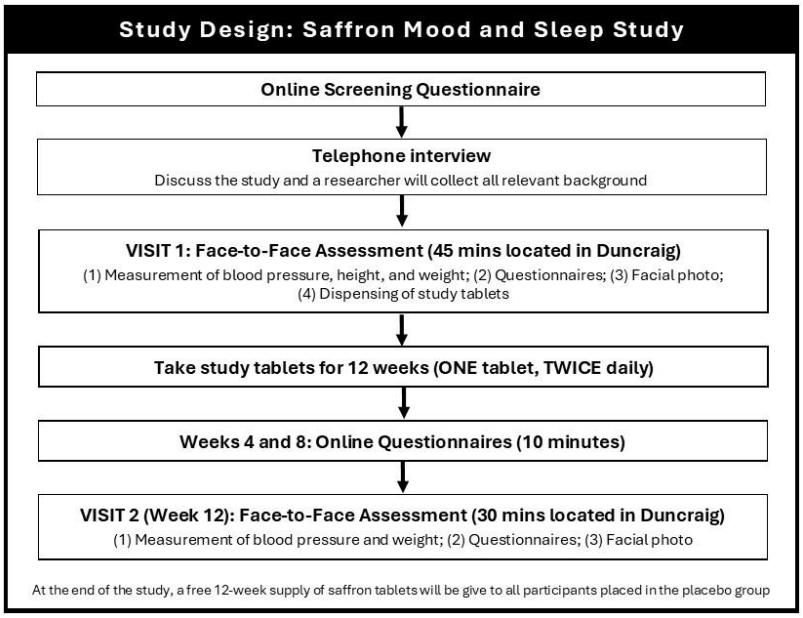
Step 5: Complete monthly questionnaires (approx. 10 mins)

At weeks 4 and 8, you will need to complete an online questionnaire assessing your mood, sleep, and general wellbeing. You will also complete questions that ask if you have been experiencing any adverse effects associated with the intake of your tablets, experienced any illnesses/injuries, or changed/started any new medications.

Step 6: VISIT 2 (week 12): Face-to-face assessment (approx. 45 mins)

During this visit, the following tasks will be completed:

1. Have your weight and blood pressure measured
2. Have your photo taken by a researcher
3. Complete questionnaires about your mood, sleep, self-esteem, and general wellbeing



Compensation for participating in this study

1. To compensate you for your travel costs and time associated with participating in this study, we will give you a $50 gift voucher at visit 1 and a $100 gift voucher at visit 2.
2. At the end of the study, volunteers placed in the placebo group will be offered a free 12-week supply of saffron tablets to try.

Criteria for inclusion/ exclusion in this study

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

1. You are a female aged between 50 to 70 years
2. You currently experience low mood.
3. You currently experience sleep disturbances
4. You are a non-smoker
5. You have a BMI between 18 and 35 kg/m^2
6. You have no plan to commence new treatments for mood, sleep, or skin quality over the study period
7. You understand and are willing and able to comply with all study procedures
8. 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 not be suitable for participation in this study:

1. You are currently receiving regular psychological therapy/ counselling
2. You are suffering from recently diagnosed or unmanaged medical conditions including but not limited to diabetes, hypertension, cardiovascular disease, gallbladder disease, autoimmune disease, endocrine disease, or cancer/ malignancy
3. You have a psychiatric disorder (other than mild-to-moderate depression and/or anxiety), or a neurological condition/ disease including but not limited to Parkinson's or Alzheimer's disease
4. You are regularly taking medication intake including but not limited to anticonvulsants, benzodiazepines, opioids, corticosteroids, or immunosuppressants.
5. You have changed your medication in the last 3 months or expect to change it during the study
6. In the last 3 months, you started or changed the dose of nutritional and/or herbal supplements that may impact treatment outcomes
7. You currently take supplements containing saffron
8. You consume more than 14 standard alcoholic drinks per week
9. You have a current or 12-month history of regular illicit drug use
10. You have planned major lifestyle changes in the next 3 months
11. You are pregnant, breastfeeding, or intend to fall pregnant during the study period
12. You have had a significant surgery that continues to affect your daily function over the last year
13. You have participated in another clinical trial in the last month

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, sleep, 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 provided 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.

Facial age estimation privacy details: As detailed previously, your photo will be taken by a researcher at the beginning and end of the study. This will be used to estimate my facial skin age. Facial photos will be uploaded on the SkinFace App by Topazium. Topazium complies with EU data protection regulations and has an established data protection risk assessment plan. The information will be used exclusively for the purposes of this study, following the principle of data minimisation (only the data strictly necessary will be collected and

stored). Images will be stored only for the duration of the clinical study and its subsequent statistical analysis. Images collected via our smartphone will be anonymous and analysed through a dedicated mobile app with user-based access control. Topazium grants app access through a username and password (minimum 8 characters, including numbers, letters, and symbols), which is renewed every three months. The algorithmic systems are hosted on Google Cloud servers located in Belgium, which comply with cybersecurity and HIPAA regulations. The images are processed automatically, and only the age prediction is stored in Firebase, a Google Cloud-hosted NoSQL database during the study period. After the study, the data will be securely deleted to prevent any recovery. Topazium has appointed a Data Protection Officer to ensure ongoing compliance with applicable regulations. Topazium's privacy policy can be found on the following webpage: https://topazium.com/privacy-policy/

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, injuries, or side effects that have commenced since starting your tablets, please immediately contact Dr Adrian Lopresti or Dr Stephen Smith (contact details are below). You may be asked to stop 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 mid-2026. 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 (usually 6 to 12 months after the completion of the study).

Questions

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

We would like to thank you in advance for your assistance with this research project.

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: 0155E_2025). If you have any reservations or complaints 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 email hrec@niim.com.au). Any issues you raise will be treated in confidence and investigated fully, and you will be informed of the outcome.