**Trial registered on ANZCTR**

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<th>Trial ID</th>
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<td><strong>Ethics application status</strong></td>
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<td><strong>Date submitted</strong></td>
<td>17/12/2015</td>
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<tr>
<td><strong>Date registered</strong></td>
<td>18/01/2016</td>
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<tr>
<td><strong>Type of registration</strong></td>
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**Titles & IDs**

**Public title**
The efficacy of adjunctive Garcinia mangostana linn (mangosteen) pericarp for bipolar depression: A 24-week double-blind, randomised, placebo controlled trial.

**Scientific title**
The efficacy of adjunctive Garcinia mangostana linn (mangosteen) pericarp for bipolar depression: A 24-week double-blind, randomised, placebo controlled trial.

**Secondary ID [1]**
Nil Known

**Universal Trial Number (UTN)**
MANGO BD

**Health condition**

**Health condition(s) or problem(s) studied:**
Bipolar depression

**Condition category**
Mental Health

**Condition code**
Depression
Mental Health
Other mental health disorders

**Intervention/exposure**

**Study type**
Interventional

**Description of intervention(s) / exposure**
1000mg/day of oral (2 capsules, once a day) of adjunctive Garcinia Mangostana Linn. (mangosteen) pericarp will be trialled against placebo for 24 weeks to determine the efficacy of mangosteen pericarp for the treatment of bipolar depression. Adherence will be monitored by participants returning all bottles of investigational product, including any unused capsules.

**Intervention code [1]**
Treatment: Drugs

**Comparator / control treatment**
Placebo (inactive starch)

**Control group**
Placebo

**Outcomes**

**Primary outcome [1]**
change in severity of mood symptoms, measured using the Montgomery Asberg Depression Rating Scale (MADRS)

**Timepoint [1]**
Conducted at all trial visits - Baseline (week 0) and every four weeks after that (week 4, 8, 12, 16, 20, 24)

**Secondary outcome [1]**
Change in Clinical Global Impressions - Improvement Scale (CGI-I)

**Timepoint [1]**
Conducted at all trial visits - Baseline (week 0), every four weeks after that (week 4, 8, 12, 16, 20, 24) and week 28 (4 weeks post discontinuation).

**Secondary outcome [2]**
Change in Clinical Global Impressions - Severity Scale (CGI-S)

**Timepoint [2]**
Conducted at all trial visits - Baseline (week 0), every four weeks after that (week 4, 8, 12, 16, 20, 24) and week 28 (4 weeks post discontinuation).

**Secondary outcome [3]**
Change in anxiety symptoms based on the Hamilton Anxiety Rating Scale (HAM-A)

**Timepoint [3]**
Conducted at all trial visits - Baseline (week 0), every four weeks after that (week 4, 8, 12, 16, 20, 24) and week 28 (4 weeks post discontinuation).

**Secondary outcome [4]**
Change in bipolar symptomatology as measured by Bipolar Depression Rating Scale (BDRS)

**Timepoint [4]**
Conducted at all trial visits - Baseline (week 0), every four weeks after that (week 4, 8, 12, 16, 20, 24) and week 28 (4 weeks post discontinuation).

**Secondary outcome [5]**
Change in mania symptomatology measured by the Young Mania Rating Scale (YMRS)

**Timepoint [5]**
Conducted at all trial visits - Baseline (week 0), every four weeks after that (week 4, 8, 12, 16, 20, 24) and four weeks post-discontinuation at week 28

**Secondary outcome [6]**
Change in Patient Global Impression Scale (PGI)

**Timepoint [6]**
Conducted every four weeks after baseline (week 4, 8, 12, 16, 20, 24) and week 28 (4 weeks post discontinuation).

**Secondary outcome [7]**
Change in quality of life measured by Quality of life Enjoyment and Satisfaction Questionnaire - Short Form (Q-LES-Q-SF)

**Timepoint [7]**
Conducted at all trial visits - Baseline (week 0), every four weeks after that (week 4, 8, 12, 16, 20, 24) and week 28 (4 weeks post discontinuation).

**Secondary outcome** [8]
Change in Functioning measured by Social Occupational Functioning Scale (SOFAS)

**Timepoint** [8]
Conducted at all trial visits - Baseline (week 0), every four weeks after that (week 4, 8, 12, 16, 20, 24) and week 28 (4 weeks post discontinuation).

**Secondary outcome** [9]
Change in Functioning measured by Range of Impaired Functioning Tool (LIFE-RIFT)

**Timepoint** [9]
Conducted at all trial visits - Baseline (week 0), every four weeks after that (week 4, 8, 12, 16, 20, 24) and week 28 (4 weeks post discontinuation).

**Secondary outcome** [10]
Change in oxidative stress (malondialdehyde) markers

**Timepoint** [10]
Bloods collected from consenting participants at baseline, week 24 and week 28

**Secondary outcome** [11]
Changes in severity of mood symptoms following discontinuation of trial medication, measured using MADRS

**Timepoint** [11]
The post-discontinuation of treatment (week 28) will be analysed both between week 24 and week 28.

**Secondary outcome** [12]
Change in inflammatory (IL-6, TNF-alpha and CRP) markers

**Timepoint** [12]
Bloods collected from consenting participants at baseline, week 24 and week 28

**Secondary outcome** [13]
Change in neuroprotection (Bcl-2) markers

**Timepoint** [13]
Bloods collected from consenting participants at baseline, week 24 and week 28

**Eligibility**

**Key inclusion criteria**
1. Must be required to meet DSM-5 criteria for bipolar disorder I or II, cyclothymic disorder or bipolar disorder not elsewhere classified (NEC),

2. Have a current episode of depressive illness with a MADRS score greater than or equal to 20

3. Have capacity to consent to the study and comply with study procedures

4. Any form of therapy must be stable for the last month

5. Using effective contraception if female, sexually active and of child bearing potential

6. Be able to speak, read, write and understand the English language,

7. Participants will be required to nominate a current treating physician and will not be eligible to enter the study until one is identified.

8. Have the capacity to consent to the study and comply with study procedures,

**Minimum age**
18 Years
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<th>Maximum age</th>
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<tr>
<td>Gender</td>
<td>Both males and females</td>
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<td>Can healthy volunteers participate?</td>
<td>No</td>
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<td>Key exclusion criteria</td>
<td>1. Participants with a known or suspected active systemic medical disorder,</td>
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<td>2. Individuals who are pregnant or lactating (participants will be requested to conduct a urine pregnancy test if sexually active and of child-bearing age),</td>
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<td>3. Participants currently enrolled in any other intervention study will be excluded,</td>
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<td>4. Individuals who are intolerant, allergic to or have had an anaphylactic reaction to any components of the preparation,</td>
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<td>5. Inability to comply with either the requirements of informed consent or the treatment protocol.</td>
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### 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)**
An independent researcher utilising a block design will develop the computer-generated randomisation plan. Trial clinicians will allocate packs sequentially, and bottles are identical so as to conceal treatment allocation and blinding. To facilitate the double-blinding process, the trial medications will be dispensed by an independent pharmacist in identical numbers and capsule forms in sealed containers.

**Methods used to generate the sequence in which subjects will be randomised (sequence generation)**
Permutated block randomisation utilising a block design on a computer-generated randomisation.

**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** | 1/02/2016 |
| **Actual date of first participant enrolment** | |
| **Anticipated date last participant enrolled** | 31/01/2018 |
| **Actual date last participant enrolled** | |
| **Anticipated date of last data collection** | |
| **Actual date of last data collection** | |
| **Target sample size** | 80 |
| **Actual sample size** | |
| **Recruitment status** | Not yet recruiting |
| **Recruitment in Australia** | |
| **Recruitment state(s)** | VIC |
| **Recruitment hospital [1]** | The Melbourne Clinic - Richmond |
| **Recruitment hospital [2]** | Albert Road Clinic - Melbourne |
| **Recruitment postcode(s) [1]** | 3121 - Richmond |
| **Recruitment postcode(s) [2]** | 3004 - Melbourne |

**Funding & Sponsors**

<p>| <strong>Funding source category [1]</strong> | University |
| <strong>Name [1]</strong> | Deakin University, IMPACT SRC Seed Funding Grant |
| <strong>Address [1]</strong> | IMPACT SRC PO BOX 281 Geelong Victoria 3220 |
| <strong>Country [1]</strong> | Australia |
| <strong>Primary sponsor type</strong> | Hospital |
| <strong>Name</strong> | Barwon Health |
| <strong>Address</strong> | Research Ethics, Governance and Integrity (REGI) Unit PO BOX 281 Geelong Victoria 3220 |
| <strong>Country</strong> | Australia |
| <strong>Secondary sponsor category [1]</strong> | None |
| <strong>Name [1]</strong> | |
| <strong>Address [1]</strong> | |
| <strong>Country [1]</strong> | |</p>
<table>
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<tr>
<th>Other collaborator category</th>
<th>University</th>
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<tbody>
<tr>
<td>Name</td>
<td>University of Melbourne</td>
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**Ethics approval**

**Ethics application status**
Approved

**Ethics committee name**
Barwon Health Human Research Ethics Committee

**Ethics committee address**
Research Ethics, Governance and Integrity (REGI) Unit
PO BOX 281
Geelong Victoria 3220

**Ethics committee country**
Australia

**Date submitted for ethics approval**
26/08/2015

**Approval date**
18/11/2015

**Ethics approval number**

**Ethics committee name**
The Melbourne Clinic Research Ethics Committee

**Ethics committee address**
130 Church St
RICHMOND, VIC 3121

**Ethics committee country**
Australia

**Date submitted for ethics approval**
31/07/2015

**Approval date**
26/08/2015

**Ethics approval number**

**Ethics committee name**
Deakin University Human Research Ethics Committee

**Ethics committee address**
Burwood Campus
Postal: 221 Burwood Highway
Burwood Victoria 3125

**Ethics committee country**
Australia

**Date submitted for ethics approval**
02/12/2015

**Approval date**
16/12/2015

**Ethics approval number**
Summary

Brief summary
Aims
The primary aim of this study is to investigate the efficacy of adjunctive mangosteen pericarp 1000mg/day for the treatment of bipolar depression using a 24 Week randomised, placebo controlled trial. The primary outcome measure will be the change in severity of mood symptoms, measured using the Montgomery Asberg Depression Rating Scale (MADRS). Secondary outcomes include global psychopathology, substance use, functioning, quality of life, and safety and tolerability data. A follow-up interview will be conducted 4 weeks posttreatment to determine any outcomes following cessation of the trial agent.

Method
We plan to recruit a total of 80 participants aged 18+years with moderate to severe bipolar depression (having a DSM5 diagnosis of bipolar I or II, cyclothymic disorder or bipolar disorder not elsewhere classified (NEC), determined using the Structured Clinical Interview for DSM Disorders 5 (SCID5) and meeting criteria of a Montgomery Asberg Depression Rating Scale (MADRS) score of greater than or equal to 20.

Participants will attend a screening visit to ascertain suitability and once randomized they will receive a month’s supply of either 1000mg/day of mangosteen or matched placebo to be taken in addition to their treatment as usual. Participants take two capsules per day.

Participants will visit the study site at weeks 4, 8, 12, 16, 20 24 and 28 (4 weeks posttreatment discontinuation) where a battery of validated outcome measures will be administered by trained research staff. Participants will be asked to discuss their symptoms, side effects and any issues the participant would like to raise regarding the trial. Participants will be notified of which arm of the study they took part in and a summary of results at the completion of the study.

Trial website
Trial related presentations / publications
Public notes

Contacts

Principal investigator
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Geelong, Victoria
3220
Country
Australia
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+61 3 4215 3300
Fax
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Email
oliviad@barwonhealth.org.au
Contact person for public queries
Name
Dr Olivia Dean
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<tr>
<td><a href="mailto:oliviad@barwonhealth.org.au">oliviad@barwonhealth.org.au</a></td>
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**Contact person for scientific queries**

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