Trial registered on ANZCTR

Trial ID	
ACTRN12616000859482	
Ethics application status	
Approved	
Date submitted	
6/04/2016	
Date registered	
30/06/2016	
Type of registration	
Prospectively registered	

Titles & IDs

Public title	
The efficacy of mangosteen pericarp fruit extract for the treatment of schizophrenia.	
Scientific title	
The efficacy of adjunctive Garcinia mangostana Linn. (mangosteen) pericarp for the treatment of schizophrenia: A 24-week double blind randomised placebo controlled trial	
Secondary ID [1]	
Nil	
Universal Trial Number (UTN)	
Trial acronym	
MANGO SZ/CADENCE-M	

Health condition

Health condition(s) or problem(s) studied:	
Schizophrenia	
Condition category	**Condition code**
Mental Health	Schizophrenia
Alternative and Complementary Medicine	Other alternative and complementary medicine

Intervention/exposure

Study type	
Interventional	

Description of intervention(s) / exposure

Total daily dose of 1000mg of Garcinia mangostana L. (mangosteen dried fruit pericarp encapsulated in ge latine capsules): 500mg 2 capsules once a day with food.
Duration of treatment: 24 weeks
Participants will be instructed to return unused medication which will be calculated and documented to det ermine medication adherence.

Intervention code [1]

Treatment: Other

Comparator / control treatment

Total daily dose of 1000mg of rice flour weighted gelatine capsules: 500mg 2 capsules once a day with foo d.
Duration of treatment: 24 weeks

Control group

Placebo

Outcomes

Primary outcome [1]

The primary outcome will be the change in schizophrenia symptom severity on PANSS total score.

Timepoint [1]

Baseline, weeks 4,8,12,16,20, primary endpoint week 24, post-discontinuation week 28.

Secondary outcome [1]

The change in PANSS Positive subscale.

Timepoint [1]

Baseline, weeks 4,8,12,16,20, primary endpoint week 24, post-discontinuation week 28.

Secondary outcome [2]

The change in depressive symptoms using MADRS.

Timepoint [2]

Baseline, weeks 4,8,12,16,20, primary endpoint week 24, post discontinuation week 28

Secondary outcome [3]

The change in participant life satisfaction rated on the self-reporting scale (Q-LES-Q)

Timepoint [3]

Baseline, week 4,12,16,20, primary endpoint week 24 and post-discontinuation week 28.

Secondary outcome [4]

The change in functioning measures using the Global Assessment of Functioning Scale (GAF)

Timepoint [4]

Baseline, weeks 4,8,12,16,20, primary endpoint week 24 and post-discontinuation week 28.

Secondary outcome [5]

The change in functioning measures using the LIFE-RIFT scale.

Timepoint [5]

Baseline, week 4,8,12,16,20, primary outcome week 24 and post-discontinuation week 28.

Secondary outcome [6]

The change in participant perception using the Patient Global Impression Scale (PGI).

Timepoint [6]

Week 4,8,12,16,20, primary endpoint week 24 and post-discontinuation week 28.

Secondary outcome [7]

The change in participant cognition using Cogstate computerised cognitive testing (Cogstate).

Timepoint [7]

Baseline and primary endpoint week 24.

Secondary outcome [8]

The changes in tobacco use will be recorded using the Opiate Treatment Index (OTI).

Timepoint [8]

Baseline and primary endpoint week 24.

Secondary outcome [9]

Blood samples are being collected at baseline and the end of the treatment phase (week 24). We expect to e xplore oxidative stress factors, including cytokines, thiobarbituric acid reactive substances and total antioxi dant capacity. However, as the field of biological psychiatry is rapidly moving, these will be exploratory in vestigations for which the targets may change by the end of the trial. Participants are providing blood samp les as an optional extra to the trial and have signed unspecified consent to allow all relevant and unforeseen investigations to occur at the completion of the study.

Timepoint [9]

Baseline, primary endpoint week 24 and post-discontinuation week 28.

Secondary outcome [10]

The change in PANSS Negative subscale

Timepoint [10]

Baseline, weeks 4,8,12,16,20, primary endpoint week 24, post-discontinuation week 28.

Secondary outcome [11]

The change in PANSS General Psychopathology subscale

Timepoint [11]

Baseline, weeks 4,8,12,16,20, primary endpoint week 24, post-discontinuation week 28.

Secondary outcome [12]

The changes in alcohol use will be recorded using the Opiate Treatment Index (OTI).

Timepoint [12]

Baseline and primary endpoint week 24.

Secondary outcome [13]

The changes in heroin use will be recorded using the Opiate Treatment Index (OTI).

Timepoint [13]

Baseline and primary endpoint week 24.

Secondary outcome [14]

The changes in other opiates use will be recorded using the Opiate Treatment Index (OTI).

Timepoint [14]

Baseline and primary endpoint week 24.

Secondary outcome [15]

The changes in cannabis use will be recorded using the Opiate Treatment Index (OTI)

Timepoint [15]

Baseline and primary endpoint week 24.

Secondary outcome [16]

The changes in amphetamine use will be recorded using the Opiate Treatment Index (OTI)

Timepoint [16]

Baseline and primary endpoint week 24.

Secondary outcome [17]

The changes in cocaine use will be recorded using the Opiate Treatment Index (OTI)

Timepoint [17]

Baseline and primary endpoint week 24.

Secondary outcome [18]

The changes in (illicit) benzodiazepine use will be recorded using the Opiate Treatment Index (OTI)

Timepoint [18]

Baseline and primary endpoint week 24.

Secondary outcome [19]

The changes in barbiturates use will be recorded using the Opiate Treatment Index (OTI)

Timepoint [19]

Baseline and primary endpoint week 24.

Secondary outcome [20]

The changes in hallucinogens use will be recorded using the Opiate Treatment Index (OTI)

Timepoint [20]

Baseline and primary endpoint week 24.

Secondary outcome [21]

The changes in inhalants use will be recorded using the Opiate Treatment Index (OTI)

Timepoint [21]

Baseline and primary endpoint week 24.

Secondary outcome [22]

The changes in synthetic drugs use will be recorded using the Opiate Treatment Index (OTI)

Timepoint [22]

Baseline and primary endpoint week 24.

Secondary outcome [23]

The changes in the occurence of tardive dyskinesia using the Abnormal Involuntary Movement Scale

Timepoint [23]

Baseline, weeks 4,8,12,16,20, primary endpoint week 24, post-discontinuation week 28.

Secondary outcome [24]

The changes in overall illness severity, improvement or change and therapeutic response using the Clinical Global Impression

Timepoint [24]

Baseline, weeks 4,8,12,16,20, primary endpoint week 24, post-discontinuation week 28.

Secondary outcome [25]

The changes in alcohol use using the Alcohol Use Disorders Identification Test

Timepoint [25]

Baseline and primary endpoint week 24.

Secondary outcome [26]

The changes in level of nicotine dependence using the Fagerstrom Test for Nicotine Dependence

Timepoint [26]

Baseline and primary endpoint week 24.

Eligibility

Key inclusion criteria

1. Being 18 years or older
2. Have a DSM-V diagnosis of schizophrenia or schizoaffective disorder.
3. Score greater than or equal to 54 on the PANSS total score or have a CGI-S score of greater than or equa l to 3.
4. Participants currently under therapy for schizophrenia or schizoaffective disorder will need to have been on that primary therapy for at least four weeks prior to randomization.
5. Have the capacity to consent to the study and comply with the procedures.
6. Be using effective contraception if female, sexually active and childbearing age.
7. Be able to speak, read, write and understand English language.
8. Participants will be required to nominate a current treating physician and will not be eligible to enter the study until one is identified.

Minimum age

18 Years

Maximum age

No limit

Gender

Both males and females

Can healthy volunteers participate?

No

Key exclusion criteria

1. Participants with a known or suspected active systemic medical disorder.
2. Individuals who are pregnant or lactating.
3. Participants currently enrolled in any other intervention study.
4. Individuals who are intolerant, allergic to or have had an anaphylactic reaction to any of the components of the preparation.
5. Inability to comply with either the requirements of informed consent or treatment protocol.

Study design

Purpose of the study

Treatment

Allocation to intervention

Randomised controlled trial

Procedure for enrolling a subject and allocating the treatment (allocation concealment procedures)

Participants will be recruited through various recruitment avenues including advertisements through local newspapers, flyers in medical waiting rooms, pharmacies and university campuses. Direct contact will be made with potential referral sources consisting of general practitioners, community mental health teams, th e disability support sector, support groups, private psychiatrists and local psychiatric inpatient unit.
Trial clinicians will contact all participants referred to the trial to schedule an initial face-to-face screening interview to establish written consent, that inclusion criteria are satisfied and confirm the DSM-V diagnosi s of schizophrenia or scizoaffective disorder with a PANSS total score of greater than or equal to 54 or CG I greater than or equal to 3. Participants will be randomised in the Garcinia mangostana Linn group or plac ebo group and will be allocated a study number for trial identification purposes. Packs will be allocated seq uentially and bottles are identical so as to conceal treatment allocation and blinding. To facilitate the doubl e-blinding process, the trial medications will be dispensed by an independent pharmacist in identical numb ers and capsule forms in sealed containers. The trial statistician and trial clinicians will be blinded to the gr oup allocation.

Methods used to generate the sequence in which subjects will be randomised (sequence generation)

Allocation to treatment arm will be randomly assigned using 1:1 ratio (active to placebo) using permutated block randomisation. An independent researcher will develop the computer-generated randomisation plan.

Masking / blinding

Blinded (masking used)

Who is / are masked / blinded?

The people receiving the treatment/s
The people administering the treatment/s
The people assessing the outcomes
The people analysing the results/data

Intervention assignment

Parallel

Other design features

Phase

Phase 2

Type of endpoint(s)

Efficacy

Recruitment

Anticipated date of first participant enrolment

6/07/2016

Actual date of first participant enrolment
Anticipated date last participant enrolled
1/09/2018
Actual date last participant enrolled
Anticipated date of last data collection
Actual date of last data collection
Target sample size
150
Actual sample size
Recruitment status
Not yet recruiting
Recruitment in Australia
Recruitment state(s)
QLD,VIC
Recruitment hospital [1]
Royal Brisbane & Womens Hospital - Herston
Recruitment hospital [2]
Ipswich Hospital - Ipswich
Recruitment hospital [3]
The Prince Charles Hospital - Chermside
Recruitment hospital [4]
Gold Coast Hospital - Southport
Recruitment hospital [5]
Logan Hospital - Meadowbrook
Recruitment hospital [6]
Princess Alexandra Hospital - Woolloongabba
Recruitment hospital [7]
Barwon Health - Geelong Hospital campus - Geelong
Recruitment hospital [8]
The Geelong Clinic - St Albans Park
Recruitment postcode(s) [1]
3220 - Geelong
Recruitment postcode(s) [2]
4305 - Ipswich
Recruitment postcode(s) [3]
4006 - Herston
Recruitment postcode(s) [4]
4032 - Chermside
Recruitment postcode(s) [5]
4215 - Southport
Recruitment postcode(s) [6]
4122 - Upper Mount Gravatt
Recruitment postcode(s) [7]
4131 - Meadowbrook
Recruitment postcode(s) [8]
3219 - St Albans Park
Recruitment postcode(s) [9]
3214 - Corio
Recruitment postcode(s) [10]
3215 - Bell Park
Recruitment postcode(s) [11]
3228 - Torquay

Recruitment postcode(s) [12]
3216 - Belmont

Funding & Sponsors

Funding source category [1]
Other
Name [1]
The Stanley Medical Research Institute
Address [1]
8401 Connecticut Avenue, Suite 200
Chevy Chase, MD 20815
Country [1]
United States of America
Primary sponsor type
Hospital
Name
University Hospital-Barwon Health
Address
P.O. Box 281
Geelong VIC 3220
Country
Australia
Secondary sponsor category [1]
University
Name [1]
University of Queensland, Queensland Brain Institute
Address [1]
The University of Queensland
QBI Building 79, University of Queensland,
St Lucia QLD 4072

Country [1]
Australia

Ethics approval

Ethics application status
Approved
Ethics committee name [1]
Barwon Health Human Research Ethics Committee
Ethics committee address [1]
Research Ethics Office
University Hospital-Barwon Health
P.O.Box 281
Geelong, Victoria
3220
Ethics committee country [1]
Australia
Date submitted for ethics approval [1]
29/06/2015
Approval date [1]

10/03/2016

Ethics approval number [1]

15/26

Ethics committee name [2]

Metro South Human Research Ethics Committee

Ethics committee address [2]

Metro South HREC Office
PAH Centres for Health Research
Level 7, Translational Research Institute
37 Kent Street
Woolloongabba QLD 4102

Ethics committee country [2]

Australia

Date submitted for ethics approval [2]

08/01/2016

Approval date [2]

15/02/2016

Ethics approval number [2]

HREC/16/QPAH/15

Summary

Brief summary

There is evidence of anomalies in redox biology in schizophrenia; (i) the presence of oxidative stress (where the levels of antioxidants are decreased or the levels of free radicals are increased to a point that is damaging to the function of the cell, increasing inflammation) particularly implicating the glutathione system ; (ii) changes in oxidative status with treatment; and (iii) evidence that other glutathione and redox active agents have therapeutic value.

Garcinia mangostana Linn, known colloquially as mangosteen, is a tropical evergreen fruit tree originating from Indonesia. Its rind or pericarp contains an exudate containing a large number of bioactive compounds called xanthones that have robust effects on the glutathione system and many other pathways germane to schizophrenia. Motivated by the results of the first pilot randomised, double blind placebo trial of adjunctive Garcinia mangostana Linn for the treatment of schizophrenia we speculate that this research may uncover a new class of agents for the treatment of the disorder, and uncover novel pathophysiological pathways.

The trial involves 150 participants aged 18 years or older with a DSM-V diagnosis of schizophrenia or schizoaffective disorder. Participants referred to the trial will have an initial face–to-face screening interview. All randomised participants will receive two 500mg mangosteen pericarp capsules once a day to a total dose of 1000mg daily or placebo, in addition to treatment as usual, for 24 weeks. Assessment will occur at regular 4 weekly intervals throughout the 24 weeks and 1 month after completion of the study. The primary outcome will be the change in schiaophrenia symptom severity using the PANSS total scale at the end of the 24-week treatment phase. The secondary outcomes will include changes in depressive symptoms, quality of life, functioning and life satisfaction which will be measured using the PANSS subscales, Q-LES-Q scale, GAF, LIFE-RIFT, PGI and Cogstate. Blood biomarkers will also be analysed. Blood samples will be obtained at baseline and at weeks 24 and 28. Blood will be analysed for relevant markers based on preclinical evidence including markers of antioxidant defence, oxidative stress and markers of inflammation. The research will have immediate and direct translational benefits. The safety and tolerability of Garcinia mangostana Linn, its affordability and accessibility and that the general public are accepting of plant-derived compounds, raise its attraction as a potential therapeutic agent.

Trial website

Trial related presentations / publications
Public notes
Attachments [1]

http://www.anzctr.org.au/AnzctrAttachments/368490-MANGO S StudyProtocol-V1-12-5-15-update.doc

Contacts

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