INFORMATION SHEET

A further examination of the short-term anxiolytic effects of an Echinacea extract (EP107™) in adults experiencing increased anxiety: A randomised, double-blind, placebo-controlled trial

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You are invited to participate in this study.

Background

Echinacea angustifolia is a commonly used natural ingredient. It has traditionally been used to treat cold and respiratory infections. However, in previous studies we conducted, it was shown to improve mood in adults. In this study, we are interested in examining the effects of an Echinacea extract (EP107™) on:

- Stress and anxiety symptoms
- Sleep quality

As a result, we are inviting you to participate in this 3-week, randomised, double-blind, placebo-controlled study.

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 Anxiofit Ltd, the company that produces the patented Echinacea extract (EP107™) that will be used in this study. However, this study is independently managed by Clinical Research Australia without external influence from Anxiofit Ltd.

Aim of the study

We would like to know whether taking Echinacea tablets twice daily for 7 days can reduce anxiety and improve sleep in adults experiencing anxiety.

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

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 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. 15 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 anxiety and confirmation of your current medication and supplement intake.

If you meet our eligibility criteria, an assessment appointment at our offices in Duncraig will be arranged in 3 to 7 days time.

Step 3: In-person assessment (30min)

During this assessment, the following tasks will be completed:

1. Completion of informed consent form
2. Completion of a mood questionnaire. You must score within a specific range to be eligible to participate in this study.
    a. If you score out of the range on the mood questionnaire, you will be ineligible, and we will provide you with a 14-day free supply of echinacea tablets and a $30 Coles/Myer group gift voucher.
3. Measurement of weight, height and blood pressure
4. Completion of a sleep questionnaire
5. Provision of a 7-day supply of study tablets

Step 4: Next morning, start taking tablets for 7 days (Echinacea or placebo)

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 Echinacea tablets, and the other half will be placed on placebo (dummy) tablets.

Neither you nor the investigator will know which group you have been placed into. This random, placebo allocation is important for assessing the true effects of Echinacea on anxiety and wellbeing.

You will be required to take 2 tablets, twice daily (morning and evening), with or without food for 7 days

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

Step 5: On days 3 and 7, complete an online questionnaire (5-10 min)

3 and 7 days after you take your tablets, you will be asked to complete a brief questionnaire that assesses your anxiety symptoms, sleep quality, and if you have experienced any side effects from taking your tablets.

Step 6: On day 7, stop taking your tablets

After you have been taking your tablets for 7 days, you will stop taking your tablets.

Step 7: On day 21, complete an online questionnaire (5 to 10 min)

After you have stopped taking your tablets for 2 weeks, you will be asked to complete a final questionnaire that assesses your anxiety and sleep symptoms.

Compensation for participating in this study

1. Participants who attend the in-person visit but are ineligible to progress further in the study will be given a $30 Coles/Myer Group gift voucher.
2. Participants who complete the study in full will be given a $40 Coles/Myer Group gift voucher.
3. All people who attend the in-person visit (eligible and ineligible participants) will be offered a free 1-week supply of Echinacea tablets.

Criteria for inclusion/ exclusion in this study

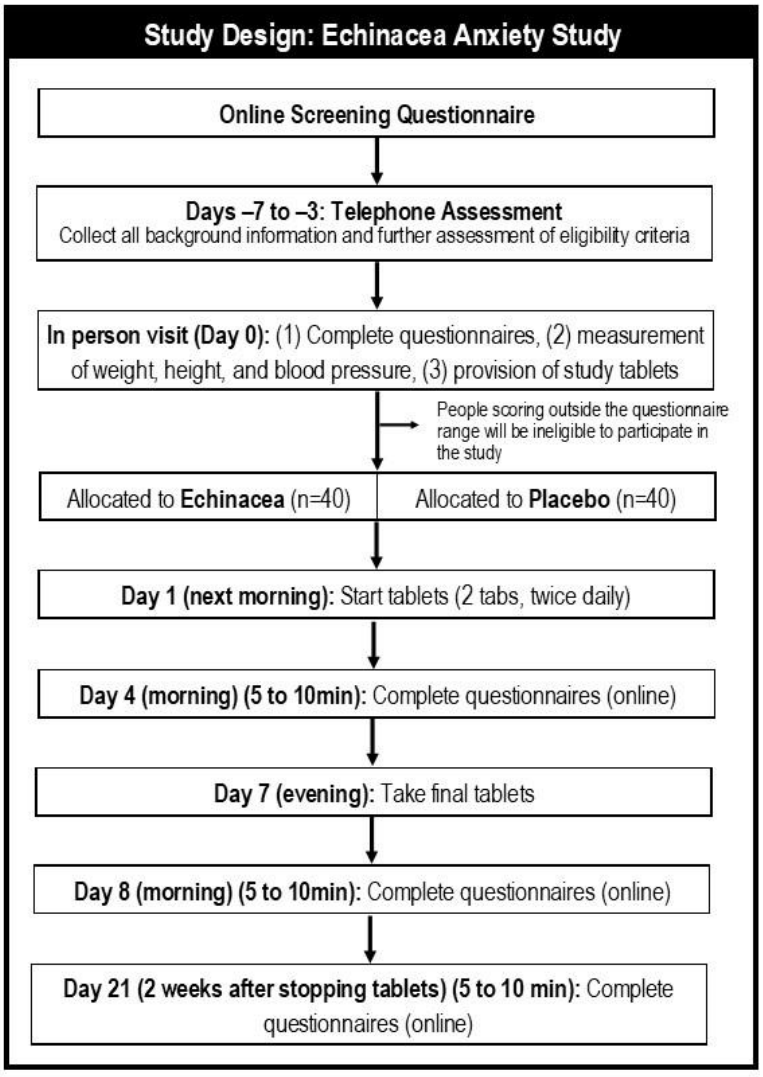
To be included in the study, the following inclusion criteria must be met:

1. Generally, healthy adults (male and female) aged 18 to 80 years
2. Currently experiencing high stress and/or anxiety
3. Scoring within a specified range on a mood-related questionnaire at both screening and the in-person visit
4. Non-smoker
5. BMI between 18 and 30 kg/m^2
6. No plan to commence new treatments over the study period
7. Understand, willing and able to comply with all study procedures

8. 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 suffer from a recently diagnosed or unmanaged medical condition including but not limited to: diabetes, hyper/hypotension, cardiovascular disease, a gastrointestinal disease requiring regular use of medications, gallbladder disease, autoimmune disease, endocrine disease, acute or chronic pain condition, or cancer/malignancy
2. You have been diagnosed with a psychiatric or neurological condition including but not limited to: any psychiatric disorder, neurological disease (Parkinson's, Alzheimer's disease, intracranial haemorrhage, head or brain injury)
3. You regularly take medications including but not limited to anticholinergics, anti-epileptics, antihistamines, benzodiazepines, opioids, or corticosteroids.
4. You have changed your medication (dose or type) in the last 3 months, or you expect to change it during the study
5. You currently take supplements containing Echinacea
6. In the last 6 months, you have commenced or changed your dose of nutritional and/or herbal supplements that may impact on treatment outcome
7. You currently (or in the last 12 months) have a problem with the use of illicit drugs
8. You drink more than 14 standard servings of alcohol per week
9. You are pregnant, breastfeeding, or intend to fall pregnant in the next 3 months
10. You have had a significant surgery in the last 12 months
11. You are an overnight shift worker
12. You have participated in another clinical trial in the past 3 months
13. You plan on making major lifestyle change in the next 2 months
14. You have a known allergy to Echinacea, chamomile, or sunflower oil



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 choose 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 anxiety or mood, or you require medical and/or psychological treatment for any other condition during the study, this will result in 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

Echinacea is a commonly used natural ingredient primarily used to treat colds and upper-respiratory infections. As a result, taking these tablets may provide some immune-supporting health benefits

If Echinacea angustifolia (EP107™) is found to be effective, it will provide a natural option to help improve symptoms of anxiety and stress.

Possible risks

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

- Echinacea is well-tolerated by most people and is a commonly sold natural ingredient. However, side effects cannot be totally ruled out, and we ask you to contact us immediately if you are experiencing any adverse effects (whether or not you believe they are associated with the intake of the tablets).
- Further details about Echinacea and its intake are included in the 'Echinacea 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 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 of study results

It is estimated the results of this study will be finalised in mid-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: 0129E_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.