

A clinical study on the management of generalized anxiety disorder with *Vaca (Acorus calamus)*

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In Ayurveda, *Vaca (Acorus calamus, Family: Araceae)*, is reputed for its beneficial effects in various neurological disorders. The present investigation was undertaken to evaluate the role of 70% hydro-ethanolic extract of *Vaca* or *Acorus calamus* (ACE) on generalized anxiety disorder (GAD) in human. Hamilton's Brief Psychiatric Rating Scale (BPRS) and thorough clinical investigations were used to screen the subjects. Thirty-three participants (20 male and 13 female; average age 36.2 yrs) were medicated with ACE 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 scale also includes a number of direct queries about current levels of experienced stress. Moreover, the questions are of a general nature and hence are relatively free of content specific to any subpopulation group. The observations exhibited that, ACE not only significantly ($p < 0.001$) attenuated anxiety related disorders but it also significantly ($p < 0.001$) reduced stress phenomenon and its correlated depression. ACE further significantly ($p < 0.001$) improved the willingness to adjustment. Therefore, it may be concluded that *Vaca* may be useful in the treatment of GAD in human and may be a promising anxiolytic agent in near future.

Keywords: Anxiety disorders, Psychological stress, Depression, *Vaca, Acorus calamus*, Ayurvedic medicine

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The facets of stress are essentially limitless; however, broad categories include physical exertion, emotional upset, persistent psychological pressure, existential crisis and the residual effects of emotional trauma. It has consistently been shown that individuals experiencing stress have impaired physical and mental functioning and increased use of healthcare services¹. The World Health Organization (WHO) Global Burden of Disease Survey estimates that mental disease, including stress-related disorders, will be the second leading cause of disability by the year 2020². Current therapies for dealing with 'stress' are extensive but perhaps not ideally targeted in most cases. Pharmacological approaches are principally focused on the treatment of depression and the manifestations of both acute and chronic anxiety disorders³. A potentially beneficial use of herbal medicine involves the use of herbs as 'adaptogens' in order to prevent stress-induced morbidity⁴. Ayurveda,

Indian system of traditional medicine has described CNS-activity under *Rasayana* categories. *Sushruta* describes *Rasayana* deals with the drugs and the methods to maintain youth, to increase longevity, intellectual capacity and strength as well as to enable the patient to be freed from diseases⁵. A number of medicinal plants from Ayurveda have been shown to have activity by the traditional methods of psychopharmacology, *Vaca* or *Acorus calamus* (Family: Araceae), is one of them⁶. *Acorus calamus* (AC) is a semiaquatic, perennial, aromatic herb with creeping rhizomes. The plant is found in the northern temperate and subtropical regions of Asia, North America, and Europe. The plant exhibits polyploidy⁷. The bioactive constituents so far identified are *asarones*, *shyobunones*, *acorones*, *octanoic acid*, *α -cedrene*, *α -phellandrene*, *β -farnesene*, *γ -elemene*, etc.⁸. Many ethnomedicinal and ethnobotanical uses have been ascribed to the rhizomes of the plant. Moreover, pharmacological studies have revealed that AC rhizome and its constituents α - and β - *asarones*,

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wide range of pharmacological activities such as sedative, CNS depressant, behavior modifying, anticonvulsant, memory enhancing, antioxidant, antiepileptic, etc⁸⁻¹¹. Although the plant has been in traditional use to treat neurological disorders for thousands of years in India and China, but till date there is no evidence-based clinical report. In this context, we aimed to investigate the *Rasayana* plant, *Vaca* (*Acorus calamus*) for its role in mental disorders, especially *Generalized Anxiety Disorders (GAD)* in human subject.

Methodology

Rhizomes of *Acorus calamus* were washed, dried and made into fine powder. This powder was soaked in 70% hydro-ethanol. After 24 hrs 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)¹². The product has been thorough quality control testing and has demonstrated consistent concentration of the plant extract. The Programmed clinical trail was done in the Out-Patient Clinics of the State Ayurvedic Medical College & Hospital, Govt. of West Bengal, Kolkata. The trial was conducted in accordance with good clinical practice guidelines and conforming to the declaration of Helsinki, following approval by the Institutional Ethical Committee. Participants of both sexes, of age group 18-60 yrs, suffering from GAD, diagnosed during initial observation of the participant and filling up of the Proforma for detailed general examination of the participants and Brief Psychiatric Rating Scale (BPRS)¹³ and in whom the exclusion criteria were absent, were included in this study, after getting their informed written consent either in mother tongue (Bengali or Hindi) or in English as the case may be. The exclusion criteria of the study were hepatic and/or renal disease, severe depression, organic lesion, uncontrolled diabetic patient, and pregnant and lactating mother.

Participants 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 (ACE) and was administered orally in dose of one capsule, twice daily after meal. Hence, each participant 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 β -blockers anti-depressants, etc. was permitted throughout the study. The participants were followed-up at day 30 and finally at day 60 from the starting of medication. Study endpoints assessed and analyzed for each of the participants consisted of both objective and subjective measures. Primary outcome measures consisted of subjective scores from five self reported questionnaires including stress scale, anxiety scale, depression scale, adjustment scale and attention scale¹³⁻¹⁵. The questionnaires were chosen because they have been validated and are widely accepted amongst healthcare professionals. The scale also includes a number of direct queries about current levels of experienced stress. Moreover, the questions are a general nature and hence are relatively free of content specific to any subpopulation group. The statistical analysis of the data was performed according to by *Chi-Square* test and percentile change compared to baseline results¹⁶.

Results and discussion

Stress is a risk factor for a number of diseases and is an important predictor of health in general. The physiology of stress has been well characterized with an emphasis on the hypothalamic-pituitary-adrenal (HPA) axis. It is well known that the immune system and the nervous system are in constant communication and are held in a subtle balance that can be distorted by the impact of stress¹⁷. Indian traditional medicine, Ayurveda has based on a mind-body medicine approach with an emphasis on relaxation techniques like yoga, meditation and the use of ingested natural health products to provide a pharmacological action in order to provide an 'adaptogenic' or protective effect against stress¹⁸.

In the study, *Vaca* was evaluated for its putative adaptogenic action to negate anxiety, stress and depression (Table 1). We enrolled 40 participants for the period of 60 days. Thirty three participants completed the trial (20 male, 13 female; average age 36.2 yrs). Regarding occupation there were

service holders (7), house wives (10), businessmen (9), students (6) and unemployed (1). Seven participants withdrew due to scheduling conflicts. The participants were selected on the basis of seven point scoring system of modified Hamilton's Brief Psychiatric Rating Scale. None of the participants reported self-perceived adverse events, nor were any observed by the monitoring physician. 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 disorders¹⁹. Table 2 displays the overall effects of ACE on subjective outcome reports results from the five

self reported questionnaires in all eight domains. The results indicated that ACE ingestion (500 mg capsule, twice daily for 60 days) significantly attenuated anxiety-stress-disorders. The overall clinical features also improved after the treatment. For our primary outcomes, we observed a 23.3% improvement in self-perceived stress. The state and trait anxiety scale reported overall changes from baseline of 95 and 18.9%. The depression scale improved by 22.5%. Adjustment score improved by 22.8%. Each of these results was statistically significant with *P*-values all <0.0001. Attention score demonstrated a modest improvement of 9.2%; however, this was not statistically significant.

The present clinical trial supports the contention that, two-month regular administration with *Vaca* or *Acorus calamus* reduced stress, attenuated anxiety, negated depression and enhanced adjustment and attention in human subject without any side effects like vertigo, nausea, and dizziness or mental weakness. The treatment also helped in mental overwork in daily life. These observations clearly indicate that ACE has potential action in the regulation of hypothalamic-pituitary-adrenal (HPA) axis especially, during stress related disorders in human. The findings of this trial should be of interest to physicians and patients alike. It appears that *Vaca* or *Acorus calamus* may be a safer alternative to Benzodiazepines for the therapy of stress related clinical disorders.

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Table 1—The distribution of subjects for trial

Total Subjects (N)	33
Male	20
Female	13
Religion	
Hindu	26
Muslim	7
Average age (36.2 yrs)	
<18 years	0
18-35 years	17
36-50 years	12
>50 years	4
Occupation	
Service holder	7
House wife	10
Student	6
Business	9
Others	1

Table 2—Effect of *Vaca* or *Acorus calamus* rhizomes extract on GAD in human Psychological Rating Scales (score)
[Values are mean ± SD of 33 participants]

	Baseline (Day 0)	Visit I (Day 30)	% Change	p-value	Visit II (Day 60)	% Change	p-value
<i>Anxiety</i>	94.96±7.80	85.36±9.22	-10.1	0.001	77.0±9.05	-18.9	0.001
<i>Stress</i>	77.93±9.25	66.96±8.02	-14.1	0.001	59.75±7.60	-23.3	0.001
<i>Depression</i>	63.36±7.15	55.96±6.82	-11.6	0.001	49.06±8.34	-22.5	0.001
<i>Adjustment</i>	41.90±7.12	46.81±6.90	-10.4	0.02	51.51±6.17	-22.8	0.001
<i>Attention</i>	3.24±0.85	3.34±0.62	-3.1	NS	3.54±0.75	-9.2	NS

The dose of ACE is 500 mg capsule, twice daily, p.o. after meal

The results were statistically compared to baseline (before treatment) using *Chi-Square test*

Per cent change over baseline

NS = non-significant

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