Clinical Evaluation of Chandana (Santalum album, Linn.) in the Generalized Anxiety Disorder (GAD) with Special Reference to Aromatherapy

INTRODUCTION
Intervention

Mental disorders are outcomes of the fast mechanical and materialistic age, in which people come increasingly under the influence of stress and strain. The incidence of anxiety is increasing day by day. The prevalence of anxiety states has been variously given as 2-5% of the total population (Rees, 1988). The generalized anxiety disorder (GAD) is the commonest type among the nine types of anxiety. Among all anxiety states, the lifetime prevalence of generalized anxiety disorder (GAD) has been estimated as 5% (Parikh, 1999); and according to another study the one year prevalence of GAD has been reported as 3.8% (Hollander and Simeon, 2003). As a result, the use of Allopathic anxiolytic agents is also increasing, which have further deleterious effects on the brain, nervous system and other organs. The drugs like diazepam, alprazolam may also cause dependence. Their adverse effects include aggression, excitement, confusion, headache, giddiness, alimentary tract upset, skin rashes, reduced libido etc. (Laurence and Bennett, 1987).

According to Ayurveda the GAD can be considered as Chittodvega, as its symptoms are almost similar to the generalized anxiety. The GAD causes clinically significant distress or impairment in social, occupational and other important areas of functioning, and the sufferer becomes like a handicapped person and cannot perform his work and duties properly, that affects the whole set-up of the family. Therefore this problem was selected for the present study.

Since many available modern drugs have their own limitations when the dangerous side effects are taken into account; hence, it has become the need of the medical community to find out safer and cost-effective anxiolytic alternatives from the natural forms of medicines, used in the health care systems like Ayurveda and Unani Medicine. It is also considerable that the natural medicines, which are already proven effective and safe on the basis of experiences of the Vaidyas and Hakeems over thousands of year’s time,
are more valuable than the unknown drugs to be tested directly (reverse pharmacology way).

There are many herbs which are in use for the treatment of psychiatric disorders especially anxiety and stress. However, a lot of work has already been carried out and published on the herbs, like Shankhapushpi (*Convolvulus pluricaulis*), Mandukparni (*Centella asiatica*), Brahmi (*Bacopa monnieri*), Jyotismati (*Celastrus paniculatus*), Jatamansi (*Nardostachys jatamansi*), Ashwagandha (*Withania somnifera*), Yashtimadhu (*Glycyrrhiza glabra*) regarding their promising effects on anxiety and stress.

History reveals the use of Chandana for its soothing effects on minds. Particularly, the Sandalwood paste application on the forehead between the eyebrows is the common Indian tradition, practiced by the religious personalities for the purpose of peace of mind. Interestingly, Ayurveda says there is a central nerve or node of nerves on the forehead (*sthapani marma*), so the application of cooling Sandalwood at this spot serves to tranquilize the individual (Patnaik, 1994).

The modern form of Aromatherapy is developed basically by the integration of the literature of aromatic natural substances and their use in Chinese Medicine, Ayurveda, and Greek Medicine. The modern Aromatherapists also recommend the use of the essential oil of Sandalwood to treat insomnia, nervous tension and stress related conditions (Lawless, 1999).

There are many references found in the literature of Ayurveda and Unani Medicine regarding Chandana for its soothing effects on the mind (Patnaik, 1994; Kabiruddin, 1978). However, its anxiolytic effect is yet to be screened on the scientific parameters. Therefore, Chandana is selected for the present study.

**Aims and Objects:**

The main aim of the present study is to clinically evaluate the effects of Chandana (Sandalwood) oil used as aroma inhalation in Generalized Anxiety Disorder (GAD) in the human individuals.
The objective of this study was to evaluate whether the Aromatherapy could prove, as an effective route of administration for the treatment of G.A.D. with the Chandana oil.

**Review of Literature:**
A thorough review of literature on Chandana (Santalum album, Linn.) was taken from vedic era till date. Also the review of Generalized Anxiety Disorder and Chittodvega was taken. Latest updates regarding the pharmacological actions, chemical constituents and pharmacognostic studies of the Chandana as well as G.A.D. were also taken from various journals, authentic Internet websites, information centres like N.I.C. and different libraries.

**Materials and Methods:**
1. **Test drug standardization:**
The test drug i.e. Sandalwood essential oil, was procured from the Fragrance and Flavour Development Centre (FFDC), Kannauj, U.P. India. Standardization of the essential oil of Chandana was made to ensure its identity, purity and quality. The authentication of the oil was done through the Holistic Health Care & Research Organization, Pune, India with arrangements of GC-MS made by the Aromatics International Inc., United States.

2. **Clinical Study:**
A controlled, randomized, single-blind clinical trial was conducted, as per G.C.P. guidelines, on the individuals suffering from generalized anxiety disorder (GAD). The permission of the Institutional Ethics Committee (IEC) was taken prior to the initiation of the clinical trial.

The human individuals of same socio-economic status, irrespective of sex and religion, between the age group of 25 to 40 years, suffering from mild to moderate Generalized Anxiety Disorder (GAD) and willingly accepting the treatment were included in the clinical trial. Informed Consent Form was given to each individual. The clinical trial was conducted on 100 completed patients.

The individuals having other types of anxiety disorders were not included in the study. The patients having tuberculosis, diabetes,
hypertension, renal disorders, cardiac disorders and other psychiatric problems and life threatening diseases were excluded from the study. The patients suffering from severe GAD, and / or not willingly accepting the treatment were also excluded from the clinical trial.

In the initial (baseline) phase of the clinical trial, the patients were diagnosed through the DSM-IV-TR diagnostic criteria (Hollander and Simeon, 2003). Initially, the Daśavidha Parikṣa was performed, in which the parameters observed were viz. Prākṛti, Viṅkṛti, Sāra, Saṃhanana, Pramāṇa, Saṭmya, Saṭvā, Ahāra Śakti, Vyayama Śakti and Vaya. Further diagnosis and assessment of the severity of was G.A.D. done through the Hamilton Rating Scale for Anxiety (HAM-A) on each fifteen days.

They patients were divided by random sampling, according to lottery method, into two groups, viz. Test group, those treated with Sandalwood oil by inhalation + Placebo (starch) capsules orally; and Control group, those were administered only Placebo (starch) capsules orally.

**Observations:**

The assessments regarding symptoms of G.A.D. were made on each fifteen days, for two months. The observations were recorded on separate sheets based on changes in scores of the Hamilton Rating Scale for Anxiety (HAM-A).

The analysis of all the results was done statistically by the One-way Analysis of Variance (ANOVA) – Dunnett Multiple Comparisons Test, using Graph Pad InStat.

**Conclusion:**

The conclusion was drawn based upon the observations and results of the statistical analysis. As a whole the results were encouraging, and the study opened a new dimension for the researchers to further work in this field.

**Layout of the Thesis:**

The Chapters included in this study are viz. Abstract, Introduction, Review of Literature, Materials and Methods, Observations and Results, Discussion, Conclusion, Summary, Bibliography and Appendices.
A thorough **Review of Literature** has been done on the test drug, viz. essential oil of Chandana (Sandalwood) and the disease Generalized Anxiety Disorder (G.A.D.). The **Drug Profile** of Chandana covers detailed information on Classification, Vernaculars, Interpretation of Sanskrit Vernaculars, Historical Background, Varieties, Drug Description (Morphology), Habitat and Geographical Distribution, Parts Used, Actions & Uses, Rasapancaka, Dose, Miscellaneous Uses, Pharmacognosy, Phytochemistry, Chemical Constituents, Pharmacological Actions, Adverse Reactions, Toxicology, Adulterants and Substitutes, Important Formulations (Kalpa), Miscellaneous Preparations, Soil and Climate, Propagation and Cultivation, Essential Oil of Sandalwood, Commercial Aspects, Threats, Range and Population, Conservation Measures. Drug profile also includes information of Chandana (Sandal Sufaid) in Unani Medicine that covers *Mizâj* (Constitution), *Afāl Wa Ista’Mâl* (Actions and Uses) and Dose.

The **Disease Review** includes two major parts, i.e. Ayurvedic Approach Towards Generalized Anxiety Disorder (G.A.D.) and information on Generalized Anxiety Disorder (G.A.D.) in main-stream medicine. In Ayurvedic Approach Towards G.A.D., the topic covered are - Manas And Its Functions, Causes of Mental Diseases, Types of Mental Diseases, Chittodvega, Preventive Measures In Ayurveda, Management In Ayurveda. The information on Generalized Anxiety Disorder (G.A.D.) covers comprehensively – Introduction, Epidemiology, Symptoms, Differential Diagnosis, Mechanisms And Theories, Course And Prognosis, Hamilton Rating Scale For Anxiety (Ham-A), Treatment In Main-Stream Medicine.

The chapter **Materials and Methods** is divided into two parts, i.e. **Test Drug Standardization, Clinical Trial Protocol and Assessment Criteria**. The Clinical protocol further divided in different parts like Trial Design, Sample Size, Ethical clearance, Criteria of Selection (Baseline Screening), Inclusion Criteria, Exclusion Criteria, Grouping, Dosage and Route of Administration, Time of Administration, Duration of administration of the drugs, Drop-outs and Follow ups. The Assessment Criteria part includes Case Report Form (CRF), Psychometric Analysis of Generalized Anxiety
Disorder (GAD), Statistical Analysis, Adverse Drug Reactions (ADR) and Criteria of Withdrawal.

The chapter of Observations and Results includes reports of Test Drug Standardization, Observations of Demographic Data and Results of Clinical Trial in tabular as well as graphic forms.

The chapter of Discussion includes General discussion, Probable mode of action and Scope and limitations of the study. The chapter of Conclusion contains a brief to the point information of the final outcome of the present clinical study.

The chapter of Summary includes a summarized version different parts of the complete study. The chapter Bibliography covers all detailed references cited in whole thesis. The Appendices included in the last of Thesis are – Appendix 1 (DSM-IV-TR Diagnostic Proforma for Generalized Anxiety Disorder), Appendix 2 (Informed Consent), Appendix 3 (Case Report Form), Appendix 4 (Proforma for Prakruti Parikshan), Appendix 5 (Sara Pariksha), Appendix 6 (Satwa Pariksha) and Appendix 7 (Hamilton Anxiety Scale).