INFORMATION SHEET

The effects of a saffron extract on mood and sleep in children aged 6 to 11 years with emotional difficulties: a randomised, double-blind, placebo-controlled trial

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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 children aged 6 to 11 years experiencing low mood.

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 takes approximately 10 minutes to complete. It provides us with information relating to the eligibility criteria.

If, based on the screening questionnaire results, your child is assessed as 'likely' eligible, you will be contacted for a phone interview. Ineligible volunteers will be informed by email that their child does not fulfil the eligibility criteria.

Step 2: Phone Interview for an assessment of eligibility

If your child is 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., medication use, current treatments, mental health history, life stressors, living arrangements, sleep quality, etc.) and assess other relevant eligibility criteria. We will also provide you with further details about the study. If your child meets our eligibility criteria and agrees to participate in the study, you will proceed to the next step.

Step 3: Discuss the study with your child and sign the consent forms

If your child is eligible to participate in the study, and he/she is willing to participate, you will be emailed copies of the Parent and Child Study Information Sheets/ Video and Consent Forms. After reading the information and watching the video, both you and your child will need to sign the Consent Forms. This will be done online (electronically).

Step 4: We will send out the study tablets

After you and your child have completed the Consent Forms, the study tablets will be sent by express post/freight.

Step 5: Complete questionnaires (Day 0)

You and your child will need to complete a series of questionnaires. This will take less than 10 minutes and must occur before your child starts his/her tablets.

Step 6: Your child takes his/her tablets (Day 1 to 42)

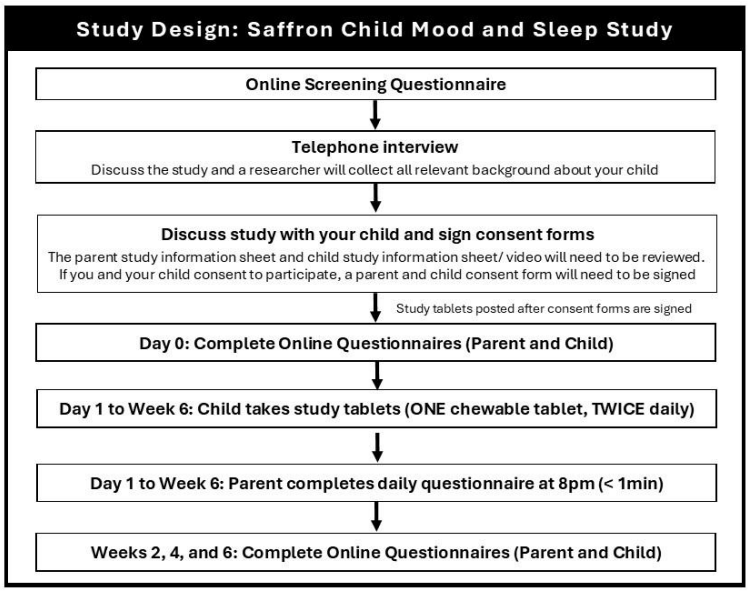
The child will start taking his/her tablets. He/she will be required to take 1 chewable tablet twice daily (morning and evening) with or without food.

Step 7: Parent completes daily child mood ratings (Day 1 to 42)

Every evening, you will be required to complete a rating of your child's overall mood and whether your child has had any difficulties taking the tablets. We will send a text message to your phone. This will take less than 1 minute.

Step 8: Complete questionnaires (Weeks 2, 4, and 6)

You and your child will need to complete a series of online questionnaires every 2 weeks during the study (sent via email). This will take approximately 10 minutes.



Compensation for participating in this study

1. To compensate you and your child for the time associated with participating in this study, we will send you a $150 gift voucher.
2. At the end of the study, children placed in the placebo group will be offered a free 6-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. Males & females aged 6 to 11 years.
2. Parent-reported emotional difficulties in the child.
3. Child attends mainstream schooling/ classes.
4. Child has a healthy body mass index.
5. Child and parent understand, are willing, and are able to comply with all study procedures.
6. Child is willing and able to take the prescribed placebo/saffron tablets.

7. Child lives with the reporting parent for at least 5 days a week.

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

1. Child has a known allergy to saffron.
2. Child is currently receiving treatment for emotional or behaviour-related difficulties, or there is a plan to start a new treatment during the study period.
3. Child has a diagnosis of a sleep disorder, including but not limited to, insomnia, night terrors, and/or sleepwalking.
4. Child has a medical/physical condition that significantly affects daily function.
5. Child has been diagnosed with a psychiatric condition that significantly affects daily function.
6. Child engages in self-harm behaviours or has suicidal ideation.
7. Child has had any injury, surgery, or illness in the last 3 months that significantly affected his/her daily function.
8. Child has been currently taking, or in the last 8 weeks, taken a pharmaceutical medication.
9. Child has been currently taking, or in the last 8 weeks, taken a nutritional or herbal supplement that may affect the treatment outcomes.
10. Any plan to commence a pharmaceutical medication, nutritional, or herbal supplement during the study period.
11. Child is experiencing a significant family or lifestyle stressor that may impact his/her emotional function.
12. A planned significant lifestyle, dietary or environmental change during the study period for the child and/or parent.
13. Child has participated in a clinical research trial within 30 days.
14. Child has a significant learning or cognitive impairment.
15. Any other condition which, in the Investigator's opinion, may adversely affect the child's and/or parent's ability to complete the study, its measures, or which may pose a significant risk to the child.

Voluntary participation and withdrawal from the study

It is important that you understand that your (and your child's) 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 or your child decides to discontinue participation in the study 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 child's mental health, sleep, or if your child requires medical treatment for any other condition during the study, this may result in withdrawal from the study. Your child's 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 (and your child's) participation in this study and any information provided will be treated in a confidential manner. Your name, your child's name, and any identifying details will not be used in any publication arising out of this 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 children experiencing a low mood.

Possible risks

Saffron is considered safe and is well-tolerated by most users. It is used throughout the world as a spice/ seasoning with few reported side effects. There have been several studies using doses of 30 to 60mg daily, conducted in children and teenagers, which have demonstrated that it was well-tolerated. In this study, we will be administering a dose of 28mg a day. Although reported side effects are infrequent, there have been reports of mild nausea and headaches in some people taking saffron. No studies have reported any serious side

effects from its intake, although this cannot be totally ruled out. Further details about saffron and its intake are included in the 'Saffron Information Sheet'.

What to do if your child experiences significant side effects

If your child experiences any significant illness, injuries, or side effects that have commenced since starting his/her tablets, please immediately contact Dr Adrian Lopresti or Dr Stephen Smith (contact details are below). Your child 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 that the results of this study will be finalised in late 2026. A summary of the results obtained from 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: 0162E_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.