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A single-arm clinical trial to evaluate the safety and efficacy of Mentacalm tablets in reducing stress and anxiety in adults

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Abstract

Introduction: The prevalence of stress and anxiety has significantly increased in recent years, with approximately one-third of the population reporting symptoms. Mentacalm tablets contain ingredients that have the potential to calm the mind, reduce brain hyperactivity, and improve mood and anxiety.

Materials and Methods: This was a single-arm, open-label clinical trial of Mentacalm tablets for reducing stress and anxiety in adults. The study lasted 68 days, and each participant was administered one Mentacalm tablet twice a day after food, orally. The research objectives were to evaluate changes in the Perceived Stress Scale (PSS) score, Serum cortisol levels, Depression Anxiety Stress Scale (DASS), Hamilton Anxiety Rating Scale (HAM-A) score, Penn State Worry Questionnaire (PSWQ) score, Profile of Mood State (POMS) questionnaire score, and World Health Organization Quality of Life Questionnaire (WHOQOL-BREF) score were done at screening, day 30 and day 60. Changes in Modified Sleep Regularity and Medication Withdrawal Questionnaire (MSRMWQ) score were assessed after stopping treatment for 1 week (day 68).

Results: Administration of the Mentacalm tablets yielded significant positive effects as demonstrated by the reduction in stress-related symptoms and markers indicated by cortisol levels, PSS score, DASS score, HAM-A score, PSWQ score, Bad Mood- POMS score, and increase in Good Mood- POMS score, MSRMWQ score and WHOQOL- BREF score.

Conclusion: Research suggests that Mentacalm tablets are a promising supplement for managing stress and anxiety in adults, enhancing mental health, mood, and overall quality of life.

Keywords: Mentacalm Tablet; Perceived Stress; Safety; Efficacy; Stress; Anxiety

1. Introduction

Stress constitutes a multifaceted physiological response to a perceived challenge (stressor), characterized by emotional dysregulation (anxiety, depression, mood swings), sleep disturbances, and alterations in physical, cognitive, and behavioral domains. Stress can be defined as a state of worry or mental tension caused by a difficult situation and is a natural human response that prompts us to address challenges and threats in our lives. Everyone experiences stress to some degree. The way we respond to stress, however, makes a big difference to our overall well-being. -WHO (1).

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The International Classification of Diseases (ICD) by the World Health Organization (WHO) and the Diagnostic and Statistical Manual of Mental Disorders (DSM) by the American Psychiatric Association (APA) serve as foundational nosological frameworks for mental health, facilitating standardized diagnosis through common terminology and criteria. (2). Emotion regulation refers to the dynamic processes by which individuals influence the intensity, duration, and quality of their emotional experiences and related physiological responses, encompassing both basic emotions and complex affective states in response to life challenges. (3). Various psychosocial stressors (illness, loss, abuse, etc.) and unhealthy lifestyle factors (substance use, inadequate sleep, etc.) can act as precipitants or exacerbating factors for psychiatric conditions.

In response to stress, a coordinated physiological response ensues. The sympathetic-adreno-medullary (SAM) axis stimulates catecholamine release from the adrenal medulla, while the hypothalamic-pituitary-adrenal (HPA) axis triggers cortisol secretion. Upon stressor resolution, the parasympathetic nervous system facilitates homeostasis restoration (4). Cortisol exerts a multifaceted physiological influence, encompassing catecholamine release, suppression of insulin and the immune response, mobilization of energy stores via gluconeogenesis and glycogenolysis, and a delay in wound healing (5). Stress may impact the gut-brain axis, potentially causing functional GI disorders (IBS, inflammation, ulcers) (6). Heidt et al. linked stress to elevated circulating inflammatory leukocytes via direct stimulation of hematopoietic stem cell proliferation (7). Chronic stress poses a significant threat beyond its psychological toll. It may directly promote tumorigenesis (cancer development) through uncontrolled cell proliferation induced by stress signaling. Furthermore, the cascading effects of chronic stress, anxiety, and mood disorders can disrupt metabolic processes, lead to cognitive decline, and exacerbate existing mental health issues. These physiological and psychological consequences can manifest as reduced focus, hindered work performance, and a general decline in quality of life (8,9,10).

The global prevalence of anxiety disorders sits around 4%, yet a significant treatment gap exists, with only a limited number receiving proper evidence-based psychological interventions (8, 11). A cross-sectional investigation utilizing the Depression, Anxiety and Stress Scale-21 (DASS-21) assessed psychological distress in a college student cohort (n=1074). The study revealed a moderate prevalence of depressive symptomatology (18.4%), anxiety symptoms (23.6%), and stress symptoms (34.5%) within the study population (12).

Subclinical stress and anxiety disorders often remain undetected during routine medical evaluations. However, timely intervention becomes crucial once these conditions progress to clinically significant emotional distress or functional impairment in daily life.

Stress management interventions encompass a diverse range of modalities tailored to individual needs and preferences. Techniques incorporating mind-body practices, such as Tai Chi and yoga, alongside various forms of exercise, are frequently cited for their efficacy in reducing stress levels (13). A study by Ramos-Sanchez et al. demonstrated a statistically significant, yet modest, anxiolytic effect (reduction in anxiety symptoms) of exercise compared to a control group in individuals diagnosed with anxiety disorders (14).

CBT (cognitive behavioral therapy) has established empirical support as an efficacious treatment for prevalent mental health disorders like depression and anxiety, often demonstrating equivalence or superiority to alternative modalities (15). A clinical trial further confirms its effectiveness in the CPdC (chemotherapy-induced psychiatric comorbidity) population, demonstrating reductions in depressive, anxiety, and stress symptoms (16). Notably, CBT also significantly lessened death anxiety, improved overall quality of life, and enhanced self-esteem.

SSRIs (selective serotonin reuptake inhibitors), SNRIs (serotonin-norepinephrine reuptake inhibitors), tricyclic antidepressants, and benzodiazepines are first-line pharmacotherapies for depression and anxiety disorders. However, these medications may be associated with adverse effects including nausea, fatigue, appetite dysregulation, sexual dysfunction, and bowel disturbances (17). Notably, SSRIs and SNRIs can transiently exacerbate anxiety during treatment initiation, potentially compromising adherence (17). Additionally, chronic benzodiazepine use has been linked to a potential risk of dementia (18). These limitations of conventional pharmacotherapies (SSRIs, SNRIs, tricyclics, benzodiazepines) highlight the need for safer and more readily integrated interventions within contemporary lifestyles (17, 18). Given the bidirectional relationship between sleep disturbances and stress/anxiety disorders, exploring natural remedies for insomnia presents a promising avenue for potentially mitigating both conditions concurrently.

The purpose of this study was to assess safety and efficacy of Brahmi, Shankhpushpi, Aswagandha, Jyotishmati, Arjuna, Vacha, and Tagar extract in management of stress and anxiety in adults.

2. Materials and methods

2.1. Study Design

A single-arm, open-labelled clinical study was conducted on 35 individuals. Each subject is advised to take one Metacalm tablet two times a day after food orally for 60 days. Subjects were recruited at the study centre i.e. Lokmanya Medical Research Centre & Hospital, Pune, India. The study was approved by the Institutional Ethics Committee (IEC) Lokmanya Medical Research Centre. The trial was registered on the Clinical Trial Registry of India (CTRI) website **(CTRI/2024/09/073264 [Registered on: 03/09/2024])**. The product used in this study, the Mentacalm Tablet, is formulated from the compositions of the investigational products depicted in Table 1.

Table 1 Investigational product and standard of care product composition

Sr. No.	Name of the Ingredient	Scientific Name
1	Brahmi	*Bacopa monnieri*
2	Shankhpushpi	*Convolvulus prostratus*
3	Ashwagandha	*Withania somnifera*
4	Jyotishmati	*Celastrus paniculatus*
5	Vacha	*Acorus calamus*
6	Arjuna	*Terminalia arjuna*
7	Tagar	*Valeriana wallichii*

2.2. Inclusion criteria

Male and female participants aged 21-50 years (both inclusive) were included in the study. Those participants suffering from self-reported mild to moderate stress on the PSS scale score of ≤26, had no severe anxiety and depression i.e, generalized anxiety disorder (GAD) score of ≤10 and Patients' health questionnaire-9 (PHQ-9) score ≤14 and no history of substance use disorder other than the use of nicotine and recreational use of alcohol (not having used for the last 14 days and consent not to use the same during the period of the trial) were included in the study. A female participant who was of reproductive potential, had a negative pregnancy test, and agreed to use contraception throughout the study period was included. Participants willing to limit caffeine consumption while in the study and willing to participate in clinical trials and who have read understood and signed the informed consent form were included in the study.

2.3. Exclusion criteria

Participants who could not perform any of the assessments required for endpoint analysis, and Participants who showed signs of dementia, such as those caused by Alzheimer's Disease, acquired immunodeficiency syndrome (AIDS), Creutzfeldt-Jakob disease (CJD), Lewy Bodies dementia (LBD), Cerebrovascular dementia (CVD), Progressive Supranuclear Palsy (PSP), multiple cerebral infarctions, or normal pressure hydrocephalus (NPH) were excluded. Participants currently using any nutraceutical, allopathic, or ayurvedic supplement for stress management, and participants having any other neurodegenerative diseases or seizure disorder were excluded. Participants having known hypersensitivity to investigational products, and a history of malignancy diagnosed within the past 5 years or currently diagnosed with malignancy were excluded. Participants having a history of substance abuse, drugs, heavy use of alcohol, and/or smoking within the last 5 years, and sitting or resting systolic blood pressure >180 mm Hg or diastolic blood pressure >110 mm Hg at screening were excluded from the study. Pregnant or lactating women, as well as women of childbearing potential who were not using contraception or intending to conceive during the study, were also excluded. Participants with serious illness or any other condition that, in the opinion of the investigator, may compromise the safety or compliance of the participant or can preclude the successful completion of the study were excluded.

2.4. Sample Size

Thirty - five subjects were planned to enroll in the study based on the clinical and research judgment of the investigators. All subjects received one Mentacalm tablet two times in a day after food orally for 60 days. Overall, 34 subjects completed the study with one participant drop-out due to loss of follow-up.

2.5. Methodology

This was a single-arm, open-labelled clinical trial of Mentacalm tablets in reducing stress and anxiety in adults. The study duration was 68 days. Each participant participated in the study for approximately 68 days and was administered one Mentacalm tablet two times in a day after food orally. Assessment of Perceived Stress Scale (PSS) score, Serum cortisol levels, Depression Anxiety Stress Scale (DASS), Hamilton Anxiety Rating Scale (HAM-A) score, Penn State Worry Questionnaire (PSWQ) score, Profile of Mood State (POMS) questionnaire score and World Health Organization Quality of Life Questionnaire (WHOQOL-BREF) score were done at screening, day 30 and day 60. Changes in Modified Sleep Regularity and Medication Withdrawal Questionnaire (MSRMWQ) score were assessed after stopping treatment for 1 week (day 68).

Assessment of changes in vital sign parameters was done at screening, baseline, Day 30, and Day 60. Physical examination (BP, pulse, and weight) and assessment of changes in complete blood count, liver function test, and kidney function test were assessed at screening and Day 60. Treatment compliance and tolerability were assessed at Day 30 and Day 60.

Safety of the investigational product in terms of adverse events (AEs), and serious adverse events (SAEs) was assessed from baseline, Day 30, and Day 60.

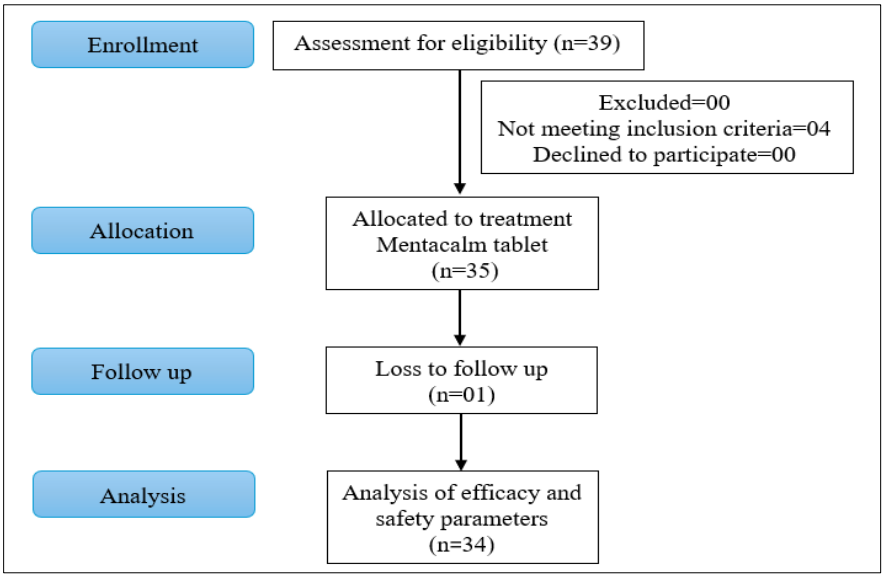

Figure 1 CONSORT diagram for the study

2.6. Statistical Analysis

The data's normality was assessed using the Kolmogorov-Smirnov test. In this study, weight, height, BMI, and modified sleep regularity score were represented in mean ± SD. PSS score, cortisol levels, HAM-A score, PSWQ score, POMS score, and MSRMWQ score were analyzed within the group by using the Student T test dependent test. DASS score and WHOQOL-BREF score were analyzed using the Student T dependent test and Wilcoxon Signed-Rank test for within-group analysis. The medication withdrawal questionnaire score was represented as mean ± S.D and number of participants.

3. Results

3.1. Demographic characteristics and lifestyle habits

The demographic data of the study population comprising 34 participants (24 females and 10 males) were analyzed. The following Table 2 presents demographic characteristics. Participants ranged in age from 21 to 50 years, with an average age of 41.82 years. Out of 34 participants, one participant was an occasional alcohol consumer while 31 participants were caffeinated drinks consumers. No participant reported as a smoker. Participants exhibited mild depression (PHQ-9 mean score: 5.35 ± 0.98) and mild anxiety (GAD-7 mean score: 5.47 ± 1.40) at screening. Given these, they were deemed eligible for inclusion in the study. Only four participants had concomitant diseases, including two

participants with diabetes mellitus, one participant with hypertension, and one participant with hypothyroidism. Anthropometric parameters such as weight, height, and BMI are represented in (Table 2).

Table 2 Assessment of demographic characteristics and anthropometric parameters

Demographic characteristics and anthropometric parameters				
Parameters	**Observations**			
Gender Distribution	**Female (n=24)**		**Male (n=10)**	
Age (years)	41.58±7.13		42.4±6.70	
Visits	Screening	Baseline	Day 30	Day 60
Weight (kg)	58.62 ± 10.46	58.62±10.46	58.59±10.47	58.82±10.34
Body Mass Index (BMI) (Kg/m^2)	23.46 ± 4.07	23.46 ±4.07	23.44±4.05	23.53±3.92

Data is represented as Mean ± S.D.

3.2. Assessment of Perceived Stress Scale (PSS) score

The PSS is a widely used self-report measure designed to assess the degree to which individuals perceive life events as stressful. PSS scores ranging from 0-13, 14-26, and 27-40 would be considered low stress, moderate stress, and high perceived stress respectively.

At screening, the participants receiving the Mentacalm tablet had moderate stress with a PSS score of 19.74 ± 3.16. The participants exhibited a statistically significant reduction in PSS scores i.e. 21.16% and 32.04% (figure 2) by Day 30 and Day 60 respectively, compared to screening with a shift of score toward low stress by Day 60. This substantial reduction suggests the efficacy of the Mentacalm tablet in mitigating stress in adults (Table 3).

Table 3 Assessment of parameters

Parameter	**Screening**	**Day 30**	**Day 60**
Assessment of PSS score			
Total PSS Score	19.74 ± 3.16	15.56 ± 3.96	13.41 ± 3.54
Mean Difference	-	4.18 ± 4.62	6.32 ± 1.63
Percent change (%)	-	21.16	32.04
P value	-	<0.001	<0.001
Assessment of HAM-A score			
Total HAM-A score	19.94 ±1.97	12.15 ±1.86	11.18 ±1.85
Mean Difference	-	7.79 ±2.67	8.76 ±2.73
Percent change (%)	-	39.09	43.95
P value	-	<0.001	<0.001

Data was represented as Mean ± S.D (percent change). Data was analyzed using the Student T-dependent test for within-group analysis.

3.3. Assessment of Hamilton Anxiety Rating Scale (HAM-A) score

The HAM-A is a widely used clinical tool designed to quantify the severity of anxiety symptoms. Each item is scored on a scale of 0 (not present) to 4 (severe), with a total score range of 0–56, where scores below 17 are considered mild, 18-24 mild to moderate, and 25-30 moderate to severe anxiety. At screening, the participants receiving the Mentacalm tablet had mild to moderate anxiety with a HAM-A score of 19.94 ±1.97. A statistically significant and consistent reduction in total HAM-A score i.e. 39.09% and 43.95% (figure 3) was observed in participants receiving Mentacalm tablets by Day 30 and Day 60 respectively. This substantial reduction, shifting the mean HAM-A score toward mild anxiety by Day 30 and Day 60 suggests the efficacy of the Mentacalm tablet in mitigating anxiety in adults (Table 3).

3.4. Assessment of cortisol levels

Cortisol, often referred to as the "stress hormone", plays a significant role in the body's response to stress, helping regulate various bodily functions. While no statistically significant difference was observed by Day 30, a statistically significant reduction in cortisol levels (32.82%) (figure 4) was observed in participants receiving Mentacalm tablets by Day 60 compared to screening as shown in (figure 4). This substantial reduction of cortisol levels by Day 60, suggests the efficacy of the Mentacalm tablet in mitigating stress and anxiety in adults (Table 4).

Table 4 Assessment of cortisol levels

Parameter	Screening	Day 30	Day 60	Reference Range
Total Serum Cortisol Level	108.65±44.16	103.81±33.37	72.99±37.41	57.2-194.2 ng/mL
Mean Difference	-	4.84±31.13	35.65±40.41	
Percent change (%)	-	4.45	32.82	
P value	-	0.371	<0.001	

Data was represented as Mean ± S.D (percent change). Data analyzed using the Student T-dependent test for within-group analysis.

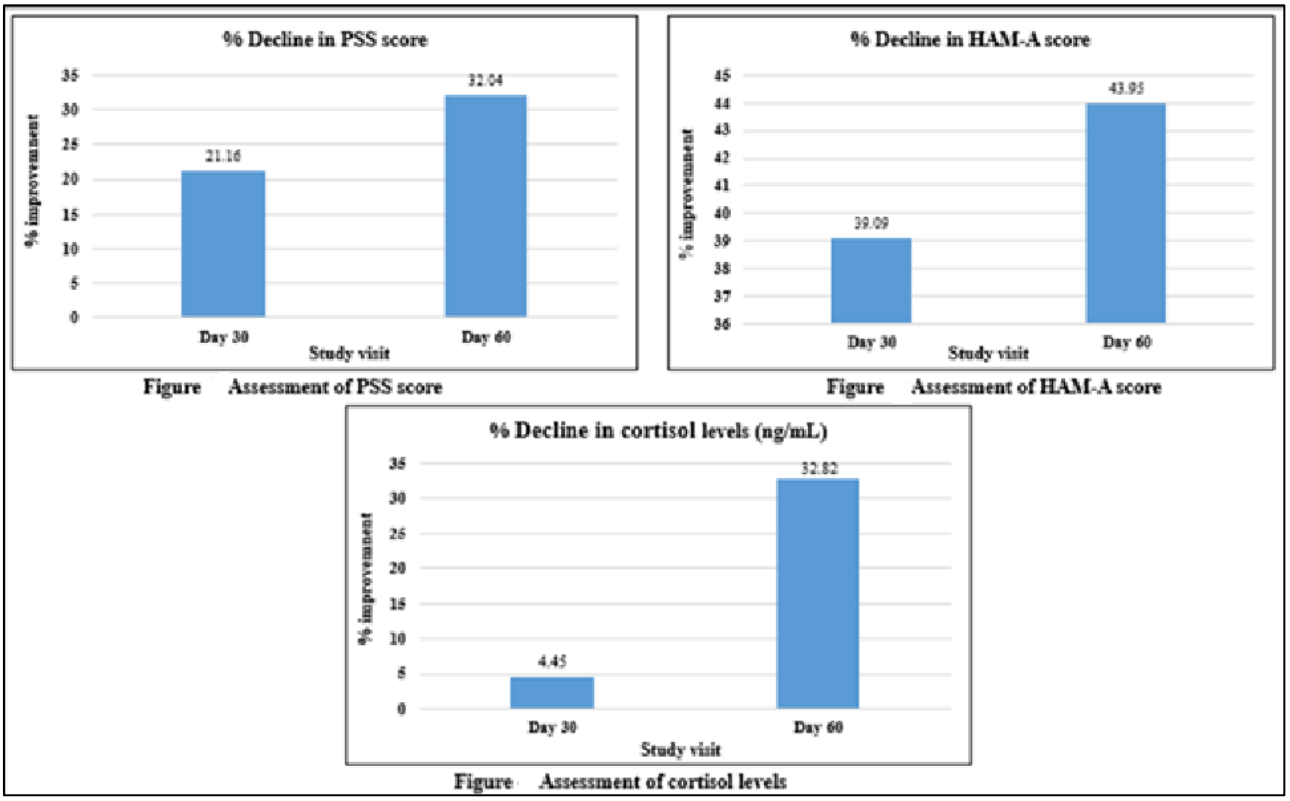

Figure 2 Assessment of cortisol levels

3.5. Assessment of Depression Anxiety Stress Scale (DASS) score

The Depression, Anxiety, and Stress Scale - 21 Items (DASS-21) is a set of three self-report scales designed to measure the emotional states of depression, anxiety, and stress. A statistically significant and consistent reduction in total DASS score i.e. 42.47% and 73.89% was observed in participants receiving Mentacalm tablets by Day 30 and Day 60 respectively. This gradual reduction in total DASS score suggests the efficacy of the Mentacalm tablet in mitigating depression, anxiety, and stress in adults.

Depression scores ranging from 0-9, 10-13, 14-20, 21-27, and more than 28 would be considered normal, mild, moderate, severe, and extremely severe depression respectively. Statistically significant reduction of 46.46% and 76.65% was observed at Day 30, Day 60 as compared to a screening where participants had a score of 12.47 ±2.40

suggesting mild depression which gets reduced to no depression, suggests the efficacy of the Mentacalm tablet in mitigating depression in adults.

Anxiety scores ranging from 0-7, 8-9, 10-14, 15-19, and more than 20 would be considered normal, mild, moderate, severe, and extremely severe anxiety respectively. At screening, the participants had moderate anxiety with an Anxiety score of 11.35 ± 2.59. The participants exhibited a statistically significant reduction in Anxiety scores i.e. 45.60% and 73.83% by Day 30 and Day 60 respectively, suggesting the efficacy of the Mentacalm tablet in mitigating anxiety in adults.

Stress scores ranging from 0-14, 15-18, 19-25, 26-33, and more than 34 would be considered normal, mild, moderate, severe, and extremely severe stress respectively. At screening, the participants had mild stress with a Stress score of 16.71 ± 2.33. The participants exhibited a statistically significant reduction in Stress score i.e. 36.80% and 71.48% by Day 30 and Day 60 respectively, compared to screening. This substantial reduction, shifting the mean Stress score toward the normal stress category by Day 60, suggests the efficacy of the Mentacalm tablet in mitigating stress in adults (Table 5).

Table 5 Assessment of DASS score (Total DASS score, Anxiety score, Depression score, and Stress score)

Parameters	Screening	Day 30	Day 60
Total DASS score			
Total DASS Score	40.44 ±4.54	23.26 ±4.45	10.56 ±3.30
Mean Difference	-	17.18 ±2.14	29.88 ±3.12
Percent change (%)	-	42.47	73.89
P value	-	<0.001	<0.001
Depression			
Depression score	12.47 ±2.40	6.68 ±2.01	2.91 ±1.03
Mean Difference	-	5.79±1.12	9.56 ±1.81
Percent change (%)	-	46.46	76.65
P value	-	<0.001	<0.001
Anxiety			
Anxiety score	11.35 ±2.59	6.18 ±2.38	2.97 ±1.31
Mean Difference	-	5.18 ±1.06	8.38 ±1.74
Percent change (%)	-	45.60	73.83
P value	-	<0.001	<0.001
Stress			
Stress score	16.71 ±2.33	10.56 ±2.09	4.76 ±2.31
Mean Difference	-	6.15 ±1.13	11.94 ±2.27
Percent change (%)	-	36.80	71.48
P value	-	<0.001	<0.001

Data was represented as Mean ± S.D (percent change). Data was analyzed using Student T-dependent test and Wilcoxon Signed-Rank Test for within-group analysis.

3.6. Assessment of Profile of Mood State (POMS) questionnaire score

The POMS is a self-report questionnaire used to assess six distinct mood dimensions: tension-anxiety, anger-hostility, vigor-activity, fatigue-inertia, depression-dejection, and confusion-bewilderment.

Total POMS scores ranging from 0-40, 41-80, 81-120, and 121-160 were considered a little, quite a lot, moderate, and extreme stress respectively. At screening, the participants receiving the Mentacalm tablet had quite a lot of stress with a POMS score of 42.32 ±7.43. A statistically significant and consistent reduction in total POMS score i.e. 23.00% and 31.13% was observed in participants receiving Mentacalm tablets by Day 30 and Day 60 respectively. This substantial reduction, shifting the total POMS score toward a little stress category by Day 30 and Day 60 suggests the efficacy of the Mentacalm tablet in mitigating stress in adults.

A statistically significant and consistent increase in total Good Mood- POMS scores i.e. 129.50% and 181.61% was observed in participants by Day 30 and Day 60 respectively. Additionally, a statistically significant and consistent reduction in total Bad Mood- POMS scores i.e. 75.25% and 85.74% was observed in participants receiving Mentacalm tablets by Day 30 and Day 60 respectively. This substantial improvement in both total Good Mood and Bad Mood POMS scores by Day 30 and Day 60 suggests the efficacy of the Mentacalm tablet in improving overall mood in adults.

3.7. Assessment of Penn State Worry Questionnaire (PSWQ) score

The PSWQ is a 16-item self-report scale designed to measure the trait of worry in adults. Worry is regarded as a dominant feature of generalized anxiety disorder. The scale measures the excessiveness, generality, and uncontrollable dimensions of worry. A total PSWQ score of 30-52 is mild, 52-65 is moderate, and 66 or more is a severe worry, indicating a need for clinical intervention.

At screening, the participants receiving the Mentacalm tablet had moderate worry or anxiety with a PSWQ score of 60.68±3.77. A statistically significant and consistent reduction in total PSWQ score i.e. 12.41% and 33.45% was observed in participants receiving Mentacalm tablets by Day 30 and Day 60 respectively. This substantial reduction, shifting the total PSWQ score toward a little stress category by Day 30 and Day 60 suggests the efficacy of the Mentacalm tablets (Table 6).

Table 6 Assessment of PSWQ score

Parameters	Screening	Day 30	Day 60
Total PSWQ Score	60.68±3.77	53.15±4.13	40.38±4.08
Mean Difference	-	7.53±3.05	20.29±5.02
Percent change (%)	-	12.41	33.45
P value	-	<0.001	<0.001

Data was represented as Mean ± S.D (percent change). It was analyzed using the Student T-dependent test for within-group analysis.

3.8. Assessment of World Health Organization Quality of Life Questionnaire (WHOQOL-BREF) score

The WHOQOL-BREF is a self-report questionnaire that measures the QoL across domains: overall QOL and general health, physical health, psychological health, social relationships, and environment. Higher scores indicate better quality of life in each domain.

A statistically significant and gradual increment in total physical health domain score i.e. 84% and 147.7% was observed in participants receiving Mentacalm tablets by Day 30 and Day 60 respectively, indicating the efficacy of Mentacalm tablets in improving physical health and thereby, quality of life. Mentacalm tablet has also shown statically significant and gradual improvement in other domains such as in the psychological domain score of 79.8% and 140.9% was observed by Day 30 and Day 60 respectively, the social relationships domain also followed a similar trend showing 74.4% and 134.1% improvement by Day 30 and Day 60 respectively, indicating the efficacy of Mentacalm tablets in improving social relationships and thereby the quality of life.

The total environment domain score showed statistically significant improvement of 79.9% and 143.2% at Day 30 and Day 60 respectively, indicating the efficacy of the Mentacalm tablet in improving the total environment domain score.

A statistically significant and gradual increment in total overall QOL and general health domain score i.e. 63.8% and 126% was observed in participants receiving Mentacalm tablets by Day 30 and Day 60 respectively. The significant increase in total domain scores across all domains including overall QOL and general health, physical health, psychological, social relationships, and environment by Day 30 and Day 60 indicates the efficacy of Mentacalm tablets

in ameliorating overall physical and psychological health, as well as improving social relationships, environmental adaptability, and overall QOL in adults (Table 7).

Table 7 Assessment of WHOQOL-BREF score

Parameters	**Total Domain Score**		
	Screening	**Day 30**	**Day 60**
Overall QOL and general health	3.74±0.99	6.12±1.15	8.44±1.24
Mean Difference	-	2.38±0.89	4.71±1.36
Percent change (%)	-	63.8	126
P value	-	<0.001	<0.001
Physical health	11.41±1.81	21.00±2.07	28.26±2.11
Mean Difference	-	9.59±1.54	16.85±1.73
Percent change (%)	-	84	147.7
P value	-	<0.001	<0.001
Psychological	10.06±1.70	18.09±2.04	24.24±1.78
Mean Difference	-	8.03±1.34	14.18±1.45
Percent change (%)	-	79.8	140.9
P value	-	<0.001	<0.001
Social relationships	5.18±0.97	9.03±1.14	12.12±1.09
Mean Difference	-	3.85±0.82	6.94±0.89
Percent change (%)	-	74.4	134.1
P value	-	<0.001	<0.001
Environment	13.47±2.16	24.24±2.30	32.76±2.15
Mean Difference	-	10.76±1.46	19.29±1.45
Percent change (%)	-	79.9	143.2
P value	-	<0.001	<0.001

Data was represented as Mean ± S.D (percent change). Data was analyzed using the Student T-dependent test and Wilcoxon Signed-Rank Test for within-group analysis.

3.9. Assessment of Modified Sleep Regularity and Medication Withdrawal Questionnaire (MSRMWQ) score

Modified sleep regularity and medication withdrawal questionnaires were employed to evaluate the post-treatment effects on the study participants one week after stopping the treatment i.e., on Day 68, through telephonic interviews.

3.9.1. Part I: Sleep Regularity Questionnaire Assessment

In Part I of the questionnaire, individuals' sleep regularity over the past seven days using a 4-point Likert scale was assessed. They rated ten statements on a scale from 0 (indicating "Not at all") to 4 (indicating "Very much"). The scores were then added up to calculate a total score. Lower scores indicated poorer sleep regularity, while higher scores pointed to better sleep regularity, with a total score ranging from 0 to 40. Participants who scored between 00-10 were categorized as having poor sleep regularity, scores between 11-20 were categorized as having good sleep regularity, scores between 21-30 indicated better sleep regularity, and scores between 31-40 indicated excellent sleep regularity. This scoring system provided a way to measure and understand an individual's sleep patterns based on their self-reported experiences.

By Day 68, the participants exhibited a modified sleep regularity score of 19.03±3.43 which indicates better sleep regularity even after stopping the treatment of Mentacalm tablet.

3.9.2. Part II: Medication Withdrawal Questionnaire Assessment

The questionnaire evaluated medication withdrawal symptoms over the past seven days, with participants indicating the presence or absence of various symptoms. Symptom scoring is based on a 4-point scale: 0 (indicating No symptom), 1 (indicating Resolved symptom), 2 (indicating Ongoing symptoms requiring no medical assistance), and 3 (indicating Ongoing symptoms requiring medical assistance). A higher score implies a greater burden of withdrawal symptoms.

Following 1 week of discontinuation of treatment, all participants experienced a complete resolution of confusion. Five participants reported ongoing changes in mood while the remaining participants had resolution of symptoms/recovered without the use of any medication. Medicine cravings were reported by five participants but required no medical assistance. Physical symptoms including sweating, increased heart rate, and tremors were reported as resolved by five participants. No participant reported with memory loss**.**

3.10. Assessment of vital signs and laboratory parameters

No statistically and clinically significant change was observed in vital signs throughout the trial, suggesting safety of Mentacalm tablet. Hematocrit levels were increased and lymphocytes were decreased after 60 days which was clinically non-significant, and no clinically significant change is observed in major organ function throughout the trial.

3.11. Assessment of tolerability, adverse events, and treatment compliance

All participants exhibited a tolerability score of 3, indicating excellent tolerability. No adverse events were observed throughout the study. All participants exhibited higher compliance rates throughout the study.

4. Discussion

This was a single-arm, open-label clinical trial to evaluate the efficacy and safety of the Mentacalm tablet in reducing stress and anxiety in adults. Results of the present study have shown beneficial and statistically significant improvement in parameters such as Stress, anxiety, and depression which is confirmed by a reduction in stress hormone cortisol levels. Other parameters such as the Profile of Mood State (POMS) questionnaire score indicating the mood state of participants, Penn State Worry Questionnaire (PSWQ) score indicating the worry state of the participants, show statistically significant improvement suggesting effectiveness of the Mentacalm tablet. Assessment of the World Health Organization Quality of Life Questionnaire shows improvement in the overall quality of life of patients. Numerous studies have linked chronic stress to a wide range of physical and mental health problems, including heart disease, depression, and weakened immune systems which ultimately affect the quality of life. Neutraceuticals, with their potential to address these concerns naturally, offer a promising avenue for mitigating the rising incidence of these conditions. Mentacalm tablets are a unique formulation rooted in Ayurvedic principles concurrently supported by previous studies.

A 12-week, randomized, double-blind, placebo-controlled study was conducted to study the effect of *Bacopa monnieri* Extract (BME) on memory and cognitive skills in adult humans. The BME group showed significant improvements in both memory (verbal short-term memory, spatial short-term memory, working memory, visuospatial working memory, and episodic memory) and cognition skills (concentration, alertness, reasoning, and mental flexibility) over placebo from baseline to Day 84, with effects on cognitive skills as early as May 14 and Day 28 for memory. Further, a significant acute effect on concentration was observed as early as 3 hours post single dose consumption of BME. Anxiety score and sleep quality were significantly improved for the BME group on Days 28, 56, and 84 as compared to placebo. Serum cortisol levels were significantly reduced from baseline to Day 56 and 84, whereas serum BDNF was significantly increased on Day 84 for the BME group as compared to placebo. Similar findings were observed for cortisol levels, anxiety, mood, and sleep regularity in the present study (19).

A prospective, randomized double-blind, placebo-controlled study of high-concentration full-spectrum extract of ashwagandha root (300 mg) in reducing stress and anxiety in adults was conducted in 64 participants for 60 days. The treatment group that was given the high-concentration full-spectrum Ashwagandha root extract significantly outperformed the placebo group, demonstrating substantial reductions in stress-assessment scores (PSS, DASS, ($P<0.0001$) and serum cortisol levels ($P=0.0006$) after 60 days. The differences are highly statistically significant, suggesting a substantial effect of Ashwagandha in improving the well-being of participants with respect to these focal aspects of stress. This finding provides evidence of the strong anti-stress adaptogenic activity of Ashwagandha (20). Similar results are also observed in the present study.

Serum cortisol is a frequently cited correlate of stress and is therefore worth elaborating on in this discussion. Acute stress increases heart rate and arterial blood pressure, and stimulates gluconeogenesis, glycogenolysis, lipolysis, and hepatic glucose secretion. These in turn elevate the catecholamines and cortisol levels in the body. Stress, either physical or mental leads to enhancement of Adrenocorticotropic hormone secretion, which in turn increases cortisol levels; at times, the level may increase even 20-fold (21). The present study found that Mentacalm tablet containing Ashwagandha root extract reduces levels of serum cortisol, which elevates in stressful conditions. Similar findings were observed in a previous study by Auddy et al. in participants with stress (22).

Previous studies have indicated that *C. pluricaulis* (both crude herb and its metabolites) possesses a wide range of neuropharmacological properties, including memory enhancement, anxiolytic, antidepressant, and anti-stress effects, both in vitro and in vivo (23). These findings are consistent with our clinical study, as demonstrated by the significant reduction in stress and anxiety levels, as evidenced by lower cortisol levels and scores on the PSS, HAMA-A, POMS, DASS, and PSWQ scales.

This study uniquely employs a multi-faceted approach to assess stress, utilizing established stress scales and serum cortisol levels, a physiological stress biomarker. This comprehensive methodology distinguishes itself from typical studies that often rely on a limited set of measures. While the study's sample size achieved statistical significance, it would benefit from a larger, more diverse population to strengthen the generalizability of the findings. Additionally, the study's focus on a relatively healthy population limits its scope. Future research should explore the effects of Mentacalm tablets on individuals with various psychological and systemic conditions. Lastly, longer-term studies are necessary to comprehensively assess the long-term impact of Mentacalm tablets on stress and anxiety resilience.

The study found that administration of the Mentacalm tablets yielded significant positive effects as demonstrated by the reduction in stress-related symptoms and markers indicated by cortisol levels, PSS score, DASS score, HAM-A score, PSWQ score, Bad Mood- POMS score, and increase in Good Mood- POMS score, MSRMWQ score and WHOQOL- BREF score. The results affirm the value of the Mentacalm tablet as a promising supplement in managing stress and anxiety-related disorders in adults, underscoring its potential role in promoting mental health, positive mood, and overall quality of life.

5. Conclusion

By Day 68, the participants exhibited a modified sleep regularity with a score of 19.03±3.43 which indicates better sleep regularity even after stopping the treatment of Mentacalm tablet.

Following a one-week treatment discontinuation, all participants experienced a complete resolution of confusion and memory loss. Five participants reported ongoing mood changes, while the remaining participants fully recovered without additional medication. Five participants experienced medicine cravings but did not require medical intervention. Physical symptoms, including sweating, increased heart rate, and tremors, resolved in five participants.

The present study, emphasizes the efficacy and safety of the intervention, reinforcing its potential as a reliable option for the management of stress and anxiety in adults.

Compliance with ethical standards

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Disclosure of conflict of interest

Dr. Sandeep Mali is a part of Vedisrty Pvt. Ltd. and other authors declares no conflict of interest.

Statement of ethical approval

Ethical approval was obtained.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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