

## Controlled programmed trial of *ocimum sanctum* leaf on generalized anxiety disorders

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### ABSTRACT

*Ocimum sanctum*, an Indian medicinal plant, has been on trial for its role in generalized anxiety disorder (GAD) in hospital based clinical set-up. Hamilton's brief psychiatric rating scale (BPRS) and thorough clinical investigations were used to screen the subjects. Thirty-five subjects (21 male and 14 female; average age 38.4 years) were medicated with the plant extract in a fixed dose regime (500 mg/capsule, twice daily, p.o. after meal). They were thoroughly investigated clinically and using standard questionnaires based on different psychological rating scale at baseline (day 0), mid-term (day 30) and final (day 60). The observations exhibited that, *O. sanctum* significantly ( $p < 0.001$ ) attenuated generalized anxiety disorders and also attenuated its correlated stress and depression. It further significantly ( $p < 0.001$ ) improved the willingness to adjustment and attention in human. Therefore, it may be concluded that *O. sanctum* may be useful in the treatment of GAD in human and may be a promising anxiolytic agent in near future.

**Keywords:** Anxiety, stress, depression, adjustment, *O. sanctum*.

### INTRODUCTION

Generalized anxiety disorder (GAD) is a cardinal symptom of many psychiatric disorders and an almost inevitable component of many medicinal and surgical conditions. Symptoms of anxiety commonly associated with panic disorder, agoraphobia, obsessive-compulsive disorder, eating disorder and many personalities disorders.<sup>1,2</sup> Throughout human history there have been searches for antidotes for the symptoms of anxiety and stress. Since the development of the first benzodiazepine, more than 2,000 related compounds have been synthesized, but few of them have been found to be clinically useful.<sup>3</sup> This provides impetus in the search for newer and more effective anti-stress drugs. Natural products have played a significant role in the management of neuropsychiatric disorders.

Ayurveda, Indian system of traditional medicine has described CNS-activity under different categories. A number of medicinal plants from India have been shown to have activity by the traditional methods of psychopharmacology, *Ocimum sanctum* is one of them.<sup>4</sup> *O. sanctum*, an herbaceous plant exceedingly common and also cultivated throughout India. An essential oil, *circa* has been isolated from cell culture of *O. sanctum*. GLC of *circa* revealed the presence of *eugenol* as a major constituent.<sup>5</sup> The ethanolic extract of *O. sanctum* leaves contains *ursolic acid*. Earlier studies with *O. sanctum* indicated that the plant has hypoglycemic,

hypolipidemic, adaptogenic, antidepressant, antiepileptic, hepatoprotective, anticancer, radioprotective, analgesic and anti-inflammatory properties.<sup>6-12</sup> Although the plant has been in traditional use for thousands of years in India, but till date there is no evidence-based clinical report. In this context, we aimed to investigate the Indian medicinal plant, *O. sanctum* for its role in mental disorders especially generalized anxiety disorder (GAD) disorders in human.

### MATERIALS AND METHODS

The leaves of *O. sanctum* were washed, dried and made into fine powder. This powder was soaked in 70.0% ethanol. After 24 h at room temperature, the materials were filtered under vacuum. This process of extraction was further repeated for three times. The combined alcoholic extract of the plant was concentrated under reduced pressure in a rotary evaporator. The concentrated material was then lyophilized and the ultimate product was filled in gelatin capsules (500 mg equivalent weight).<sup>13</sup>

The Programmed clinical trail was done in the Out-Patient Clinics of the J. B. Roy State Ayurvedic Medical College and Hospital, Govt. of West Bengal, Kolkata, India. The trial was conducted in accordance with good clinical practice guidelines and conforming to the declaration of Helsinki, following approval by the Institutional Ethics committee.

Patients of both sexes, of age group 18-60 years,

suffering from GAD, diagnosed during initial observation of the patient and filling up of the proforma for detailed general examination of the patient and brief psychiatric rating scale (BPRS)<sup>14-15</sup> and in whom the exclusion criteria were absent, were included in this study, after getting their informed written consent either in English, Bengali or Hindi as the case may be. The exclusion criteria of this study were: (i) hepatic and/or renal disease, (ii) severe depression, (iii) organic lesion, (iv) uncontrolled diabetic patient.

Subjects judged eligible by the inclusion and exclusion criteria were formally informed about the study and those who gave written informed consent were enrolled. The encapsulation contained 500 mg of the plant extract and was administered orally in dose of one capsule, twice daily after meal. Hence, each patient ingested two capsules per day. The dose remained constant throughout the study (i.e., no increase or decrease in dose). Any concomitant illness and medication during study period were recorded throughout the study. No other anxiolytic medication including b-blockers anti-depressants etc. was permitted throughout the study. The subjects were followed-up at day 30 and finally at day 60 from the starting of medication. They were thoroughly investigated clinically and using questionnaires based on different psychological rating scale.<sup>14-15</sup> The statistical analysis of the data was performed according to by *Chi-*

*Square test* and percentile change compared to baseline results.<sup>16</sup> The p value smaller than 5.0% was considered as statistically significant.

**RESULTS**

The distribution of subjects was tabulated in Table-1. This study included 35 subjects. Regarding sex, 21 patients were male and 14 were female. There were 15 patients (42.8%) who belonged to the age group of 18-35 years, 11 patients (31.4%) belonged to the age group of 36-50 years and only 9 (25.7%) patient was above 50 years. The average age of the subjects was 38.4 years. Regarding occupation there were service holders (9 patients), house wives (11 patients), businessmen (7 patients), students (6 patients) and others (2 patients) including unemployed, retired person etc.

The patients were selected on the basis of seven point scoring system of modified Hamilton’s brief psychiatric rating scale. The results indicated that *O. sanctum* ingestion (500mg capsule, twice daily for 60days) significantly attenuated anxiety-stress-disorders (Table-2). The overall clinical features also improved after the treatment. Before the test drug, *O. sanctum* therapy, the baseline score of anxiety index was 84.42±7.56, but it declined to 68.17±7.84 (-19.2%) after 30 days and 55.54±7.20 (-34.2%) after 60 days. Further, stress index at baseline was 95.65±8.42, while, *O. sanctum* treatment showed significant reduction to 84.32±9.08 (-11.5%) after 30 days and to 68.45±9.60 (-27.5%) on 60 days. On the other hand, depression index also reduced from 66.45±5.68 (at baseline) to 57.65±5.04 (30 days) and 45.97±6.27 (60 days), decline was 13.2% and 30.8% respectively. These results clearly indicated that the test drug, *O. sanctum* has significant anti-stress and anxiolytic properties. Furthermore, it significantly improved the willingness of adjustment (10.6% on day 30 and 25.1% on day 60) and attention (16.3% on day 30 and 33.9% on day 60) when it was compared with baseline score in the selected subjects.

**Table-1:** The distribution of subjects for trial

<b>Total Subjects (N)</b>	35
Male	21
Female	14
<b>Religion</b>	
<i>Hindu</i>	29
<i>Muslim</i>	6
<b>Average age</b>	38.4
18-35 years	15
36-50 years	11
50 years	9
<b>Occupation</b>	
Service holder	9
House wife	11
Business	7
Student	6
Others	2

**DISCUSSION**

The human society has become complex and, in many ways, more demanding. However, our physiological responses designed to cope with the ever-increasing adverse situations have not evolved appreciably during the past thousand years. The failure of successful adaptation during stressful situations has resulted in stress-related illness that result from, or are associated with, dysregulation of the stress response.<sup>17</sup> Various attempts have been made to counter the aversive

**Table-2:** Role of *Ocimum sanctum* leaves extract (500mg/capsule, twice daily, p.o.) on Generalized Anxiety Disorders in human subject

	Psychological Score (mean ± SD)						
	Baseline (Day 0)	Visit I (Day 30)	% Change	p-value	Visit II (Day 60)	% Change	p-value
Anxiety	84.42 ± 7.56	68.17 ± 7.84	-19.2	<0.001	55.54 ± 7.20	-34.2	<0.001
Stress	95.65 ± 8.42	84.32 ± 9.08	-11.5	<0.001	68.45 ± 9.60	-27.5	<0.001
Depression	66.45 ± 5.68	57.65 ± 5.04	-13.2	<0.001	45.97 ± 6.27	-30.8	<0.001
Adjustment	45.22 ± 6.80	50.02 ± 5.63	10.6	<0.001	56.57 ± 5.82	25.1	<0.001
Attention	2.45 ± 0.70	2.85 ± 0.65	16.3	<0.02	3.28 ± 0.82	33.9	<0.001

N=35; The results were statistically compared to baseline using Chi-Square test.

effects of stress, ranging from meditation to anti-stress drugs, particularly the anxiolytic benzodiazepines (BDZ). However, despite claims to the contrary, these nonpharmacological and pharmacological methods appear to have limited utility.<sup>18</sup> An answer to this perplexing problem of countering stress-induced perturbations of physiological homeostasis came from the plant kingdom. A group of plant-based drugs, the adaptogens, appears to induce a state of nonspecific resistance, enabling the organism to counteract and adapt to various stressors that can adversely affect the physiological system. The topic of adaptogens and their likely utility in stress medicine has been reviewed.<sup>19</sup> Several plants have been shown to have adaptogenic activity.<sup>20</sup> Indian ancient medicinal system, *Ayurveda* documents several plants, including *O. sanctum*, which are, categorized as *rasayana*.<sup>6</sup> The properties ascribed to *rasayanas* in *Ayurveda* are remarkably similar to those of adaptogens.<sup>21</sup> In this study, *O. sanctum* extract showed overall improvement in stress management. The treatment also helped in mental overwork in daily life. Prolonged treatment of *O. sanctum* extract showed to inhibit stress in human, without any side effects like vertigo, nausea, and dizziness or mental weakness.

Further, the present results indicate that, *O. sanctum* has good efficacy to negate anxiety related disorders in human subjects. Anxiety is a cardinal symptom of many psychiatric disorders and an almost inevitable component of many medicinal and surgical conditions. Symptoms of anxiety commonly associated with

dysthymic disorder, panic disorder, agoraphobia, obsessive-compulsive disorder, eating disorder and many personality disorders.<sup>1-2</sup>

Generalized stress, particularly if continued in nature, is known to induce melancholic depression. It has been suggested that the symptoms of endogenous depression represent tolerance of the mesocortical system to chronic activation of the stress system.<sup>17</sup> Physical changes also occur particularly in severe or melancholic depression: these include insomnia or hypersomnia, anorexia and weight loss (or sometime over eating), decreased energy and libido, and disruption of the normal circadian rhythms of activity, body temperature, and many endocrine functions.<sup>22</sup> In that study, it was revealed that, depression index was also reduced after two-month continuous treatment with *O. sanctum*. Furthermore, the plant also enhanced the willingness to adjustment and attention in human.

The present clinical trial supports the contention that, two-month regular administration with *O. sanctum* reduced stress, attenuated anxiety, negated depression and enhanced adjustment and attention in human subject. These observations clearly indicate that *O. sanctum* has potential action in the regulation of hypothalamo-hypophyseal-adrenocortical axis (HHA axis) especially, during stress related disorders in human. It appears that *O. sanctum* may be a safer alternative to Benzodiazepines for the therapy of stress related clinical disorders.

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