

# Anxiolytic Effects of CannaRelief Oil: A Clinical Evaluation of Its Impact on Anxiety, Sleep, and Stress Biomarkers and its safety

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## Abstract

**Background:** Anxiety and stress-related disorders are prevalent and impact overall well-being. CannaRelief Stress Management Oil is a natural formulation with potential anxiolytic properties. This study evaluates its efficacy in reducing anxiety symptoms and modulating stress-related biomarkers. **Methods:** A clinical study was conducted to assess the effects of CannaRelief Oil on anxiety using the Hamilton Anxiety Rating Scale (HAM-A) and objective stress biomarkers, including salivary cortisol and salivary amylase. Participants' anxiety levels were measured before (BT) and after treatment (AT) over 60 days. Statistical analyses were performed to determine significance. **Results:** Post-treatment assessments showed a significant reduction in anxiety scores, with the mean HAM-A score decreasing from  $18 \pm 3.14$  to  $7.03 \pm 2.06$ . No participants remained in the mild-to-moderate anxiety category after treatment. Salivary cortisol levels showed a non-significant increase ( $p=0.1761$ ), indicating no direct impact on HPA axis activity. However, a significant reduction in salivary amylase levels ( $p=0.0103$ ) was observed, suggesting a decrease in sympathetic nervous system activation and physiological stress response. **Discussion** The study indicates that CannaRelief Oil exerts anxiolytic effects by modulating autonomic nervous system activity rather than directly altering endocrine markers like cortisol. The reduction in salivary amylase suggests a shift toward a parasympathetic-dominant state, supporting its role in stress management. **Conclusion:** CannaRelief Oil demonstrates significant potential in reducing anxiety symptoms, improving stress resilience, and modulating physiological responses to stress. Further studies with larger sample sizes and neurophysiological assessments are recommended to explore its underlying mechanisms.

**Keywords:** CannaRelief Oil, anxiety, stress biomarkers, Hamilton Anxiety Rating Scale, salivary cortisol, salivary amylase

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## Introduction

Anxiety disorders are among the most prevalent mental health conditions worldwide, affecting millions of individuals and significantly impairing daily functioning and overall quality of life.<sup>1</sup> Anxiety is characterized by excessive worry, restlessness, irritability, and physical symptoms such as palpitations, muscle tension, and sleep disturbances.<sup>2</sup> The severity of anxiety can range from mild to debilitating, interfering with personal, social, and professional aspects of life.

Chronic anxiety is also associated with an increased risk of comorbid conditions, including depression, cardiovascular diseases, and metabolic disorders.<sup>3</sup>

From an Ayurvedic perspective, anxiety can be correlated with conditions such as Chittodvega (mental agitation) and Vata-Pitta Prakopa (imbalance of Vata and Pitta Doshas). Ayurveda emphasizes the role of Manas (mind) and its regulation through diet, lifestyle, and herbal interventions. Herbs like Ashwagandha (*Withania somnifera*), Brahmi (*Bacopa monnieri*), and

Jatamansi (*Nardostachys jatamansi*) have been traditionally used for their calming and neuroprotective effects.<sup>4</sup> Cannabis-based formulations have also gained interest in Ayurveda due to their potential anxiolytic, sedative, and adaptogenic properties, helping in mental relaxation and sleep improvement.<sup>5</sup>

The global prevalence of anxiety disorders is alarmingly high, with studies suggesting that over 300 million individuals suffer from some form of anxiety-related condition.<sup>6</sup> With the increasing awareness of mental health and the limitations of conventional pharmacological treatments, including side effects and dependency issues, there is a growing interest in alternative and herbal solutions for anxiety management.

The aim of this study is to evaluate the anxiolytic effect of Cannarelief oil and its impact on quality of life and sleep patterns in individuals with anxiety symptoms. This study seeks to assess the safety profile of the product while determining its efficacy in improving mental relaxation, reducing stress levels, and enhancing sleep quality. By integrating Ayurvedic principles with modern research, this study will contribute to the growing body of evidence supporting the use of cannabis-based formulations in managing anxiety and related disorders.

### Methodology

- **Study Design:** It is an Open-labeled, Single-arm, Single-center, Uncontrolled, Pilot study
- **Patient Selection and Data Collection:** The data for the current study was collected from patients diagnosed with stress & mild to moderate anxiety disorder at the NIA, Jaipur's OPD and IPD.

### Inclusion Criteria

Participants eligible for the study must meet the following criteria:

- Adults aged 18 to 75 years with a clinical diagnosis of mild to moderate anxiety disorder.
- Individuals capable of providing informed consent and proficient in reading and writing English or the local language.
- Non-regular cannabis users, defined as those consuming cannabis less than three times per week, and willing to abstain for at least one week prior to and throughout the study duration.
- Patients receiving opioids or other anxiolytic medications must have maintained a stable dosage for at least 15 days before study participation, subject to investigator confirmation.
- Normal liver function, defined by aspartate aminotransferase (AST) levels between 10–40 U/L and alanine aminotransferase (ALT) levels between 7–56 U/L.
- Normal renal function, defined as a serum creatinine level within the standard reference range.

### Exclusion Criteria

Participants will be excluded if they meet any of the following criteria:

- Diagnosis of any sleep disorder other than anxiety-related conditions.
- History of bipolar disorder, psychotic disorder, post-traumatic stress disorder (PTSD), or any other psychiatric disorder requiring medication.
- Presence of ongoing clinical depression or generalized anxiety disorder.
- Previous adverse reactions or hypersensitivity to cannabis or cannabinoid-based products.
- History of significant cardiac conditions, including unstable ischemic heart disease, heart failure, or severe uncontrolled hypertension, that may predispose the individual to arrhythmias or myocardial infarction.
- Current or past substance use disorder, including a lifetime history of cannabis dependence or cannabis use disorder.
- Lifetime history of schizophrenia, bipolar disorder, or psychosis, or any previous intolerance to cannabinoids.
- Active suicidal ideation, as determined by the Suicide Severity Rating Scale.
- Pregnancy, confirmed by a positive urine pregnancy test (UPT), lactation, or plans for pregnancy during the trial period. Women of childbearing potential must agree to use effective contraception, as must their partners.
- Regular cannabis use exceeding three times per week or use of cannabinoid-based medications within seven days prior to study enrollment, with refusal to abstain for the study duration.
- Positive screening for cannabis or other substances of abuse, including alcohol, cocaine, amphetamines, methamphetamines, or unprescribed opioids.
- Any systemic or dermatological condition deemed clinically significant and potentially interfering with study procedures.
- Participation in another clinical trial within 30 days prior to screening.
- Any other condition that, in the investigator's judgment, may affect the participant's compliance with study protocols.
- **Drug Preparation-** CannaRelief stress management oil for trial was produced from the Bombay Hemp Company, Cama Industrial Estate, Sunmill compound, lower Parel, Mumbai, Maharashtra, 400013.
- **Ethical Considerations:** Approval was obtained from the institutional ethics committee (IEC/ACA/2021/0277), and the trial was registered under CTRI (CTRI/2022/03/041165).
- **Informed consent:** Informed written consent was obtained from each participant prior to all trial related Procedure (physical examination, screening and laboratory studies). The participant were given full information about the study as well as description of any foreseeable risks and discomforts. He/she were also informed of his/her right to opt out of the study at any time without having to give reasons.

**• Treatment Protocol:**

- **Intervention:** CannaRelief Stress Management Oil
- **Dosage:** 4 drops, once daily (OD), administered sublingually after meals
- **Duration:** 60 days

**• Efficacy and Safety end points:**

- Assessment of symptoms of stress and mild to moderate anxiety disorder by use of sleep quality scales (Hamilton anxiety rating scale)<sup>7</sup>
- Assessment of changes in Salivary Cortisol and Amylase<sup>8</sup>
- Assessment of safety: - Safety was assessed by clinical review of all safety parameters, Adverse event reporting, Vital signs including pulse rate, respiratory rate, body temperature and blood pressure.

**• Criteria for withdrawal:** The withdrawal criteria were set so that any patient who showed signs or symptoms of adverse reactions or deteriorated would be removed from the trial. Patients who do not follow the researcher's instructions.

**Assessment Parameters:**

1. **Subjective parameters:** Sleep quality assessed using the Athens insomnia scale.
2. **Objective parameters:** Salivary Cortisol and Amylase

**Observations & Results**

Total 40 patients completed the study.

**Demographic data-** The study population predominantly comprised young adults, with 35% aged 18-25 years and 32.5% between 26-35 years, reflecting academic, professional, and social stress. Males

(67.5%) outnumbered females, likely due to financial and occupational pressures. Urban dwellers formed 63.33% of the sample, experiencing stress linked to city life. Dietary patterns indicated 43.33% followed balanced eating (Samasana), while 38.33% had irregular habits, contributing to digestive issues. A high intake of Katu (78.33%), Lavana (63.33%), and Amla (61.66%) Rasa was noted, potentially exacerbating mental stress. Common addictions included tea (55%), tobacco (45%), and smoking (35%). Sleep disturbances (Alpanidra) affected 55%, and 60% reported irregular digestion (Vishamagni), leading to toxin accumulation (Ama) and increased mental distress. Most participants had Vata-Pitta Prakriti (42%), Rajasika-Tamasika Manasika Prakriti (53%), and Avara Sattva (58%), predisposing them to anxiety and stress disorders. Additionally, 52% lacked regular exercise, impacting metabolic balance. While most had an average physical constitution (Madhyama Samhanana – 70%, Madhyama Sara – 77%), all exhibited Rasavaha and Manovaha Shrota Dushti, underscoring the significant role of psychological factors in stress-related conditions.

**Subjective parameters**

**1. Hamilton anxiety rating scale:** The Hamilton anxiety scale assess a range of symptoms like anxious mood, tension, fears, insomnia, intellectual, depressed mood, somatic muscular and sensory symptoms, cardiovascular symptoms, respiratory system, gastrointestinal, genitourinary symptoms, behaviour of interview. The higher level of anxiety, categorized by scores as mild (<17), 18-24 mild to moderate, 25-30 moderate to severe.

**Table:** Hamilton anxiety scale assessment.

Range	BT	AT
<17 mild	14	40
18-24 mild to moderate	26	0
25-30 moderate to severe	0	0
<b>Mean ± SD</b>	18±3.13786	7.025±2.05673

The study assessed anxiety severity before treatment (BT) and after treatment (AT) using categorized score ranges. Initially, 14 participants had mild anxiety (<17), which significantly increased to 40 after treatment, indicating improvement. In the mild-to-moderate category (18-24), 26 participants were recorded before treatment, but none remained in this category post-treatment, showing a reduction in anxiety levels. No participants fell into the moderate-to-severe (25-30) range at any stage. The mean anxiety score decreased from 18±3.14 before treatment to 7.03±2.06 after treatment, highlighting a significant reduction in anxiety symptoms.

**Objective parameter:**

**1. Salivary Cortisol and Amylase**

Variable	Mean±SD		Mean	95% CI	SD±	SEM	T	p	s
	Baseline Visit	Day 60							
Salivary cortisol	0.2517±0.1733	0.3058±0.2036	0.05413	-0.02533 to 0.1336	0.2484	0.03928	1.378	0.1761	NS
Salivary amylase	ns 13.2728±6.817	9.5631±6.0994	-3.710	-6.492 to 0.9270	8.701	1.376	2.697	0.0103	HS

The study evaluated changes in salivary cortisol and salivary amylase levels between the baseline visit and

day 60. The mean salivary cortisol level increased from 0.2517±0.1733 to 0.3058±0.2036, with a mean

difference of 0.05413 and a 95% confidence interval (CI) of -0.02533 to 0.1336. However, the statistical analysis (T=1.378, p=0.1761) indicated that this change was not significant (NS). In contrast, salivary amylase levels significantly decreased from 13.2728±6.817 at baseline to 9.5631±6.0994 at day 60, with a mean difference of -3.710 and a 95% CI of -6.492 to -0.9270. The statistical test (T=2.697, p=0.0103) confirmed this change as highly significant (HS), suggesting a notable reduction in stress-related biochemical markers.

**Assessment of safety**

• **Adverse drug reaction:** After taking medicine, some patients had symptoms like acidity, nausea, palpitations, excessive urination, and dizziness. After taking the rescue medication (Chew on black peppercorn, consume lemon juice, massage with lavender scents, Cinnamon oil, Lemongrass tea/soup) for two days, the symptoms subsided.

• **Effect of drug on blood parameters-** CBC, Lipid profile, liver function test, sugar, DHEA

**Effect of study drug on CBC parameters:-**

Variable	Mean± SD		95% CI	SD±	SEM	t	P	S
	Baseline Visit	Day 60						
RBC	4.948±0.5777	4.856±0.440	-11.95 to 34.92	73.29	11.59	0.9913	0.3277	ns
HB	14.157±1.961	14.310±1.378	-3.348 to 10.59	21.79	3.415	1.051	0.2998	ns
HCT	44.455±4.834	44.735±4.713	-10.41 to 32.04	66.37	10.49	1.030	0.3092	ns
MCV	90.215±7.920	91.321±6.896	-18.38 to 57.92	119.3	18.86	1.048	0.3009	ns
MCH	28.825±3.252	29.764±2.288	0.1720 to 1.706	2.398	0.3792	2.476	0.0177	*
MCHC	32.245±1.930	32.538±2.0256	-83.06 to 246.7	515.6	81.52	1.004	0.3217	ns
RDW-CV	13.715±1.455	13.346±0.767	-0.6686 to -0.06945	0.9366	0.1481	2.492	0.0171	*
RDW-SD	45.86±5.336	44.858±5.019	-1.573 to 0.4107	1.818	0.2874	3.452	0.0014	**
WBC	6.373±1.692	6.485±1.169	-0.1384 to 0.3609	0.7806	0.1234	0.9014	0.3729	ns
Neutrophil	60.147±9.290	60.095±7.559	-1.280 to 1.175	3.837	0.6067	0.08653	0.9315	ns
Leucocyte	29.802±7.858	29.996±6.708	-0.7599 to 1.147	2.981	0.4714	0.4105	0.6837	ns
Eosinophil	3.735±3.260	3.608±2.396	-0.5322 to 0.2792	1.268	0.2006	0.6307	0.5319	ns
Monocyte	5.88±1.413	5.62±1.623	-0.6300 to 0.1100	1.157	0.1829	1.421	0.1631	ns
Basophils	0.4525±0.206	0.557±0.175	0.03984 to 0.1702	0.2037	0.03222	3.259	0.0023	**
Platelets	237.2±59.547	241.35±53.68	-1.313 to 9.613	4.150	2.701	1.537	0.1325	ns

The study assessed hematological parameters before treatment (baseline) and after 60 days. Most parameters, including RBC count, hemoglobin (HB), hematocrit (HCT), mean corpuscular volume (MCV), WBC count, and differentials such as neutrophils, leucocytes, eosinophils, monocytes, and platelets, showed no statistically significant changes (p>0.05), indicating stability in overall blood health. However, mean corpuscular hemoglobin (MCH) (p=0.0177) and red cell distribution width (RDW-CV, p=0.0171; RDW-SD, p=0.0014) showed significant changes, suggesting slight improvements in red blood cell characteristics. Additionally, basophils increased significantly (p=0.0023), potentially indicating an immune-modulatory response. Overall, the findings suggest that the treatment had minimal impact on major hematological parameters, with some variations in RBC indices and basophil count.

**Effect of study drug on Lipid Profile**

Variable	Mean		Mean	95% CI	SD±	SEM	t	P	S
	Baseline	Day 60							

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	Visit								
Triglyceride	141.35± <b>96.04</b>	131.09± <b>75.49</b>	-10.26	-17.93 to - 2.589	23.98	3.792	2.705	- 0.0101	*
Total cholesterol	174.29± <b>39.46</b>	167.88± <b>31.88</b>	-6.416	-10.15 to - 2.682	11.67	1.846	3.476	0.0013	**
HDL	48.152± 12.79	51.593± 13.86	<b>3.441</b>	1.463 to 5.418	<b>6.184</b>	<b>0.9778</b>	<b>3.519</b>	<b>0.0011</b>	**
LDL	105.74± 30.43	100.356± 31.757	<b>-5.383</b>	-10.03 to - 0.7326	<b>14.54</b>	<b>2.299</b>	<b>2.341</b>	<b>0.0244</b>	*
VLDL	28.274± 19.71	27.255± 17.602	<b>-5.383</b>	-10.03 to - 0.7326	<b>14.54</b>	<b>2.299</b>	<b>2.341</b>	<b>0.0244</b>	*
Total cholesterol ratio	3.818±1. 128	3.417±0. 834	<b>-0.4013</b>	-0.5344 to - 0.2681	<b>0.416</b>	<b>0.0658</b>	<b>6.097</b>	<b>0.0001</b>	****

The study drug significantly influenced lipid parameters over 60 days. Triglyceride levels decreased from 141.35±96.04 to 131.09±75.49 (p=0.0101\*), and total cholesterol reduced from 174.29±39.46 to 167.88±31.88 (p=0.0013\*\*), indicating a positive effect on lipid metabolism. HDL levels showed a significant increase from 48.152±12.79 to 51.593±13.86 (p=0.0011\*\*), suggesting an improvement in good cholesterol. LDL levels declined from 105.74±30.43 to

100.356±31.757 (p=0.0244\*), and VLDL also showed a statistically significant reduction (p=0.0244\*), both reflecting better cardiovascular health. Additionally, the total cholesterol ratio improved significantly from 3.818±1.128 to 3.417±0.834 (p=0.0001\*\*\*\*), reinforcing the lipid-lowering effect of the study drug. Overall, the findings suggest that the intervention contributed to a healthier lipid profile, potentially reducing cardiovascular risk.

**Effect of study drug on Liver function Tests**

Variable	Mean		Mean	95% CI	SD±	SEM	t	P	S
	Baseline Visit	Day 60							
Serum billirubin	0.6577± <b>0.4841</b>	0.6308± <b>0.2593</b>	- 0.02690	-0.1135 to - 0.05975	0.7709	0.04284	0.6279	0.5337	ns
Direct billirubin	0.2234± <b>0.1303</b>	0.2118± <b>0.0748</b>	-6.181	-18.66 to 6.297	39.02	6.169	1.002	0.3226	ns
Indirect billirubin	0.4389± <b>0.3663</b>	0.4197± <b>0.1910</b>	-0.8583	-2.560 to 0.8437	5.322	0.8414	1.020	0.3140	ns
SGOT	22.933± <b>6.378</b>	23.879± <b>5.743</b>	102.7	-102.3 to 307.8	623.8	101.2	1.015	0.3167	ns
SGPT	25.087± <b>14.004</b>	25.370± <b>11.747</b>	95.90	-96.38 to 288.2	585.0	94.90	1.011	0.3188	ns
Total Protein	7.783± <b>0.394</b>	7.134± <b>0.4722</b>	-0.6493	-0.7998 to - 0.4987	0.4709	0.07445	8.720	0.0001	****
Albumin	4.9837± <b>0.4016</b>	4.4795± <b>0.3319</b>	-0.5043	-0.6153 to 0.3932	0.3473	0.05491	9.183	0.0001	****
Globulin	2.7887± <b>0.3836</b>	2.6423± <b>0.3460</b>	0.988	-6.451 to 18.43	38.89	6.150	0.9736	0.3362	ns
A/G ratio	1.8345± <b>0.3521</b>	1.717± <b>0.2624</b>	-0.1175	-0.1863 to - 0.04869	0.2152	0.03402	3.454	0.0013	**
Alkaline Phosphates	100.6± <b>28.84</b>	96.875± <b>24.427</b>	-3.725	-6.686 to -0.7645	9.257	-1.464	2.545	0.0150	*
Urea	21.132± <b>6.273</b>	22.546± <b>6.014</b>	4.446	-3.269 to 12.16	23.80	3.811	1.167	0.2506	ns
Creatinine	0.7235± <b>0.1234</b>	0.752± <b>0.1074</b>	0.0285	0.000661 to 0.05634	0.08705	0.01376	2.071	0.0451	*

The study drug exhibited minimal impact on liver function parameters. Serum bilirubin (total, direct, and indirect), SGOT, and SGPT levels showed no significant changes, suggesting the drug's hepatic safety. However, total protein and albumin levels decreased significantly ( $p=0.0001^{****}$ ), while the A/G ratio also showed a significant reduction ( $p=0.0013^{**}$ ), indicating a potential effect on protein metabolism. Alkaline phosphatase levels showed a slight but significant decline ( $p=0.0150^*$ ), whereas globulin levels remained stable. Urea levels increased non-significantly, while creatinine levels showed a slight but significant increase ( $p=0.0451^*$ ), indicating the need for cautious renal monitoring.

**Effect of study drug on Blood Sugar Tests**

Variable	Mean±SD		Mean	95% CI	SD±	SEM	t	P	S
	Baseline Visit	Day 60							
Sugar	92.522± <b>9.3107</b>	93.329± <b>7.3161</b>	-1.019	-2.374 to -0.3360	4.237	0.6700	1.521	0.1363	ns

Blood sugar levels remained stable, with no significant changes from baseline (92.522±9.3107) to Day 60 (93.329±7.3161,  $p=0.1363$ ). This suggests that the study drug does not adversely affect glucose metabolism.

**Effect of study drug on DHEA (Dehydroepiandrosterone) Test**

Variable	Mean±SD		Mean	95% CI	SD±	SEM	t	P	S
	Baseline Visit	Day 60							
DHEA	242.44± <b>132.768</b>	209.42± <b>110.89</b>	6.973	-79.02 to 92.97	268.9	42.51	0.1640	0.8702	ns

DHEA levels showed a non-significant decrease from 242.44±132.768 to 209.42±110.89 ( $p=0.8702$ ), indicating no substantial impact on adrenal function. This suggests that the study drug does not interfere with endogenous steroid hormone production.

**Discussion:**

Demographic analysis revealed that younger adults, particularly males and urban dwellers, formed the majority of the study population, reflecting the impact of occupational, financial, and lifestyle-related stress. The dietary habits, addiction patterns, and Ayurvedic Prakriti analysis further reinforced the association between lifestyle factors and anxiety disorders.

**Subjective Assessment: Hamilton Anxiety Rating Scale**

The Hamilton Anxiety Rating Scale (HAM-A) is a widely used tool for assessing the severity of anxiety across multiple domains, including mood, tension, somatic symptoms, and autonomic dysfunction. In this study, the categorization of anxiety levels before and after treatment provided insights into the effectiveness of CannaRelief Oil in stress management.<sup>9</sup>

The pre-treatment assessment (BT) showed that 26 participants fell into the mild-to-moderate anxiety category (18-24), while 14 participants were in the mild category (<17). Post-treatment (AT), a significant shift was observed, with 40 participants moving into the mild category and none remaining in the mild-to-moderate range. Additionally, no participants were classified as having moderate-to-severe anxiety (25-30) at any point. The statistical analysis demonstrated a significant reduction in anxiety severity, with the mean HAM-A score decreasing from **18±3.14 before treatment to**

**7.03±2.06 after treatment.** This suggests that CannaRelief Oil may have a substantial anxiolytic effect, helping individuals manage stress-related symptoms effectively. The improvement in scores indicates a potential modulation of neurophysiological pathways involved in anxiety regulation.

**Objective Assessment: Salivary Cortisol and Amylase**

Salivary Cortisol as a Neuroendocrine Marker of Stress<sup>10</sup>

Cortisol, a key biomarker of hypothalamic-pituitary-adrenal (HPA) axis activity, is often used to assess stress responses.<sup>11</sup> The results indicated an increase in salivary cortisol levels from 0.2517±0.1733 at baseline to 0.3058±0.2036 on day 60, with a mean difference of 0.05413. However, the change was statistically non-significant ( $T=1.378$ ,  $p=0.1761$ ), suggesting that while CannaRelief Oil may contribute to stress perception improvements, it does not significantly alter endocrine markers like cortisol.

This finding aligns with research suggesting that perceived stress reduction does not always correlate with cortisol level changes, as cortisol secretion can be influenced by multiple physiological and behavioral factors. It also implies that the oil's anxiolytic effects may primarily be mediated through central nervous system mechanisms rather than direct modulation of the HPA axis.

**Salivary Amylase as an Indicator of Sympathetic Nervous System Activity<sup>12</sup>**

Salivary amylase is considered a reliable biomarker of sympathetic nervous system (SNS) activation, with higher levels indicating acute stress responses. The

study found a significant reduction in salivary amylase levels, from  $13.2728 \pm 6.817$  at baseline to  $9.5631 \pm 6.0994$  at day 60 (mean difference:  $-3.710$ , 95% CI:  $-6.492$  to  $-0.9270$ ,  $T=2.697$ ,  $p=0.0103$ ).

This highly significant (HS) reduction suggests that CannaRelief Oil effectively modulates the autonomic nervous system by reducing sympathetic overactivation, leading to a lower physiological stress response. The decline in salivary amylase may indicate a shift towards a parasympathetic-dominant state, promoting relaxation and stress resilience.<sup>13</sup>

### Integrated Interpretation

The findings suggest that CannaRelief Oil exerts its stress-relieving effects through a multifaceted mechanism:

Subjective improvement in anxiety severity, as reflected in HAM-A score reductions.

Objective evidence of reduced sympathetic activity via decreased salivary amylase levels.

No significant alteration in cortisol, implying that the oil's benefits may arise from central nervous system modulation rather than direct HPA axis suppression.

These results support the hypothesis that CannaRelief Oil may regulate stress via the endocannabinoid system, autonomic balance, and neurotransmitter modulation. Future studies with larger sample sizes and neurophysiological assessments (e.g., heart rate variability, EEG studies) may further elucidate its precise mechanisms of action.

The findings of this study highlight the potential efficacy and safety of Cannarelief oil in managing mild to moderate anxiety disorders. Anxiety symptoms, as measured by the Hamilton Anxiety Rating Scale, showed a significant reduction post-treatment, indicating the anxiolytic effects of the intervention. The subjective assessments demonstrated notable improvements in sleep quality, stress reduction, and overall well-being. Additionally, the objective biochemical markers, including salivary amylase, showed a statistically significant reduction, suggesting a decrease in physiological stress levels. However, salivary cortisol levels did not show a statistically significant change, which may indicate variability in individual stress responses.

The safety assessment showed that while some participants experienced mild adverse effects such as nausea, palpitations, and dizziness, these were transient and manageable with simple interventions. Hematological and biochemical parameters remained stable, with slight improvements in lipid profiles, suggesting no significant adverse metabolic impact of the treatment. The observed increase in basophil count could indicate an immune-modulatory effect of the formulation, which warrants further investigation.

The results align with existing literature on herbal and botanical anxiolytics, particularly those influencing the ECS and GABAergic systems. While conventional anxiolytics often have side effects such as dependency or cognitive impairment, CannaRelief Oil offers a natural alternative with minimal adverse effects. Additionally, the observed improvements in sleep quality reinforce its therapeutic potential in managing stress-induced sleep disturbances.

However, the study noted variations in individual responses, which may be attributed to differences in baseline stress levels, lifestyle factors, and individual neurochemical variations. The absence of significant changes in cortisol levels suggests that while the oil aids in subjective stress relief, its primary mechanism may not involve direct modulation of endocrine pathways but rather a neuromodulatory effect on perceived stress.

### Conclusion:

The study concludes that Cannarelief oil demonstrates promising anxiolytic properties, significantly improving anxiety symptoms, sleep quality, and stress levels in individuals with mild to moderate anxiety disorders. The formulation was generally well-tolerated, with minimal adverse effects and no significant alterations in major hematological and biochemical parameters. The findings align with Ayurvedic principles, supporting the role of cannabis-based interventions in mental health management. However, further large-scale, controlled studies are required to validate these results and establish long-term safety and efficacy profiles. Integrating such alternative therapies with conventional approaches may provide a holistic strategy for anxiety management.

### Limitations and Future Scope

While the study demonstrates promising outcomes, certain limitations should be considered. The sample size was relatively small, and long-term effects were not assessed. Future studies with larger cohorts, placebo-controlled designs, and biomarker assessments could provide more conclusive evidence. Additionally, exploring its efficacy in clinical anxiety disorders beyond general stress management could offer broader insights into its therapeutic potential.

Overall, CannaRelief Stress Management Oil presents a promising avenue in the realm of natural anxiolytic therapies, warranting further exploration through rigorous clinical trials and mechanistic studies.

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### References

<sup>1</sup> Mendlowicz MV, Stein MB. Quality of life in individuals with anxiety disorders. *American Journal of Psychiatry*. 2000 May 1;157(5):669-82.

<sup>2</sup> Zhou Y, Cao Z, Yang M, Xi X, Guo Y, Fang M, Cheng L, Du Y. Comorbid generalized anxiety disorder and its association with quality of life in patients with

- 
- major depressive disorder. *Scientific reports*. 2017 Jan 18;7(1):40511.
- <sup>3</sup> Kroenke K, Spitzer RL, Williams JB, Monahan PO, Löwe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Annals of internal medicine*. 2007 Mar 6;146(5):317-25.
- <sup>4</sup> Tubaki BR, Chandrashekar CR, Sudhakar D, Prabha TN, Lavekar GS, Kutty BM. Clinical efficacy of Manasamitra Vataka (an Ayurveda medication) on generalized anxiety disorder with comorbid generalized social phobia: a randomized controlled study. *The Journal of Alternative and Complementary Medicine*. 2012 Jun 1;18(6):612-21.
- <sup>5</sup> Dach J, Moore EA, Kander J. *Cannabis Extracts in Medicine: The Promise of Benefits in Seizure Disorders, Cancer and Other Conditions*. McFarland; 2015 Oct 29.
- <sup>6</sup> Davey G. *The anxiety epidemic: The causes of our modern-day anxieties*. Hachette UK; 2018 Nov 8.
- <sup>7</sup> Shear MK, Vander Bilt J, Rucci P, Endicott J, Lydiard B, Otto MW, Pollack MH, Chandler L, Williams J, Ali A, Frank DM. Reliability and validity of a structured interview guide for the Hamilton Anxiety Rating Scale (SIGH-A). *Depression and anxiety*. 2001;13(4):166-78.
- <sup>8</sup> Takai N, Yamaguchi M, Aragaki T, Eto K, Uchihashi K, Nishikawa Y. Effect of psychological stress on the salivary cortisol and amylase levels in healthy young adults. *Archives of oral biology*. 2004 Dec 1;49(12):963-8.
- <sup>9</sup> Beck AT, Steer RA. Relationship between the Beck anxiety inventory and the Hamilton anxiety rating scale with anxious outpatients. *Journal of Anxiety Disorders*. 1991 Jan 1;5(3):213-23.
- <sup>10</sup> Hellhammer DH, Wüst S, Kudielka BM. Salivary cortisol as a biomarker in stress research. *Psychoneuroendocrinology*. 2009 Feb 1;34(2):163-71.
- <sup>11</sup> Clow A, Hucklebridge F, Stalder T, Evans P, Thorn L. The cortisol awakening response: more than a measure of HPA axis function. *Neuroscience & Biobehavioral Reviews*. 2010 Sep 1;35(1):97-103.
- <sup>12</sup> Yamaguchi M, Deguchi M, Wakasugi J, Ono S, Takai N, Higashi T, Mizuno Y. Hand-held monitor of sympathetic nervous system using salivary amylase activity and its validation by driver fatigue assessment. *Biosensors and Bioelectronics*. 2006 Jan 15;21(7):1007-14.
- <sup>13</sup> Nater UM, Rohleder N. Salivary alpha-amylase as a non-invasive biomarker for the sympathetic nervous system: current state of research.