STUDY PROTOCOL

REVISED Evaluation of comparative efficacy of *Celastrus paniculatus (Jyotishmati)* capsule versus sertraline capsule in the management of *Chittodvega* (generalized anxiety disorder): protocol for a randomized controlled trial [version 3; peer review: 2 approved, 1 approved with reservations]

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Abstract

Background

Generalized anxiety disorder (GAD) *(Chittodvega)* is one among many types of mental disorders explained in Ayurveda. It can be defined as a *Chitta* (mind) + *Udvega* (anxiety)= *Chittodvega*- Anxious status of a mind. *Celastrus paniculatus* also known as *Jyotishmati* stimulates and improves the digestive fire and metabolism at a cellular level (*Jatharagni and Majja dhatwagni).* It can be correlated to GAD. GAD is characterized by feelings of threat, restlessness, irritability, sleep disturbance, and tension, and symptoms such as palpitations, dry mouth, and sweating. It affects women more frequently than men and prevalence rates are high in midlife (prevalence in females over age 35: 10%) and older subjects. In modern medicine the first-line psychological and pharmaceutical treatments are selective serotonin reuptake inhibitors (SSRIs) like sertraline (SNRIs).

Aim and objectives

To evaluate the comparative efficacy of *Jyotishmati* versus sertraline in the management of *Chittodvega.*

Open Peer Review

Approval Status ? ✓ ✓

	1	2	3
version 3 (revision) 28 Oct 2024			
version 2 (revision) 17 Jun 2024		✓ view	✓ view
version 1 11 Dec 2023	? view	? view	

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Any reports and responses or comments on the article can be found at the end of the article.

Methods

In this randomized active controlled double blind equivalence trial a total of 70 patients will be enrolled and divided into two equal groups. Patients between 20–50 years age of either gender having symptoms of *Chittodvega* and a Hamilton anxiety rating (HAM-A) scale score less than 24 (i.e., mild to moderate) will be selected for the study. In Group A, sertraline capsules 25 mg for first 7 days and then dose increased to 50 mg at bedtime for next 53 days and in Group B *Jyotishmati* Capsules 500 mg will be given twice a day after food with water for 60 days.

Result and observation

The patients will be assessed on the HAM-A scale, serum cortisol and WHO Quality of Life on day 0, 30, 60 and 90 and data will be analyzed using paired and unpaired t-tests for continuous variables and chi-square tests for categorical variables to evaluate whether treatments are equivalent.

Trial registration

CTRI No. REF/2023/07/069880 Date – 15/09/2023

Keywords
Chittodvega, Celastrus paniculatus, GAD, HAM-A Scale, Jyotishmati, Medhya, Sertralin

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REVISED **Amendments from Version 2**

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Any further responses from the reviewers can be found at the end of the article

Introduction

Ayurveda, due to its psychosomatic approach considers the mind as an integral part of life. It advocates the integration between the mind, body and soul with holistic approach. In our bodies, there are two different types of mind qualities (*Manas doshas* like *Satva*, *Rajas*, and *Tamas*) and bodily humours like (*Vata, Pitta,* and *Kapha*). Because bodily humours and mind qualities frequently interact with one another,[1] Ayurveda accepts the idea of psychosomatic disorder. Of the three humours, *Vata* (Particularly *Prana, Vyana, and Udana Vata*) is primarily in charge of controlling and stimulating mental activity as well as generating enthusiasm. *Sadhaka*, a subtype of *Pitta*, has a direct connection to how the mind works. It is in charge of intelligence, memory, and cognition, as well as self-worth and enthusiasm.[2] The qualities of *Kapha* (*Tarpaka* and *Bodhaka*, types of *Kapha*) include endurance, strength, knowledge, learning, wisdom, thinking, understanding, comprehensiveness, comprehension ability, equilibrium, enthusiasm etc.[3] Generalized anxiety disorder (GAD) (*Chittodvega*) is referred to as the "anxious status of a mind" and is described as a *Chitta* (mind) + *Udvega* (anxiety).[4] It is referred to as *Raja-tama vikara* in *Charaka vimana* 6 (*Rogaanik vimaana adhyaya*).[5]

The vitiation of mind qualities like *Raja* and *Tama* leads to the development of *Chittodvega.* In Ayurveda *Chittodvega* (anxiety disorders) is described as one of the causes of psychosis (*Unmada)* rather than as a separate disease.[6] One of the minor psychiatric diseases is *chittodvega*; there is no disorientation and the patient can carry out everyday activities without much trouble (i.e neurosis),[7] whereas psychosis (*Unmada*) is a major psychological disorder (impairment of orientation, i.e. psychosis), and neurosis may leads to psychosis, so can be considered as prodromal of psychosis (*Unmada*).[8]

The symptoms of Chittodvega are similar to those of GAD, which are muscle tension, poor concentration, autonomic arousal, feeling "on edge" or restless, and insomnia. GAD manifests as persistent, excessive, and/or exaggerated worry. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) includes the following diagnostic criteria: anxiety and worry that has lasted for at least 6 months, the anxiety is connected with three or more of the following symptoms: 1. Restlessness, tenseness, or apprehension. 2. Being easily exhausted. 3. Difficulty concentrating or going blank, as well as impatience. 4. Muscle tenseness. 5. Sleep deprivation.[9]

WHO estimates that 264 million people globally, or 3.6%, suffer from an anxiety illness. Additionally, anxiety affects 4.6% of females and 2.6% of males worldwide.[10] The following primary categories of anxiety disorders are included in the DSM-5, according to the American Psychiatric Association: acute stress disorder, post-traumatic stress disorder, obsessive compulsive disorder (OCD), GAD, agoraphobia without panic, social phobia (social anxiety disorder), specific phobia, and anxiety disorder not otherwise mentioned.[11]

In modern medicine, GAD management consists of psychotherapy, like cognitive behavioral therapy (CBT) and pharmacological approaches such as cannabis, citalopram, escitalopram, sertraline, duloxetine, and venlafaxine.[12] The first-line psychological and pharmaceutical treatments are CBT and selective serotonin reuptake inhibitors (SSRIs) like sertraline; alternative possibilities include selective norepinephrine reuptake inhibitors (SNRIs). Compared to other anxiolytics, SSRIs deal with depression, which is frequently co-occurring with anxiety and has less adverse effects.[13] The World Federation of Societies of Biological Psychiatry recommends SSRIs, and SNRIs as first-line therapies for GAD. A substantial number of studies demonstrates the effectiveness of sertraline, a well-known SSRI, in treating generalized anxiety disorder. In comparison to an acknowledged gold standard, it provides a reliable baseline for assessing Jyotishmati's efficacy.[14]

One of the most significant medicinal plants in the Celatraceae family is *Celastrus paniculatus*, also known as *Jyotishmati. Jyotishmati* is a combination of the words "enlightens" (Jyoti) and "brain functions" (*mati*), which means "enlightens the psychomotor function." The seed oil (*Jyotishmati taila*) is well renowned for its intellect-promoting (*medhya*) properties. As a brain tonic, it is used to boost intelligence and improve memory.[15] With its pungent and bitter taste and hot potency, *Celastrus paniculatus* (*Jyotishmati*) has an effect on three bodily humours of the body.

It strengthens the ability of grasping and remembering (i.e *Grahana* and *Smarana*) and supports *Sadhak Pitta* (a subtype of pitta).

In *Bhavaprakash Nighantu* and *Raj Nighantu* it is mentioned as intellect promoting (*Medhya*) drug.[16]

Need for the study

One type of anxiety illness, known as generalized anxiety disorder (GAD), is marked by excessive worry and anxiety that the individual with it has trouble controlling. GAD leads to functional disability and a markedly reduced quality of life for the patient.[17] This constituted 25–30% of psychiatric outpatients.[18] International Statistical Classification of Diseases and Related Health Problems ICD 10 enlists anxiety as one of the symptoms. Its prevalence is about 2–4%, along with psychological arousal, muscle tension, sleep problems, and restlessness.[19] Many people live with GAD, which makes it difficult for them to engage in relationships, employment, and other parts of life. Due to the problems of living in a materialistic, competitive society as well as the modern way of life, these types of symptoms and diseases are becoming more and more prevalent day by day.[20]

To reduce the impact of these ongoing health hazards, treatment regimens are always being sought for the management of anxiety and the reduction of stress. Substitutes to SSRIs, benzodiazepines, and other prescribed medication are highly sought after in an effort to reduce exposure to hazardous effects related to these drugs.[21]

The intellect promoting (*Medhya*) medicines described in the Ayurvedic texts have a powerful effect on the mind, have the ability to lower anxiety, and support mental wellness.

Presently there is a need for safer and effective drugs for GAD (*Chittodvega)* and less research have been done in this regard in recent years. *Celastrus paniculatus* is one such herb mentioned having intellect promoting *(Medhya)* property.[22] Comparing Jyotishmati's effectiveness to a recognized pharmaceutical treatment like sertraline makes it possible to assess it directly, which can provide more insightful results than comparing it to other SSRIs that may not have as much evidence specifically for GAD but have a similar mechanism of action.

As a result, this study aims to assess the effectiveness of *Celastrus paniculatus* (*Jyotishmati)* capsules in the treatment of *Chittodvega.*

Aim: Evaluation of comparative efficacy of *Celastrus paniculatus* (*Jyotishmati)* capsules versus sertraline capsules in the management of *Chittodvega* (generalized anxiety disorder).

Objective

Primary

- To evaluate the efficacy of *Jyotishmati* capsules on the Hamilton anxiety rating-scale (HAM-A) and serum cortisol level.
- To evaluate the efficacy of sertraline capsules on the HAM-A Scale and serum cortisol level.
- To compare the efficacy of both on the HAM-A Scale and serum cortisol level.

Secondary

- To evaluate the efficacy of *Jyotishmati* capsules on quality of life.
- To evaluate the efficacy of sertraline capsules on quality of life.
- To compare the efficacy of both on quality of life.

Methods

Ethical considerations

The study will start after clearance from the institutional ethics committee of Mahatma Gandhi Ayurved College Hospital and Research Centre, Salod (H), Wardha. And after CTRI registration (Ref. No. REF/2023/07/069880) Date – 15/09/2023.

The committee will decide on the endpoint and oversee the trial as it progresses. The researcher will assess any adverse event and will report these to the ethics committee. The committee will decide on the endpoint and oversee the trial as it progresses.

Before conducting the trial, written informed consent will be taken from the patient in the local language while explaining every aspect of the study. The researcher will take consent from trial participants.

The personal information of the participants will be collected and kept confidential before, during, and after the trial. Physical data will be stored in a protected storage facility with only access to the researcher. Computerized data will be held in a password-protected hard drive with only access to the researcher.

Study setting

The patients will be selected from Kayachikitsa Out-patient department and In-patient department of the Mahatma Gandhi Ayurved College, Hospital & Research Centre, Salod (H) and peripheral camps, mainly the population of Wardha district including patients of all community, (Maharashtra) India.

A total of 70 patients will be recruited for the study. They will randomly be divided into two groups; Group A – sertraline capsules, and Group B – *Jyotishmati* capsules. All the baseline parameters will be recorded at the start of the study. The patients will undergo treatment for 60 days for both groups. All the parameters will be recorded at the 0^{th}, 30^{th}, 60^{th}, 90^{th} day of the study duration.

Eligibility criteria

Inclusion criteria

- Patients willing to take part in a research study and ready to give written informed consent.
- Patients will be selected according to DSM-V,[23] ICD-10[24] criteria for anxiety disorders.
- A score of less than 24 on HAM-A scale.
- Age group of 20 to 50 years of either sex.

Exclusion criteria

- Currently undertaking CBT with a psychologist.
- GAD *(Chittodvega)* due to drug abuse, a medication or due to general medical state like hyperthyroidism.
- Alcoholic, and self-harm or suicide risk.
- Diagnosed with psychosis, schizophrenia, or bipolar illness currently or in the past.
- Treatment with sertraline for two or more weeks within the previous three months.
- Pregnant and lactating mothers.

Intervention description

- **Group A** – sertraline capsules 25 mg at bedtime for 1 week, then increased to 50 mg with water for the next 53 days.
- **Group B** – *Jyotishmati* capsules containing processed seed powder of Jyotishmati, 500 mg twice a day with water for 60 days.

Preparation

Jyotishmati (Celastrus paniculatus) seed will be pulverized into powdered form which then will be sieved and three bhavanas (trituration) of *Jyotishmati phanta* will be given to it according to *Churnakriya* method mentioned in

Sharangadhara Samhita in Dattatreya Ayurved Rasashala, Salod (H), Wardha.[25] The processed powder will be filled into capsules.

Intervention modification

Any adverse effect during the treatment will be noted and will be informed to the ethical committee. The patients will be taken care of for the adverse effect. If participants want to drop out, this will be mentioned with the reason for discontinuing the treatment.

Outcomes

- **Primary –** Reduction in Hamilton A score and serum cortisol levels,
- **Secondary –** Improvement in quality of life.

Participant timeline

Patients will be treated for 60 days and assessment will be done up to 90 days as mentioned in Figure 1.

Sample size formula using mean difference

$$n1 = n2 = 2\frac{(Z_\alpha + Z_\beta)^2 \sigma^2}{(\delta)^2}$$

$$Z_\alpha = 1.96$$

$$\alpha = \text{Type I error at } 5\% \text{ at both sides two tailed}$$

$$Z_\beta = 1.28 = \text{Power at } 90\%$$

Primary Variable = Hamilton anxiety rating scale (Anxiety Assesment)

Before the treatment (sertraline) Hamilton Anxiety Rating Scale (mean ± sd) = 19.38 ± 4.318, (As per reference article).[26]

After the treatment (sertraline) Hamilton Anxiety Rating Scale at 28 day (mean ± sd) = 15.70 ± 4.550,

Mean difference (δ) = 3.68

Pooled Std. Deviation = (4.318+ 4.550)/2 = 4.434

Sample size N = 31

Considering 10 % drop out = 3

Total sample size required = 31+3 = 34 per group.

For protocol purposes and according to the calculated sample size for each group is = 34

Recruitment

As per sample size calculation, total 34 patients will be recruited which include 31 patients and 3 drop outs. Data collected will be analyzed by using appropriate statistical methods. The patients of *Chittodvega* will be selected from the Kayachikitsa Out-patient department and In-patient department of Mahatma Gandhi Ayurved College, Hospital & Research Centre, Salod (H), and from specialized peripheral camps.

A total of 70 patients will be recruited for the study.

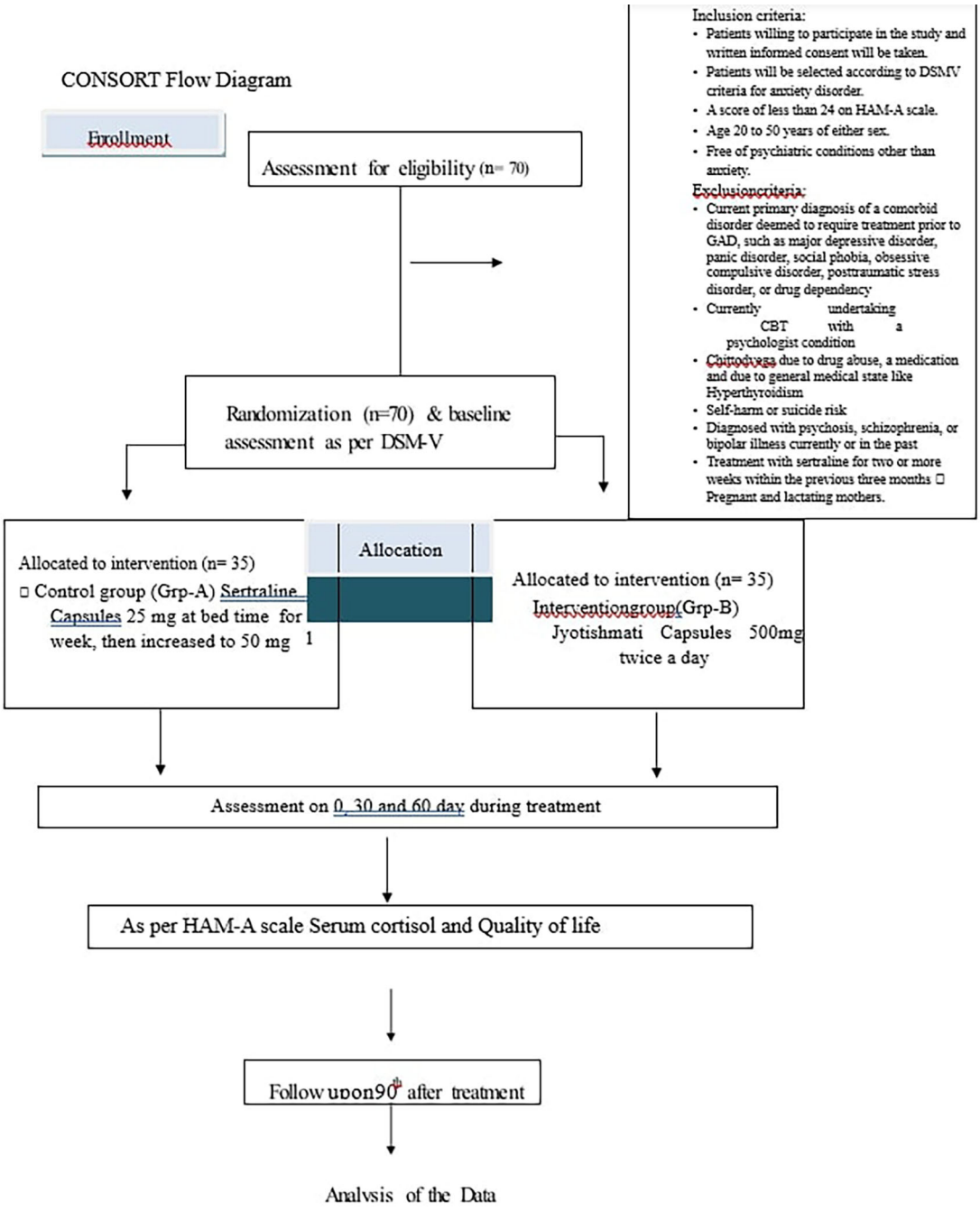

Figure 1. Showing study timeline.

Enrolment and interventions time schedule

The intervention period will be from 0 to 60 days and follow up on the 0^{th}, 30^{th}, 60^{th} and 90^{th} day.

Guidelines

This protocol follows the SPIRIT guidelines.[18]

Case definition

Patients between 20–50 years of age of both gender having symptoms of *Chittodvega* and a HAM-A scale score of less than 24, i.e., mild to moderate cases, will be selected for the study.

Type of study
Interventional study.

Study design
Randomized active controlled double blind equivalence trial.

Investigation – Serum cortisol level.

Diagnostic criteria – DSM-V Diagnostic Criteria for Generalized Anxiety Disorder.[27]

Assessment criteria
1. Hamilton Anxiety Scale – HAM-A assessment will be done on 0, 30, 60 and 90 days by asking the validated questionnaire attached in annexure.[28]

2. Serum cortisol level – will be assessed before and after treatment in our lab.

3. WHO Quality of life – assessment will be done on 0, 30, 60 and 90 days by asking the validated questionnaire attached in annexure.[29]

Assignment of interventions
Allocation sequence generation – Computer-generated random numbers.

Allocation implementation – The researcher or the first author will generate an allocation sequence, enrol participants, and assign participants to intervention.

Sampling procedure
Computer-generated random allocation software in SPSS 7.0 will be used for randomization in order to guarantee the study's objectivity and the validity of the findings. This advanced program uses algorithms to create a random sequence that is then employed in an entirely unpredictable way to place people in the treatment or control groups. With this approach, selection bias is removed, and the study's double-blind design is preserved because neither the subjects nor the researchers may affect the group assignments. Clinical trials typically employ SPSS 7.0 for randomization, which guarantees unbiased patient assignment and preserves the integrity of the investigation.

Concealment of allocation
A third person will do coding to allocate subjects in sequentially numbered, opaque, sealed envelopes in groups A or B (SNOSE Scheme) to avoid bias in the study.

Blinding – Randomized active controlled double blind equivalence trial, i.e., A robust double-blind methodology will be used in the study to ensure the accuracy of the findings. Randomization will be accomplished by enclosing the trial medicine (*Jyotishmati*) and the control drug (Sertraline) in uniformly sized and identically appearing capsules.

This methodological design will eliminate bias and maintain the study's blinding throughout the trial time by guaranteeing that neither the participants nor the healthcare professionals know the allocation of the interventions.

Establishing a thorough framework of this kind is essential to verifying the relative effectiveness of the treatments being studied.

Data collection plan
Data will be assessed according to HAM-A Scale, WHO Quality of life, on 0^{th}, 30^{th}, 60^{th} & 90^{th} day and serum cortisol at baseline and after completion of treatment. See Table 1.

Drug collection/authentication
The raw material for the drug will be purchased from an authentic shop from Nagpur (Wagh brothers) and will be identified by the department of *Dravyaguna* and *Rasashastra* of M.G.A.C.H. and RC, Salod, Wardha.

Data analysis
After the study, the data will be analyzed according to a suitable statistical test.

Table 1. Plan for collection of data.

Group	Sample size	Intervention	Dose and frequency	Anupana	Duration	Follow up
A	35	Sertraline Capsule	25 mg at bed time for 1 week, then increased to 50 mg	With water	60 days	Day 0^{th}, 30^{th}, 60^{th}, 90^{th}
B	35	*Jyotishmati* Capsule	500 mg twice a day after food	With water	60 days	Day 0^{th}, 30^{th}, 60^{th}, 90^{th}

The collected data will be entered in the software SPSS version 22. Man-Whitney and Wilcoxon tests will be used if the distribution of data was not normal. A chi squared test will be used to compare the qualitative variables. Independent t-test will be used to compare the mean of the two groups in the normal distribution of data, and for comparison before and after data, the paired t-test will be used.

Study status
Drug preparation is in process.

Discussion
The contemporary clinical diagnosis of Generalized Anxiety Disorder (GAD) closely resembles the Ayurvedic concept of chittodvega, an anxious mental condition.[30] Persistent concern and anxiety are characteristics of Generalized Anxiety Disorder (GAD), which frequently presents with somatic symptoms such insomnia and tense muscles.[31] GAD is a common mental condition in the general society as a whole with a prevalence of about 5%. Women are twice as likely as men to have this condition.[32] Medication such as selective serotonin reuptake or serotonin-norepinephrine reuptake inhibitors are the first-line treatments[33] but long-term use can have negative side effects such nausea, trouble sleeping, changes in appetite, dry mouth, headaches, and sexual dysfunction.[34] In contrast, Ayurveda states that mental disorders (*manas rogas)* is where mind promoting (*Medhya*) medicines are used. The seed oil and fruit of *Celastrus paniculatus* (*Jyotishmati*) are often used for their tranquillizing, sedative, anxiolytic, and other properties. The Ayurvedic application is primarily for its Medhya (brain tonic) activity. It can be used as a brain tonic to enhance intelligence and memory. Its *Deepana* (stimulating digestion) property help in improving deranged digestive fire (*Agni*) and thereby balancing bodily as well as mental humours (*Sharir* and *Manas dosha*).[35] With its cognitive-enhancing (*Medhya*) and digestive-stimulating (*Deepana*) qualities, *Jyotishmati* (*Celastrus paniculatus*) provides a comprehensive approach to treating GAD. The purpose of this study is to establish an Ayurvedic intervention with fewer side effects by comparing its efficacy with sertraline. To prove the efficacy of *Jyotishmati* multicentric study can be conducted. If it is found to be effective in reducing symptoms then it can be easily used in clinical practice.

Data monitoring: formal committee.

Dissemination
This protocol will be further published as a thesis to disseminate the study for GAD (*Chittodvega*). The study protocol provides a detailed overview of the study design, methodology, data collection procedures, data analysis plan, and ethical considerations. By disseminating this protocol, we hope to advance knowledge in the field and facilitate future research by posters, papers and publications.

Data availability
Reporting guidelines
Zenodo: SPIRIT checklist for 'Evaluation of comparative efficacy of *Celastrus paniculatus (Jyotishmati)* capsule versus sertraline capsule in the management Of *Chittodvega* (generalized anxiety disorder) – protocol for a randomized controlled trial'. https://doi.org/10.5281/zenodo.8125916.[36]

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Open Peer Review

Current Peer Review Status: ? ✓ ✓

Version 2

Reviewer Report 05 August 2024

https://doi.org/10.5256/f1000research.167827.r306252

✓ **Danish Javed**
[1] All India Institute of Medical Sciences, Bhopal, India
[2] All India Institute of Medical Sciences, Bhopal, India

Introduction: I have thoroughly reviewed the article. The review was conducted with a focus on the relevance, accuracy, and overall contribution of the content to the field of Ayurveda.
Content Analysis:

1. **Relevance:**
   The article is highly relevant to the current trends and practices in Ayurveda. It addresses significant issues and presents well-researched information that aligns with contemporary medical knowledge and practices.
2. **Accuracy:**
   The information presented in the article is accurate and supported by credible references. The data and facts have been cross-verified with existing literature, ensuring the reliability of the content.
3. **Clarity and Coherence:**
   The article is well-written, with clear and coherent language. The flow of information is logical, making it easy for the reader to follow and understand the concepts discussed.
4. **Contribution to the Field:**
   This article makes a valuable contribution to the field of Ayurveda. It provides new insights and practical approaches that can be beneficial for practitioners and researchers alike.
5. **Methodology:**
   The research methodology adopted in the article is robust and appropriate for the study. The methods used are well-explained and justified, adding to the credibility of the findings.
6. **References and Citations:**
   The article includes a comprehensive list of references and citations from reputable sources. This enhances the article's scholarly value and allows readers to further explore the topics discussed.

Based on my thorough review, I have found the article to be suitable for index. It meets the high standards required for scholarly work in the field of Ayurveda. The content is relevant, accurate, and contributes significantly to the existing body of knowledge. Therefore, I recommend this article for indexing without any reservations.

Is the rationale for, and objectives of, the study clearly described?
Yes

Is the study design appropriate for the research question?
Yes

Are sufficient details of the methods provided to allow replication by others?
Yes

Are the datasets clearly presented in a useable and accessible format?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Ayurveda

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 16 July 2024

https://doi.org/10.5256/f1000research.167827.r291859

Punam Khobarkar
[1] Kayachikitsa, All India Institute of Ayurveda, New Delhi, India
[2] Kayachikitsa, All India Institute of Ayurveda, New Delhi, India

Dear Authors
You have addressed the previous suggestions effectively. The introduction is now clearer, the methodology is well-detailed, and the discussion is more comprehensive
The manuscript has been significantly improved in terms of clarity, consistency, and comprehensiveness. Therefore, I recommend the acceptance of this manuscript for indexing.

Is the rationale for, and objectives of, the study clearly described?
Yes

Is the study design appropriate for the research question?
Yes

Are sufficient details of the methods provided to allow replication by others?
Yes

Are the datasets clearly presented in a useable and accessible format?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: ayurveda cardiology, diabetes, insomnia, herbsl medicine, ayurveda

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 06 June 2024

https://doi.org/10.5256/f1000research.152749.r286303

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Punam Khobarkar
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1.Title:
It is precise and informative, giving a clear indication of the research topic.
2.Abstract:
The abstract succinctly summarizes the background, objectives, methodology, and anticipated outcomes. However, it could benefit from a more detailed description of the study design, including specific statistical methods and anticipated sample size, to better inform the reader about the study's robustness and scope.
3.Introduction
The introduction provides a comprehensive overview of GAD, detailing its prevalence, symptoms, and the limitations of current pharmacological treatments, such as side effects and dependency issues. The rationale for investigating Celastrus paniculatus (Jyotishmati) is well-grounded, citing its historical use in Ayurvedic medicine and previous studies suggesting its anxiolytic properties.
4.Literature Review:
The introduction could be strengthened by including a more exhaustive review of contemporary studies and meta-analyses on the efficacy of Jyotishmati and Sertraline, thereby situating the current research within the broader scientific context.
5.Aims and Objectives
The study's aims and objectives are clearly articulated. The primary objective is to compare the efficacy of Jyotishmati and Sertraline in reducing anxiety symptoms as measured by the Hamilton Anxiety Rating Scale (HAM-A). Secondary objectives include assessing changes in serum cortisol

levels and evaluating quality of life improvements.

6.Methods

a.Study Design:

The study employs a randomized clinical equivalence trial design, which is appropriate for comparing the effectiveness of two interventions. However, further elaboration on the randomization process, blinding procedures (if any), and controls to mitigate bias would enhance the methodology's rigor.

b.Participants:

Inclusion and exclusion criteria are well-defined, ensuring a relevant study population. Yet, additional details on the demographic characteristics of the target population would be beneficial.

c.Intervention:

The interventions are described with adequate detail, specifying the dosage and duration of treatment for both Jyotishmati and Sertraline. However, the manuscript should provide more information on the standardization and quality control of the Jyotishmati capsules used.

d.Outcome Measures:

Primary and secondary outcome measures are appropriate and clearly defined. The choice of HAM-A for primary outcome and serum cortisol levels, along with quality of life assessments, as secondary outcomes are justified. Including information on the validity and reliability of these measures within the study context would be advantageous.

e.Data Collection and Analysis:

The data collection methods are thorough, but the statistical analysis section is underdeveloped. A more detailed plan, including sample size calculation, power analysis, handling of missing data, and specific statistical tests to be used, would enhance the study’s scientific rigor.

f. Ethical Considerations

The manuscript adequately addresses ethical considerations, mentioning informed consent, confidentiality, and the approval by an institutional ethics committee. This reflects adherence to ethical standards in clinical research.

7.Expected Outcomes:

While the manuscript outlines expected outcomes, it should also discuss potential challenges and limitations in greater detail, such as sample size constraints, adherence issues, and potential biases.

8.Discussion:

The discussion should provide a balanced view of the study's potential impact on clinical practice and future research. It should also elaborate on how the findings could influence the treatment paradigm for GAD, especially in contexts where traditional and alternative medicine practices intersect.

9.**Strengths:**

Comprehensive background and rationale for the study.
Clearly defined aims and objectives.
Detailed description of interventions and outcome measures.
Ethical considerations are well addressed.

10.Weaknesses:

The abstract could be more detailed regarding the study design and statistical methods.
The methodology section lacks comprehensive details on randomization, blinding, and statistical analysis.
The literature review in the introduction could be more exhaustive.
The discussion does not sufficiently address potential limitations and the broader impact of the study findings.

The manuscript presents a well-conceived study protocol to compare the efficacy of Jyotishmati and Sertraline in managing GAD. Addressing the noted weaknesses, particularly in the methodological and analytical details, will enhance the study's scientific validity and reliability. This research has the potential to provide significant insights into alternative treatments for GAD, contributing to the broader field of integrative medicine.

Is the rationale for, and objectives of, the study clearly described?

Yes

Is the study design appropriate for the research question?

Yes

Are sufficient details of the methods provided to allow replication by others?

No

Are the datasets clearly presented in a useable and accessible format?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: ayurveda cardiology, diabetes, insomnia, herbsl medicine, ayurveda

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 07 Jun 2024

Reeya Gamne

THANKS FOR THE REVIEW.

Competing Interests: No competing interests were disclosed.

Reviewer Report 05 June 2024

https://doi.org/10.5256/f1000research.152749.r281408

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Dr Savitha H P

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1. Evaluation of comparative efficacy of ***Jyotishmati (Celastrus paniculatus)*** capsule versus sertraline capsule in the management of *Chittodvega* (generalized anxiety disorder) - **A Proposed** protocol for a randomized controlled trial
2. Introduction and need for study - need to include explanation behind comparing with sertraline as control as there are many other SSRIs.
3. Introduction is very lengthy and it needs to be crisp and clear
4. Repetitions in inclusion and exclusion criteria
5. Justify about the dose of both control and study drugs
6. There is difference in the prescription of control drug in abstract and study plan which needs to be corrected
7. Inclusion of a modern psychiatrist in the study enhances the quality of proposal
7. Discussion has to be crisp

Is the rationale for, and objectives of, the study clearly described?
Partly

Is the study design appropriate for the research question?
Yes

Are sufficient details of the methods provided to allow replication by others?
Partly

Are the datasets clearly presented in a useable and accessible format?
Not applicable

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Clinical research, Survey study, Literary research

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 05 Jun 2024

Reeya Gamne

Thanks for the review.

Competing Interests: No competing interests were disclosed.