A Dissertation On

"EFFICACY OF CLARY SAGE OIL ON PRE-MENSTRUAL SYNDROME(PMS) – A CONTROLLED TRIAL"

Submitted By

Dr. GEETHANJALI.S, B.N.Y.S (Reg. No: 461613001)

Under the Guidance of

Prof. Dr. N. MANGAIARKARASI, B.N.Y.S; M.Sc.(psy)., PGDHAN,

Submitted to

The Tamilnadu Dr. M. G. R. Medical University, Chennai

In partial fulfillment of the requirements for the award of degree of

DOCTOR OF MEDICINE

IN

BRANCH – III: ACUPUNCTURE & ENERGY MEDICINE

POST GRADUATE DEPARTMENT OF ACUPUNCTURE & ENERGY MEDICINE GOVERNMENT YOGA AND NATUROPATHY MEDICAL COLLEGE AND HOSPITAL, ARUMBAKKAM, CHENNAI – 600106.

OCTOBER 2019

GOVERNMENT YOGA AND NATUROPATHY MEDICAL

COLLEGE AND HOSPITAL, CHENNAI, TAMILNADU.

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **"EFFICACY OF CLARY SAGE OIL ON PREMENSTRUAL SYNDROME(PMS) – A CONTROLLED TRIAL"** is a bonafide research work done by the post graduate **Dr. GEETHANJALI.S ,** Department of Acupuncture & Energy Medicine, Government Yoga & Naturopathy Medical College & Hospital, Chennai – 600 106 under my guidance and supervision in partial fulfillment of regulations of **The Tamilnadu Dr. M.G.R. Medical University, Chennai** for the award of **M.D. (Acupuncture & Energy Medicine) Branch – III** during the academic period from 2016-2019.

Date: **SIGNATURE OF THE GUIDE**

Place: Chennai **Dr.N.MANGAIARKARASI**

B.N.Y.S.,M.Sc.(psy),PGDHAN

Head of the Department,
Department of Acupuncture & Energy Medicine,
Government Yoga & Naturopathy Medical College & Hospital,
Arumbakkam, Chennai – 600 106.

GOVERNMENT YOGA AND NATUROPATHY MEDICAL COLLEGE AND HOSPITAL, CHENNAI, TAMILNADU.

ENDORSEMENT BY THE HEAD OF THE DEPARTMENT

I certify that the dissertation entitled **"EFFICACY OF CLARY SAGE OIL ON PREMENSTRUAL SYNDROME(PMS) – A CONTROLLED TRIAL"** is the record of original research work carried out by **Dr. GEETHANJALI. S ,** in the Department of Acupuncture & Energy Medicine, Government Yoga & Naturopathy Medical College & Hospital, Chennai – 600 106 submitted for the degree of **DOCTOR OF MEDICINE (M.D) in Yoga and Naturopathy** under my guidance and supervision, and that this work has not formed the basis for the award of any degree, associate ship, fellowship or other titles in this University or any other University or Institution of higher learning.

Date: **SIGNATURE OF THE GUIDE**

Place: Chennai **Dr.N.MANGAIARKARASI**

B.N.Y.S.,M.Sc.(psy),PGDHAN
Head of the Department,
Department of Acupuncture & Energy Medicine,
Government Yoga & Naturopathy Medical College
& Hospital, Arumbakkam, Chennai – 600 106.

GOVERNMENT YOGA AND NATUROPATHY MEDICAL COLLEGE AND HOSPITAL, CHENNAI, TAMILNADU.

ENDORSEMENT BY THE PRINCIPAL

I certify that the dissertation entitled is **"EFFICACY OF CLARY SAGE OIL ON PRE-MENSTRUAL SYNDROME(PMS) – A CONTROLLED TRIAL"** the record of original research work carried out by Dr. GEETHANJALI. S, in the Department of Acupuncture & Energy Medicine, Government Yoga & Naturopathy Medical College & Hospital, Chennai – 600 106 submitted for the degree of DOCTOR OF MEDICINE (M.D) in Acupuncture & Energy Medicine under my guidance and supervision, and that this work has not formed the basis for the award of any degree, associateship, fellowship or other titles in this University or any other University or Institution of higher learning.

Date: **SIGNATURE OF THE PRINCIPAL**

Place: Chennai **Dr. N. MANAVALAN,**

N.D.(OSM), M. A (G.T), M.Sc (Y&N), M. Phil,

P.G.D.Y, P.G.D.H.M, P.G.D.H.H,

Government Yoga & Naturopathy Medical College & Hospital,

Arumbakkam, Chennai – 600 106.

GOVERNMENT YOGA AND NATUROPATHY MEDICAL COLLEGE AND HOSPITAL, CHENNAI, TAMILNADU.

DECLARATION BY THE CANDIDATE

I, Dr. GEETHANJALI. S solemnly declare that dissertation titled **"EFFICACY OF CLARY SAGE OIL ON PRE-MENSTRUAL SYNDROME(PMS) – A CONTROLLED TRIAL"**

is a bonafide and genuine research work carried out by me at Government Yoga & Naturopathy Medical College & Hospital, Chennai from May 2018 – May 2019 under the guidance and supervision of Dr. N. MANGAIARKARASI, Head of the Department, Department of Acupuncture and Energy Medicine, Govt. Yoga & Naturopathy Medical College & Hospital, Chennai. This dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University towards partial fulfillment of requirement for the award of M.D. Degree (Branch – III) in Acupuncture & Energy Medicine.

Date: Signature of the Candidate

Place: Chennai **(Dr. GEETHANJALI.S)**

INSTITUTIONAL ETHICAL COMMITTEE

GOVERNMENT YOGA AND NATUROPATHY MEDICAL COLLEGE AND HOSPITAL, CHENNAI – 600 106.

CERTIFICATE OF APPROVAL

The Institution Ethical Committee of Government Yoga & Naturopathy Medical College & Hospital, Chennai reviewed and discussed the application for approval of **"EFFICACY OF CLARY SAGE OIL ON PRE-MENSTRUAL SYNDROME(PMS) – A CONTROLLED TRIAL"** for project work submitted by Dr. Geethanjali. S, 2nd Year M.D. Acupuncture & Energy Medicine, Post Graduate, Government Yoga & Naturopathy Medical College & Hospital, Chennai – 600 106.

The proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study and adverse drug reaction during the course of the study and any change in the protocol and patient information / informed consent and asks to be provided a copy of the final report.

COPY RIGHT

DECLARATION BY THE CANDIDATE

I hereby declare that the Tamilnadu Dr. M. G. R. Medical University, Chennai, Tamilnadu shall have the rights to preserve, use and disseminate this Dissertation / Thesis in print or electronic format for academic / research purpose.

Date: Signature of the Candidate:

Place: Chennai **(DR. GEETHANJALI.S)**

ACKNOWLEDGEMENT

Foremost, I express my sincere gratitude to Dr. N. Manavalan, Principal, Govt. Yoga & Naturopathy Medical College, Chennai, for giving me this opportunity to pursue my Post Graduation degree M.D. Acupuncture & Energy Medicine from this prestigious institute.

I extend my gratitude towards Dr. N. Mangaiarkarasi, H.O.D., Department of Acupuncture and Energy Medicine, Govt. Yoga and Naturopathy Medical College and Hospital, Chennai for her constant support and encouragement. I once again thank Dr. N. Mangaiarkarasi mam for her continuous support and provision of all necessary requirements needed for the completion of this dissertation.

I am very much thankful to Dr. S. T. Venkateswaran, H.O.D., Department of Yoga for his support and guidance.

I thank all the people who volunteered for the research by giving their most valuable time for my research.

I express my heartfelt gratitude to Dr. Rosy Ayda. Y, Dr. Prabu. P, Dr. Venugopal. V, Dr. Sujithra. T.S and my batchmates for giving their constant support and time throughout the completion of this dissertation and also for helping me through the intervention and interpretations needed for this study.

I am indebted to thank my guru (late)**Dr. R. S. HIMESWARI,** for giving me the knowledge about different styles of acupuncture and concept of Energy Medicine and encouraging me in completing the study.

I express my thanks to my family members for always being there for me, motivating and morally supporting me throughout my research.

I thank all the teaching & non-teaching staffs of GYNMCH for their support.

My sincere thanks go out to all my Post-Graduate and Undergraduate friends who have been there at all phases of this study including the preparation of this dissertation.

Above all I thank God for all that I am blessed with.

Date: Signature of the Candidate:

Place: Chennai (Dr. GEETHANJALI. S)

LIST OF ABBREVATIONS

PARTICULAR	ABBREVIATION
Pre-Menstrual Syndrome	PMS
Premenstrual dysphoric disorder	PMDD
Premenstrual syndrome screening tool	PSST
Premenstrual syndrome scale	PMSS
National association of Premenstrual syndrome	NAPS
American college of Obstetricians and Gynecologists	ACOG
Interferons	IFN
Orbito-frontal cortex	OFC
Positron emission tomography	PET
Cold pressor test	CPT
Monoamine oxidase activity	MAO
Gamma-aminobutyric acid	GABA
Diagnostic and statistical manual of mental disorders- IV	DSM-IV
Central nervous system	CNS
Autonomic nervous system	ANS
Sympathetic nervous system	SNS
Parasympathetic nervous system	PNS
Menstrual distress questionnaire	MDS
Randomized control trial	RCT

International Classification of Diseases	ICD
Oral contraceptive pills	OCP
Allopregnanolone	ALLO
Gonadotropin releasing hormone	GnRH
Catechol -O- methyltransferase	COMT
Daily record of severity of problems	DRSP
Complementary and alternative medicine	CAM
Over the counter	OTC
Contingent negative variation	CNV
Systolic blood pressure	SBP
Diastolic blood pressure	DBP
Electrodermal galvanic activity	EDG
Visual analogue scale	VAS
Isometric hand grip	IHG
Defense institute of physiology and allied sciences	DIPAS
Skin conductance level	SCL
Mental component summary	MCS
Physical component summary	PCS
The inventory to measure psychological stress	IMPS
Beck depression inventory	BDI
State trait anxiety inventory	STAI

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

AIMS & OBJECTIVE: To assess and evaluate the effects of clary sage oil in Premenstrual syndrome.

BACKGROUND: Premenstrual syndrome (PMS) is a condition that presents with distressing physical, behavioral, and psychological symptoms, in the absence of organic or underlying psychiatric disease, which regularly recurs during the luteal phase of each menstrual cycle, and which disappears or significantly regresses by the end of menstruation. It has been estimated from retrospective community surveys that nearly 90% of women have experienced at least some symptoms attributed to the premenstrual phase of menstrual cycle during their life.

Aromatherapy is the practice of therapeutic use of essential plant-based oils. Essential oils and aromatherapy have been used in the care of women for centuries. Clary sage is a gift to the female and has a rejuvenating effect on the endocrine system and balances the pituitary and is specifically indicated in treating PMS. In aromatherapy, there are limited studies on Premenstrual syndrome. Moreover most papers are based on other aroma oils.

DESIGN AND METHOD: 60 subjects were screened using Premenstrual Syndrome Screening Tool and randomized using convenient sampling method and into Study group (N = 30) and Placebo-control group (N= 30) on 1:1 ratio. The Subjects of Study group and Placebo-control group received their respective treatment three days a week

for three months. Data was collected before and after 3 months of treatment using Premenstrual Syndrome Scale.

RESULTS: The results show a high level of statistical and clinical significance and highly favours the intervention group in the reduction of all 3 components of the PMSS when compared to the placebo-controlled group.

CONCLUSION: This trial suggested that Clary sage oil helps in reducing the physiological, psychological and behavioural symptoms of Premenstrual syndrome.

KEY WORDS: Pre-menstrual syndrome, Clary sage, Aromatherapy, Premenstrual Syndrome Screening tool, Premenstrual Syndrome Scale.

1.INTRODUCTION

Premenstrual syndrome (PMS) is a condition that presents with distressing physical, behavioral, and psychological symptoms, in the absence of organic or underlying psychiatric disease, which regularly recurs during the luteal phase of each menstrual cycle, and which disappears or significantly regresses by the end of menstruation[1].Although mild symptoms occur in approximately 75% of women of reproductive age[2],40% of women are reported to suffer from clinically significant PMS[3]

The prevalence of PMS has been reported in 20-32% of premenopausal [4]and 30%-40% of the reproductive female population globally [5]. The prevalence of PMS is reported to be 67% in India [6]. Women with PMS usually complain of somatic symptoms, such as food cravings, mastalgia, bloating, headache, lack of energy, abdominal discomfort and pain, and weight gain. Frequently reported affective changes include depression, angry outbursts, crying spells, anxiety, irritability, and feelings of being unable to cope [1].

The exact etiology of PMS is unknown, but it may be related to hormone variations. Some theories state that PMS is not caused by abnormal concentration of gonadal steroids but more likely by variations in levels of the sex hormones. The differences between women with and without PMS may also be explained by increased sensitivity to variations in levels of sex hormones[7].Moreover, some studies showed that the onset and course of PMS are related to stress[8].The variations in hormone levels across the menstrual cycle cause an increase in

negative emotions in women and can influence mood regulation and sensitivity to stress[9,10]. Specifically, women have stronger responses to stressors before the menstruation or in the luteal phase, which may increase the risk for negative emotions or moods, suggesting stress may strengthen PMS symptoms [11].

The pathophysiology of PMS or PMDD have not been established and hypotheses included hormone imbalances, sodium retention, nutritional deficiencies, abnormal neurotransmitter responses to normal ovarian function and abnormal hypothalamic pituitary-adrenal axis function [12,13].

PMS symptoms, even though mild to moderate in intensity, might adversely affect and influence daily activities and work productivity [14]. It is more pronounced in cases of working females. Most of the studies done on this subject worldwide focus on women in general population or a specific subset of working females [15].

1.1 Background:

Numerous treatments have been proposed over the past sixty years, and although some have been successful, each has adverse effects which may well outweigh their benefits [16]. O'Brien [17] stated that the proposed treatments were

"*either ineffective or that the high placebo effect in premenstrual syndrome leads to over optimistic conclusions being drawn*".

Many doctors do not believe there is such condition as PMS and, consequently, fail to recognize and treat it. Of 482 women who called the National Association

for Premenstrual Syndrome (NAPS) helpline last year, 42% said that their GPs were unsympathetic or did not seem to know much about PMS[18]. Its recognition is a twentieth century event, reflecting changes in our social structure and lifestyle. In the past the time between puberty and the menopause was filled with many pregnancies when PMS disappears. Each was followed by the cessation of ovulation caused by prolonged breastfeeding. Nowadays with fewer pregnancies the effects of the menstrual cycle are more apparent [19].

1.2 Prevalence:

The true prevalence of PMS is difficult to determine because of self-treatment, differences in availability and access to health services, definition & diagnostic criteria and cultural practices [20]. It has been estimated from retrospective community surveys that nearly 90% of women have experienced at least one premenstrual syndrome. Epidemiological surveys have estimated that as many as 75% of women in their reproductive age experience some symptoms attributed to the premenstrual phase of menstrual cycle during their life [21,22].It is also estimated that up to 85% of premenopausal women experience at least one premenstrual symptom and 15-20% meet clinical criteria for premenstrual syndrome (PMS) [23]. Among the gynecological problems, menstrual problems are said to be the major ones especially among adolescent females [24].

1.3 Clinical features:

Premenstrual symptoms reappear monthly and last for an average of 6 days per month for the majority of the reproductive years. It has been calculated that

affected women experience almost 3000 days of severe symptoms during the reproductive years [25]. The significant appearance of these symptoms starts from the teen years and worsen through the process of ageing [25]. More than 200 symptoms of PMS have been described in literature, ranging from mild symptoms to those severe enough to interfere with normal activities [26].

The most important somatic symptoms are feeling overwhelmed, food craving, insomnia or hypersomnia, headache, pelvic pain and discomfort, breast tenderness, joint pain, bloating ; and the most common and distressing affective symptoms are irritability, anxiety, depression, mood swinging, hostility, poor concentration, confusion, social withdrawal and interpersonal conflicts[27,28].Of these, six symptoms identified as core symptoms suggesting that clinical diagnosis of PMS can be developed around a core symptom group. The identified core symptoms are: anxiety/tension, mood swings, aches, appetite/food cravings, cramps, and decreased interest in activities [29].

1.4 Pathophysiology of PMS:

In evolutionary terms,[30] luteal mood changes could be remnants of the oestrogen cycle-related fluctuations in behaviour shown by lower species with the original purpose of promoting reproduction: sexual receptivity being increased and aggression decreased when oestrogen is high before ovulation[31,32].

1.4.1 Role of Progesterone:

Since the 1980s, the factor responsible for provoking symptoms of PMS has been attributed to the progesterone produced by the corpus luteum [33]. During anovulatory cycles, when a corpus luteum fails to form, the symptoms of PMS are not observed [34]. Premenarchal girls, postmenopausal women and those who have undergone bilateral oophorectomy also do not experience PMS. Nevertheless, the role of progesterone in triggering adverse symptomatology is not straightforward. For example, PMS symptoms are absent during pregnancy, in spite of high progesterone and estrogen concentrations. It is unclear how long after conception the typical PMS symptoms that are linked to the luteal phase hormonal complement will diminish. Administration of exogenous progesterone or a progestogen can also engender symptoms akin to PMS. Postmenopausal women receiving hormonal therapy consisting of both estrogen and a progestogen may experience PMS-like complaints consisting of negative mood and somatic symptoms. These undesirable effects were investigated and have been attributed to the progestogen [35]. In addition, PMS-like symptoms often persist even after anovulation has been induced with a hormonal contraceptive, and again it has been hypothesized that the exogenous progestogens are responsible, although the dose of estrogen may also be relevant. There are a number of studies suggesting oral contraceptive pills (OCPs), regardless of the elimination of ovulation, can be associated with ‘PMS-like’ negative affective and physical symptoms such as irritability, depression, anxiety, bloating, fatigue and breast tenderness in a subset of women [36]. Although compelling evidence

points to the role of progesterone in the pathophysiology of PMDs, it appears that the classical progesterone receptor is not involved in this process. This observation is supported by lack of reduction in physical or behavioural manifestation of PMS with administration of the progesterone receptor antagonist, mifepristone [37]. In addition, numerous studies have been unable to provide evidence for progesterone excess or deficiency in the aetiology of PMDs. In multiple studies, measurement of serum progesterone in women with PMS compared with controls failed to show any significant differences [33]. Finally, a series of randomized double-blinded placebo-controlled trials (RCTs) failed to show efficacy of progesterone supplementation [38]. Other reproductive hormones, estradiol, testosterone, the adrenal hormones cortisol and dehydroepiandrosterone sulphate and the pituitary and thyroid hormones including prolactin and thyroxin also fail to distinguish women with PMDs from controls. Although in one study, more severe symptoms were found in cycles with higher concentrations of both estradiol and progesterone [39]. It appears that women with PMDs are more sensitive to developing negative mood and physical symptoms with the exposure to normal concentrations of ovarian sex steroids. Women with PMS, but not asymptomatic women, had a negative affective response to the administration of physiological doses of exogenous estradiol or progesterone after having achieved a ‘chemical menopause’ by receiving a gonadotrophin-releasing hormone (GnRH) agonist [40]. The metabolites of progesterone (and corticosterone) have psychoactive properties and have been known for almost a century to produce sedation in animals. These effects are not

mediated through the classical progesterone receptor. Given this evidence, researchers have postulated that a metabolite of progesterone may contribute to the generation of the affective and physical symptoms of PMDs through the modulation of a different receptor mechanism.

1.4.2 Gamma Amino Butyric Acid:

Temporal onset of PMS begins with ovulation and is likely related to progesterone production. The rising concentration of estradiol in the late follicular phase or a hormonal milieu consisting of estrogen alone fails to produce PMS symptoms. However, progesterone itself did not seem to be specifically the key, leading researchers to investigate the role of the neuroactive metabolites of progesterone that were known to affect mood and behaviour. In the ovary and the brain, progesterone is metabolized to form the potent neuroactive steroids, 3-alpha-hydroxy-5-alpha-pregnane-20-one (allopregnanolone or ALLO) and 3-alpha-hydroxy-5beta-pregnane20-one (pregnanolone). These metabolites act as positive allosteric modulators of the GABA neurotransmitter system in the brain. The main inhibitory neurotransmitter in the brain, GABA, is a widely distributed neurotransmitter in the central nervous system (CNS) and evidently is an important regulator of stress, anxiety, vigilance, alertness and seizures [41] GABA is derived from glutamate, which is synthesized in series of steps by the Krebs cycle, and is then decarboxylated to GABA by the rate-limiting enzyme, glutamic acid decarboxylase, exclusively found in GABAergic neurons. GABA is then stored in vesicles found in the presynpatic terminal of GABAergic neurons. Three

subtypes of GABA postsynaptic receptors have been identified: GABAA, GABAB and GABAC receptors. However, it is the GABAA receptor that is the site of action of endogenous agents such as neuroactive steroids derived from progesterone or synthesized de novo in the CNS, as well as exogenous agents such as progestogens (after metabolism to reduced steroids), benzodiazepines, barbiturates, alcohol and anticonvulsants [41]. GABAA receptors are transmembrane protein complexes composed of alpha, beta, delta and gamma subunits that function as ion channels. For example, when GABA binds to the GABAA receptor it causes a conformational change in the protein complex that results in rapid and transient opening of chloride ion channels. Chloride influx results in hyperpolarization of the membrane and decreases the likelihood of depolarization by excitatory neurotransmitters. This is in contrast to the slow classical genomic effect of cystosolic activation of steroid hormone receptors. Binding of alpha reduced progesterone, corticosterone and testosterone metabolites, barbiturates, benzodiazepines at an allosteric site on the GABAA receptor results in activation of receptor and increases neuronal inhibition via a direct and rapid mechanism as described above [41]. Research has shown that ALLO, by binding GABAA receptors, plays an important physiological modulatory role in changing the sensitivity of GABAA receptors for GABA. [41] This modulatory effect is accomplished by altering the subunit composition of the receptor, rending the receptor temporarily insensitive to modulation by neurosteroids. These compositional alterations of the GABAA receptor isoforms are postulated to be important in the aetiology of PMDs. Initially a deficiency of

these neuroactive steroids was postulated. For example, acute treatment with ALLO has been shown to have anxiolytic, antidepressive and anticonvulsant effects. Similarly, decreased neuroactive steroids have been associated with anxious and depressive behavior [42]. Reduced progesterone metabolites such as ALLO have been measured in PMS and asymptomatic women in the luteal phase and some but not all studies have shown a deficiency or an association with mood in women with PMS.[43,44] In addition to the importance of concentration of these neuroactive metabolites in determining agonistic effect on GABAA receptor, the duration of exposure also plays a critical role. For example, whereas acute, very short-term ALLO exposure decreases stress and anxiety, chronic exposure has been shown to produce an anxiety-like reaction [45]. Decreased expression and binding to the GABAA receptor as well as uncoupling of the receptor from anxiolytic modulators can result in increased anxiety. GABAA receptor configuration changes after exposure to ALLO in the luteal phase such that GABAA receptor function and modulation vary throughout the menstrual cycle. Studies completed in rodents have shown that acute and prolonged exposure as well as withdrawal from ALLO attribute to an increased in alpha-4,17 gamma-2 [46] and delta [47] subunit of GABAA receptors. This GABAA plasticity subsequently results in temporarily decreased sensitivity to GABA and GABA agonists and enhances anxiety-like behavioural changes. Although the GABA subunit studies were performed in rats, human studies using saccadic eye velocity as a proxy for GABAergic activity support the postulate that these alterations in GABAA subunit configuration and GABAergic activity likely

contribute to the negative mood symptoms associated with PMS [48]. Sundstro ¨m and Ba ¨ckstro ¨m (1998) [49] demonstrated that administration of a selective serotonin reuptake inhibitor (SSRI) in the luteal phase to women with PMS increased the saccadic eye velocity to that of control women, suggesting a re-instatement of GABAergic sensitivity by augmenting serotonin.

1.4.3 Serotonin:

Serotonin (5-HT, 5-hydroxytryptamine) has been implicated in the modulation of mood, eating, arousal and circadian rhythms. Serotonin depletion through dietary or pharmacological means leads to anxiety and depressive like symptoms. The role of serotonin in PMS has been supported by various lines of evidence. PMS symptoms overlap symptoms associated with reduction in serotonin transmission [50] These symptoms include depression, mood swings, irritability, self-deprecation, poor impulse control, sleep disturbance, anxiety, aggression, decreased pain threshold, carbohydrate cravings and difficulty in concentrating. In addition, serotonergic function has been shown to be altered during the luteal phase of the menstrual cycle in women with PMS. For example, decreased platelet uptake of serotonin [51], decreased baseline whole blood serotonin [52] and decreased platelet monoamine oxidase (MAO) activity [53] have all been shown to occur during the luteal phase of the menstrual cycle. Tryptophan loading tests in women with PMS are abnormal compared with the results for asymptomatic women. Serotonin metabolism is also modulated in part by ovarian sex steroids. Ovarian sex steroids have also been implicated in serotonin uptake, turnover, binding and transport. Finally, administration of

drugs augmenting serotonergic neurotransmission is effective for treatment of PMDs. The role of serotonin is further supported by lack of significant improvement of PMS symptoms with antidepressants that only augment norepinephrine and not serotonin. Taken together, the evidence suggests that serotonergic dysregulation may play an important role in symptomatology of PMS and that serotonin in concert with other neurotransmitters such as GABA are important in the pathophysiology underlying the disorder. 5-HT is synthesized in serotonergic neurons. Specifically, the amino acid, tryptophan, is sequentially altered by two enzymes in the CNS. First, tryptophan hydroxylase, the rate-limiting enzyme, produces 5hydroxytryptophan, then L-aromatic amino acid decarboxylase decarboxylates 5-hydroxytryptophan to 5-HT. 5-HT is then stored in vesicles in the presynaptic terminal, ready to be released upon arrival of nerve impulses. Once 5-HT is released into the synaptic cleft, it is subsequently inactivated primarily by reuptake through the high affinity pre-synaptic membrane serotonin transporter (SERT). An important clinical target for therapeutic drugs, SERT, is the site of action of the SSRIs. Serotonergic activity in the brain is affected by estrogen and progesterone; specifically sex steroids can modify serotonin availability at the neuronal synapses. For example, estrogen has been shown to increase degradation of MAO, enzyme responsible for oxidation of monoamines, and catechol-o-methyl-transferase (COMT), enzyme responsible for degradation of catecolamines. Estrogen's role in increasing degradation of MAO and COMT results in augmenting action of serotonin in regulating the availability of free tryptophan in the CNS and improving clinical effect of SSRIs.

In contrast, progesterone increases MAO activity, therefore decreases 5-HT availability, which may result in depressed mood [53].

1.4.4 Brain Neurocircuitry:

Neuroimaging studies focusing on hormonally mediated changes across the menstrual cycle and in women with PMDs compared with asymptomatic controls can provide valuable information regarding the underlying neurophysiological abnormalities in PMS and PMDD. For example, an early positron emission tomography (PET) study showed that regional cerebral blood flow in the prefrontal cortex was attenuated by pharmacological ovarian suppression, and this was subsequently normalized with estrogen or progesterone replacement [54]. A study employing protein magnetic resonance spectroscopy showed increased cortical GABA concentrations in the luteal phase of women with PMDD when compared with follicular phase; however, healthy subjects showed decreased cortical GABA [55]. The authors concluded that abnormal GABAA receptor functioning could reduce sensitivity to GABA agonists, including neuroactive steroids such as the pregnone metabolites [55]. A PET study looking at serotonin-1A receptors showed significantly smaller increment in receptor binding between the follicular and the luteal phase scans in women with PMDD compared with controls [56]. In one study using functional magnetic resonance imaging, neural response was evaluated to an emotional Go/No-Go task designed to provoke negative emotion [57]. Researchers found that women with PMDD were less able than controls to inhibit incorrect responses to affectively negative words. Control subjects showed more activity during the late luteal phase

compared with the follicular phase within the anterior-medial orbitofrontal cortex (OFC) and less activity in the lateral OFC, insula and posterior cingulate cortex. However, PMDD subject showed more activity in the amygdale during the late luteal compared with the follicular phase and less activity in the OFC [57]. This was interpreted as diminished impulse control via prefrontal 'top-down' modulation of the limbic system. In a more recent study, investigators desired to map functional brain abnormalities associated with negative mood states in PMDD. PET with [18F] fluorodeoxyglucose was used to assess regional cerebral metabolism across the menstrual cycle in women with PMDD and asymptomatic participants. Women with PMDD showed an increase in cerebellar activity from the follicular phase to the late luteal phase and this was correlated with worsening of mood. The increased activity was localized primarily to cerebellar regions that have been previously described as the 'limbic' cerebellum. The cerebellum is rich in GABA receptors containing the delta and alpha subunits and as noted above, animal models suggest women with PMDs may have deficiencies in mechanisms regulating GABA subunits. The increased cerebellar activity could reflect decreased GABA-mediated inhibition during the symptomatic luteal phase [58].

1.5 Impact of PMS:

Impact of PMS on various areas of life and health includes such as:

- ✓ These symptoms can vary between individuals and have the potential to affect work, personal life, and place additional stress on a relationship [59, 60].

- ✓ Significant correlations were found between the mean premenstrual severity and functional impairment. The severity of premenstrual affective symptoms was related to social impairment. The severity of psychological symptoms was correlated with occupational impairment. These findings confirm the prominent role of premenstrual affective symptoms and support classification guidelines focusing on both affective and physical changes [61].
- ✓ The marital relationship of PMS couples deteriorated in the luteal cycle phase [62].
- ✓ Moderate-to-severe PMS/PMDD seems to be associated with work productivity impairment and increased absenteeism, and thus poses a potential economic burden [63].
- ✓ Premenstrual period is a risk period for associated psychiatric disorders exacerbations, as the obsessive-compulsive disorder, more severe alcohol intakes in case of alcoholism, symptoms increase in schizophrenics, or higher rates of suicide attempts [64].
- ✓ Women with PMS are likely to have sexual difficulties and a higher level of sexual distress, emphasizing the importance of the sexual aspects of PMS in clinical practice [65].
- ✓ The presence of PMS is a risk factor for sexual dissatisfaction in women of reproductive age [66].

- ✓ Women with PMS and PMDD have a higher odds of BN, independent of co-morbid mental health conditions. PMS and PMDD may be important co-morbidities to BN to consider in clinical settings, and future research should investigate whether PMS and PMDD affect the onset and duration of bulimic symptoms as well as the potential for shared risk factors across disorders [67].

- ✓ This study demonstrates a strong, independent association between PMS/PMDD and trait anger among a representative sample of female suicide attempters. It is of major interest for clinicians in view of addressing a substantial public health problem among women of reproductive age [68].

- ✓ Serum levels of inflammatory markers, including interleukin (IL)-2, IL-4, IL-10, IL-12 and interferon (IFN)-γ were positively associated with menstrual symptom severity and/or PMS in young women [69].

- ✓ PMS/PMDD is an important risk factor for PPD. Women endorsing a history of PMS/PMDD should be monitored during the perinatal period [70].

- ✓ The diastolic blood pressure is elevated in young adult women experiencing PMS [71].

- ✓ PMS had an elevated frequency in medical students. In students with PMS, rate of depression was higher than students without PMS [72].

1.6 Diagnosis:

There are no specific physical findings or laboratory tests that can be utilized to make the diagnosis of PMS. In a Practice Bulletin published in the year 2000, The

American college of obstetricians and gynecologists (ACOG) defined diagnostic criteria for PMS based on the work of Mortola (1990) describes that PMS can be diagnosed if at least one of the affective and one of the somatic symptoms are reported five days prior to the onset of menses in the three prior menstrual cycles. The symptoms must be prospectively recorded in at least two cycles and must cease within 4 days of onset of menses and not recur until after day 12 of the cycle. These symptoms must be recorded in the absence of pharmacologic therapy, or use of hormones, drugs, or alcohol, and cause identified dysfunction in social or work-related activities [73]. Premenstrual symptoms may cause several difficulties for women including impairment in physical functioning, psychological health and severe dysfunction in social or occupational realms [74]. In young adolescents, symptoms might particularly affect school functions, and social interactions in a negative way [75]. Previous studies have also shown that women with premenstrual disorders have a poor health-related quality of life [76, 77].

1.7 Conventional therapies:

1.7.1 General Principles of Treatment:

When managing women with PMS, there are certain principles that should be adhered to. Even though not evidence-based, there is little doubt that reduction of stress for instance is a great help in ameliorating the symptoms. Also, dietary measures such as avoidance of carbohydrate binges and limitation of alcohol and caffeine intake are often of benefit. There are data from non-randomised trials suggesting that exercise improves PMS symptoms.However, in cases of moderate

to severe PMS, it is important that medical therapy is instituted sooner rather than later to avoid unnecessary suffering. Women with marked underlying psychopathology as well as PMS should be referred to a psychiatrist. Symptom diaries (e.g. the DRSP) should be used to assess the effect of treatment [78].

1.7.2 Service Delivery:

Primary care should deal with most cases of PMS. Awareness of the condition and training in its management is essential. Ideally, women with severe PMS should be managed by a multidisciplinary team, which might comprise a hospital or community gynaecologist, psychiatrist or psychologist, dietician and counsellor. While such services are rarely provided in any National Health Service (NHS) setting, referral to gynaecologists should be reserved for women who have been fully evaluated as having severe PMS and when simpler forms of therapy have been explored. Where there is multidisciplinary provision of care, this is of benefit both from the diagnostic and therapeutic point of view, giving the ability to offer a broad range of interventions from lifestyle interventions and cognitive behavioural therapy (CBT) to gynaecological interventions [79].

1.7.3 Complementary Therapies (CAMs):

When treating women with PMS, complementary medicines may be of benefit, but clinicians need to consider that data from clinical studies are limited and underpowered. Interactions with conventional medicines should also be considered. The referring clinician retains legal responsibility for the patient's well being when they refer patients to complementary therapists. It is difficult to

assess the true value of most of these therapeutic interventions because they are freely available without prescription or physician recommendation, with little regulation of efficacy or safety. Most are not licensed or registered for treatment of PMS. The Medicines and Healthcare products Regulatory Agency (MHRA) and European regulatory authorities are aiming to rectify the situation by insisting that all complementary therapies are registered by 2011 or withdrawn from sale. This section reviews the recent evidence for some of the evidence-based 'alternative' interventions that have been used to treat PMS. Treatments have been selected where reasonable efficacy data exist [randomised controlled trial (RCT) data if possible [79].

1.7.4 Vitamin B6 OTC:

Vitamin B6 is often used to treat PMS without clear evidence of its efficacy [80]. The recommended dietary allowance for vitamin B6 is around 2.0 mg/day and deficiency of vitamin B6 is rare. Due to unproven efficacy of vitamin B6 in treating PMS, a systematic review of published and unpublished randomised placebo-controlled trials of effectiveness of vitamin B6 in the management of PMS was undertaken. Nine published trials representing 940 patients were reviewed. The main outcome measure was an improvement in overall premenstrual symptoms. The overall methodology of the trials identified was of poor quality, with none of the trials justifying patient numbers with a power calculation. The odds ratio (OR) in favour of vitamin B6 relative to placebo for an improvement in overall PMS was 2.32 (95% CI 1.95–2.54). No conclusive evidence of vitamin B6 toxicity was reported and there was no dose-related

response to treatment. There is no rationale for giving daily doses of vitamin B6 in excess of 100 mg, especially following the recommendation from the Department of Health and the Medicine Control Agency in 1999 to restrict the dose of vitamin B6 available generally to 10 mg and to limit the dose sold by a pharmacist to less than 50 mg[81].

1.7.5 Magnesium OTC:

Preliminary studies suggest that magnesium may also be helpful in PMS. A double-blind, placebo-controlled study of 32 women found that magnesium taken from Day 15 of the menstrual cycle to the onset of menstrual flow could significantly improve premenstrual mood changes [82]. Another small, double-blind, preliminary study found that regular use of magnesium could reduce symptoms of PMS related fluid retention [83].In this study, 38 women were given magnesium or placebo for 2 months. One small, double-blind study (20 participants) found that magnesium supplementation with vitamin B6 might help prevent menstrual migraine [84].

1.7.6 Calcium/Vitamin D OTC:

Studies suggest that blood calcium and vitamin D levels are lower in women with PMS and that calcium supplementation may reduce symptom severity, but it is unknown whether this may prevent the initial development of PMS. In a recent case control study, after adjustment for risk factors, women in the highest quintile of total vitamin D intake (median, 706 IU/day) had a relative risk of 0.59 (95% CI 0.40–0.86) compared with those in the lowest quintile (median, 112 IU/day)

(p = 0.01 for trend) [85]. The intake of calcium from food sources was also inversely related to PMS; compared with women with a low intake (median, 529 mg/day), participants with the highest intake (median, 1283 mg/day) had a relative risk of 0.70 (95% CI 0.50–0.97) (p = 0.02 for trend). The intake of skimmed or low-fat milk was also associated with a lower risk (p<0.001). A high intake of calcium and vitamin D may therefore reduce the risk of PMS but large-scale clinical trials addressing this issue are required. At present, the only interventional data are from small trials. More data are required to determine efficacy and to optimise regimens[86-88].

1.7.7 Isoflavones (e.g. soy/red clover) OTC:

In a 24-week, double-blind study, 49 women with menstrual migraines received either placebo or a combination supplement containing soy isoflavones, dong quai and black cohosh extracts. The treatment group showed a significantly greater improvement than the placebo group [89]. Recent data from the author's unit demonstrate a benefit with red clover isoflavones but this is not statistically significantly different to placebo [90].

1.7.8 Agnus castus OTC:

Agnus castus is the best researched CAM for PMS but a lack of standardised quality controlled preparations is a problem. The fruits of Vitex agnus castus (the chaste tree) contain a mixture of iridoids and flavonoids. The mechanism of action may be related to modulation of stress-induced prolactin secretion via dopamine, without directly affecting luteinising or follicle-stimulating hormones.

A study was undertaken to compare the efficacy and tolerability of agnus castus with placebo in 170 women with PMS. Results showed improvement in the main variable was greater in the active group compared with placebo group [91]. Patient acceptance was high and side effects were few and mild. A previous double-blind trial compared agnus castus to vitamin B6 (pyridoxine) instead of placebo [92]. The two treatments proved equally effective. In a recently published study, 217 women were randomised. Efficacy was assessed using the Chinese version of the PMS diary (PMSD). The total PMSD score in the third cycle was highly significantly lower than the baseline in both groups ($p<0.0001$). The difference in the mean scores from the baseline to the third cycle in the treatment group (22.71 ± 10.33) was significantly lower than the difference in the placebo group (15.50 ± 12.94, $p<0.0001$) [93].

1.7.9 St John's Wort OTC (Hypericum perforatum):

(St John's Wort) is a herbal remedy shown to alleviate mild to moderate depression. However, there has been no clinical investigation on its effectiveness in treating PMS apart from one case report and a small, prospective, open, uncontrolled, observational pilot study [94, 95] The study investigated whether Hypericum could relieve PMS in a small group of women and tested the methods for conducting future RCTs with this preparation. Nineteen women with PMS used Hypericum tablets for two complete menstrual cycles. There were significant reductions in all outcome measures. The improvement was 51% when the PMS scores were measured between the baseline and the end of the trial, with over two-thirds of women demonstrating at least a 50% decrease in symptom

severity. Symptoms which improved the most were emotional and cognitive, which correlates with evidence showing that Hypericum has positive effects on mood and that it may moderate brain neurotransmitters.

1.7.10 Evening primrose oil OTC IE:

Evening primrose oil, a rich source of gamma linoleic acid, is often used as a treatment for severe PMS. However, the evidence for efficacy in this condition is poor. A prospective, randomised, double-blind and placebo-controlled trial showed that there was no significant difference in the scoring between the active and placebo groups over six cycles. These findings indicate that the improvement experienced by these women with moderate PMS was solely a placebo effect [96]. A metaanalysis of the data has also concluded that evening primrose oil is ineffective in the treatment of severe PMS [97]. Only cyclical mastalgia has been shown to respond to this treatment [98].

1.7.11 Exercise and Yoga:

A primary example of a nonpharmacologic therapy with is exercise. Most of the published studies on exercise and PMS have shown a benefit. These studies are hampered by small study size and the inability to double blind. Exercise seems to reduce mood symptoms and physical symptoms of breast tenderness and bloating. One pro- posed underlying pathophysiology is the enhancement of central opiate activity associated with exercise. Because of other significant health benefits of regular exercise and data suggesting the relief of PMS

symptoms, exercise can be considered a first-line therapy among the nonpharmacologic interventions [99].

1.8 Aromatherapy

Aromatherapy, also referred to as Essential Oil therapy, can be defined as the art and science of utilizing naturally extracted aromatic essences from plants to balance, harmonize and promote the health of body, mind and spirit. Aromatherapy is the practice of therapeutic use of essential plant-based oils. Essential oils and aromatherapy have been used in the care of women for centuries [100].

Aromatherapy can be defined as a controlled use of aromatic plant oils for therapeutic or preventive purposes. It can be applied through aerial diffusion, direct inhalation, and topical applications. The use of essential oils for therapeutic and spiritual purposes can be dated back to ancient civilizations, including the Chinese, Indians, Egyptians, Greeks, and Romans. However, the beginning of contemporary aromatherapy is often attributed to the pioneer work of the chemist René-Maurice Gattefossé and Doctor Jean Valnet from the early twentieth century in France. It was not until the 1980s that aromatherapy became popular in the United States and began to gain attention for its potential clinical applications. Nevertheless, despite its popular use in both the community and health care settings today [101, 102], there is still a paucity of empirical evidence supporting the efficacy of aromatherapy in many therapeutic claims [103].

1.8.1 Mechanism of aromatherapy:

Essential oils are absorbed into the body in many different ways. Once inside the body, essential oils have the ability to enter the bloodstream and therapeutic benefits can be achieved. They can enter the body through inhalation, ingestion, or absorption through the mucous membranes and skin. Essential oils can enter the bloodstream by being inhaled through the nose, which is the fastest direct route into the body. Researchers Gatti and Cajola noted that odors produced an immediate effect on respiration, pulse, and blood pressure, and concluded that odors had produced by reflex action a dramatic effect on the functioning of the nervous system [104].

The olfactory system allows the sense of smell. The nose is the first part of the olfactory system. Smell is a chemical reaction – receptors in the brain respond to chemicals in the essential oil [105]. The process of olfaction consists of five stages – detection, transmission, perception, analysis, and storage. An aroma must pass through all five stages in order to be stored in the brain for future recall.

The Olfactory and Limbic Systems

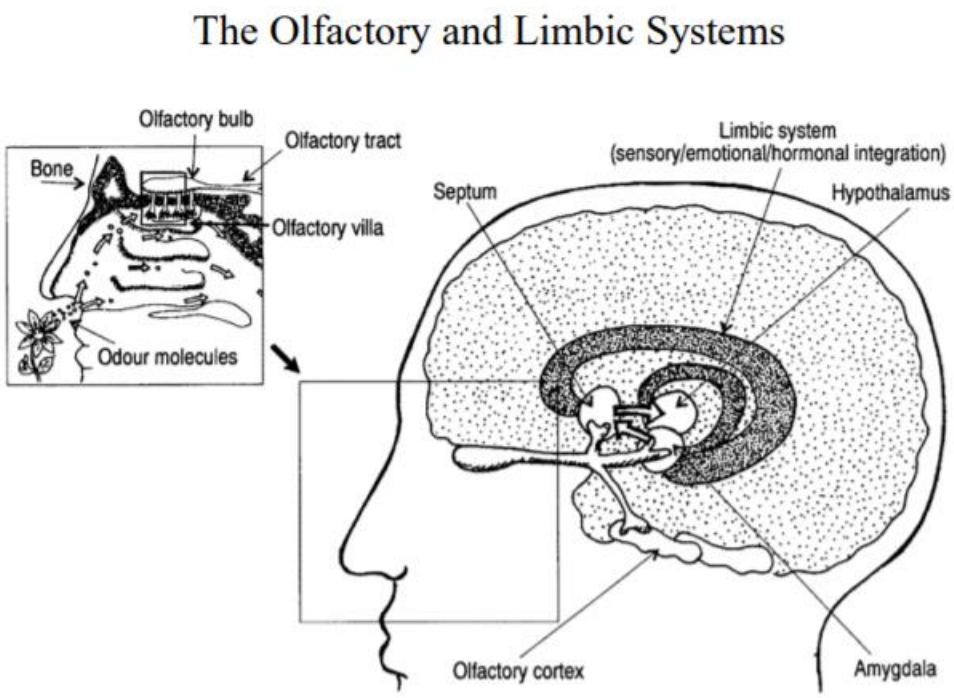


Figure 1: (From Battaglia S. 1995. A schematic of the olfactory system with its primary and secondary paths to other regions in the brain. In Battaglia, S (ed.), The Complete Guide to Aromatherapy, Australia: The Perfect Potion, p. 101)

During detection, a scent is carried into the nostril and the molecules move up the nose to the olfactory epithelium. Here the molecules attach to millions of hair like receptors that are connected to the olfactory bulb. Different scents bind to different receptors. Once the scent binds to a receptor, it is transmitted into an electromagnetic impulse and travels to the two olfactory bulbs. These bulbs connect directly to the limbic system of the brain where the scent is perceived. The limbic system is comprised of the amygdala, septum, hippocampus, anterior

thalamus, and hypothalamus. The limbic system influences emotions, motivation, instinctive behaviors, learning, and memory [106].

It can activate emotional reactions from aromas, and send these coded aroma messages to other parts of the brain. Once the aroma is perceived, the mind and body analyze the scent. This is accomplished by the reticular system of the brain, which integrates emotions with memories. The hypothalamus, the brain's basic center for drives and emotions may be activated, which stimulates the pituitary gland. The pituitary gland produces hormones that affect the body's other glands. These hormones trigger physiological, psychological, and emotional reactions that influence feelings and behavior. The brain will then store the aroma. It may compare input about the aroma with other senses in the body. The brain will form a conclusion as to what the aroma is, and store the information for future recall. In this manner, certain aromas or scents will trigger particular emotional reactions. Once an aroma is stored in the brain, each subsequent time it is inhaled the brain and the body will evoke the same response. By directly inhaling an essential oil, the brain is able to analyze and store the scent, as well as the responses in the body the scent invokes. In this way, essential oils are therapeutic by inhalation. Essential oils are also effective through inhalation if the desired therapeutic effect concerns the respiratory system, as the oils will travel down the trachea and into the lungs when inhaled. Once in the respiratory system, the oils can have dramatic effects on respiratory disorders as they come in contact with the mucous membranes in the nose, as well as the tissue of the lungs and bronchi. Essential oils can be inhaled using an atomizer, diffuser,

vaporizer, through steam vapor, or directly from the bottle. Essential oils are lipid soluble and can be absorbed directly into the bloodstream through the skin. The study of where essential oils go when they are absorbed into the body and how they are absorbed and eliminated is called pharmacokinetics. Straehli, who researched pharmacokinetics in 1940, found that all the essential oils appear in the breath following absorption through the skin, although the time interval differs with each essential oil [107].

The lipophilic nature of essential oils means they can pass the blood brain barrier. Their affinity for lipid rich tissues like those of the central nervous system facilitates an exchange of essential oil constituents from the blood into the nervous system. Once the oils have reached the central nervous system, their effects can travel through the body very quickly. When essential oils are applied to the skin surface, they are absorbed into the epidermis, the stratum corneum, and to the lower layers of the dermis. The oils can travel down into the dermis via the sweat glands or the hair follicles. Once in the dermis, the oils move into the capillaries located here and travel into the bloodstream. Once in the blood stream, they are able to quickly travel through the body [108].

1.8.2 Physiological effects of aromatherapy:

Physiological effects of aromas can be divided into two types: those which act via the stimulation of the nervous system and those which act directly on an organ or tissue via an effector receptor-mechanism [109]. The physiological measures are all under the control of the nervous system. In general, the nervous

system of higher organisms can be classified into two major sections, the central nervous system (CNS) and the peripheral nervous system. The CNS includes the brain and spinal cord. Two important functions of the CNS are to receive and process sensory information and to regulate bodily movements. The peripheral nervous system refers to the nervous tissues outside the brain and spinal cord, including the cranial and spinal nerves. The peripheral nervous system is further divided into the somatic nervous system, concerned with muscular activities, and the autonomic nervous system (ANS) which controls visceral structures (glands and organs of body). In addition, the function of the ANS is to regulate the internal and relatively involuntary responses that are associated with emotions. Finally, the ANS is subdivided into the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS). These two branches differ in functions. The SNS is dominant in situations requiring mobilization of energy whereas the PNS is dominant in a rest situation. Some organs are innervated by only one division of the ANS (e.g., the sweat glands, peripheral blood vessels, and adrenal glands are innervated solely by the SNS). Most organs are innervated by both the SNS and the PNS. In those cases, the SNS and the PNS branches usually produce opposite reactions. Among the most significant of the bodily reactions produced by the SNS are pupil dilation, inhibition of salivation (causing a dry mouth), secretion of sweat (causing clammy hands), constriction of blood vessels in the periphery of the body (causing cold hands and feet), dilation of blood vessels in the muscles and brain, increase of heart rate, increase of blood pressure, speeding of breathing rate, and inhibition of digestive processes.

Among the bodily reactions produced by the PNS are pupil constriction, increase of salivation, decrease of heart rate, decrease of blood pressure, decrease of breathing rate and increase of digestion and peristaltic processes [110]. Evaluation of the effects of aromas on the nervous system may be divided into two different forms of arousal, the cortical arousal such as brain wave activity and the autonomic arousal such as heart rate, skin conductance. Decreases of the cortical arousal and/or the autonomic arousal are interpreted in terms of a sedative/relaxing effect of aromas. In contrast, increases of the cortical arousal and/or the autonomic arousal are interpreted in terms of a stimulating effect of aromas. The changes of physiological parameters in response to aromas are reviewed throughout this paper. They are heart rate, blood pressure, electrodermal activity, electroencephalogram (EEG), contingent negative variation (CNV), and eye blink rate or pupil functions [111].

1.8.3 Clary sage and Aromatherapy:

Clary sage is a gift to the female and has a rejuvenating effect on the endocrine system and balances the pituitary and is specifically indicated in treating PMS [100]. The composition of the essential oils obtained from different parts of both wild and cultivated forms of Salvia sclarea L. were investigated by both GC and GC/MS. The principal components of the oils were linalool (22–32%) and linalyl acetate (25–51%). It was found that the oil composition was not influenced by the part of the plant from which oil was obtained, except for the leaves [112].

Figure 2: Clary Sage

Tisserand [113] suggested that clary sage has functions similar to estrogen, such as normalizing the menstrual cycle, promoting menstruation, and strengthening the uterus [114]. Aromatherapy is perceived to be a safe therapy [115]. Essential oils have been used for several hundred years and are used regularly today by the public for stress-management and for minor ailments [116]. However, the therapeutic effects of aromatherapy are not well supported by clinical studies.

Clary sage oils contain linalyl acetate. Linalyl acetate has been shown to decrease blood pressure, heart rate and respiratory rate, and decrease salivary cortisol and CgA concentrations [117, 118]. Research has also revealed that clary sage oils act on neurotransmitters in the brain.

Salvia sclarea L. (Lamiaceae) essential oil was tested in a pilot trial for modulation of depression signs in 22 women [119]. Normal and depressive

tendencies and serum parameters in menopausal women acutely inhaling clary sage oil were assessed before and after exposition. Given the comparison between pre-inhalation and post-inhalation of clary sage oil, 5-HT plasma concentrations increased significantly, and plasma cortisol levels decreased significantly for both normal and depressive menopausal women [119]. It should be mentioned that this pioneering clinical trial contributed by measuring physiological changes alongside of behavioral alterations in women with depressive symptoms after acute clary sage oil inhalation. The antidepressant effects of essential oil of Salvia sclarea L. were assessed in the FST in rats. The acute exposition to this oil, via intraperitoneal and inhalation, reduced immobility time similar to conventional antidepressant drugs [120]. The antidepressant effects of this essential oil seem to be mainly mediated by the activation of dopamine and 5-HT neurotransmission [120]. In fact, the pretreatment with haloperidol (Dopamine receptor antagonist), SCH-23390 (D1 receptor antagonist), but also buspirone (5-HT1A partial agonist) blocked the antidepressant effect of this essential oil [120]. The principal constituents of Salvia sclarea L. oil include linalyl acetate (64%), linalool (21%), and geraniol (2.6%) [121]. Linalool and geraniol have showed consistent antidepressant actions inrodents after acute administrations [122, 123–125. This effect of linaloolin rodents were prevented with WAY100,635 (5-HT1A receptor antagonist) and yohimbine (α2-receptor antagonist), thus reinforcing the role mediated by monoaminergic neurotransmission in the antidepressant effects of linalool [123]. Ultimately, the antidepressant of the Salvia sclarea L. essential oil

seems to be due to the synergic effects of bioactive isolated compounds. The most studied isolated compounds are eugenol [126,127] and linalool [122,123,124]. Studies suggest robust antidepressant-like actions as demonstrated in distinct behavioral tests (FST and TST) performed in different labs around the world. The main target of the antidepressant action of eugenol is the MAO enzyme [127]. This compound preferentially inhibits the MAOA activity, and after chronic administrations increases the neurotrophic factor, BDNF, a mechanism of action shared with conventional antidepressants. Concerning linalool, main constituent of the extracted lavender and clary sage oil [119,128], acute studies suggestive of antidepressant actions support the activation of monoamine 5-HT1A and α2-receptors [123].

2. AIMS AND OBJECTIVES

AIM:

To evaluate the effects of clary sage oil in relieving the symptoms of Premenstrual syndrome.

OBJECTIVES:

To assess the effects of clary sage oil on physiological, psychological and behavioural symptoms of Premenstrual syndrome.

3. REVIEW OF LITERATURE

According to a study conducted in May 2013, it indicates that lavender aromatherapy has a potential therapeutic modality could alleviate premenstrual emotional symptoms, which, at least in part, is attributable to the improvement of parasympathetic nervous system activity. This study further implies that HRV could evaluate the efficacy of aromatherapy using various fragrances to relieve premenstrual symptoms, and ultimately, support the mind and body health of women [129].

Premenstrual Syndrome is a psycho-neuroendocrine stress related disorder and more than 300 treatment modalities for PMS show that the existing remedies have not provided satisfactory help to relieve PMS. 61points relaxation exercise (61-PR), a relatively less known hatha yoga technique, is a successful means of stress relaxation and is expected to relieve PMS as well. Therefore, Dvivedi et al., (2008) conducted a study on 50 clinically healthy women volunteers who were in their reproductive age group and in their premenstrual period, from which a control group (n = 20) and a PMS group (n = 30) based on the symptoms were identified. In both groups basal heart rate (HR/min), systolic (SBP; mmHg) and diastolic blood pressure (DBP; mmHg), electromyogram (EMG; mV), electrodermal galvanic activity (EDG; microv), respiratory rate (RR/min) and peripheral temperature (T; degrees F) were recorded and the subjects were taken through a guided 61PR. The results suggested a reduction in sympathetic activity by 61-PR, also the high basal sympathetic tone present in subjects of PMS group due to stress is considerably reduced by relaxation. 61-PR is effective in providing

relief from PMS and may be a useful adjuvant to medical therapy of PMS and other stress disorders [130].

Pullon, Reinken and Sparrow (1989) conducted a survey among 1826 females in Wellington in order to collect data about their gynecological health and general health along with detailed history of last menstrual period. Majority of females had had their menstrual cycle within last one month. Out these females, 85% had suffered from premenstrual symptoms of some or the other kind and were asked whether they followed any advice, treatment, medical help or self-help for PMS. Self-help was tried by 990 women and 416 went for medical help. Exercise, vitamin B6 supplement, and rest were the most common self-help practices tried by half of the females surveyed. Rest, exercise and keeping a record of PMS were helpful in 80% of females. There was a marked placebo effect. Treatments offered by doctors included mefenamic acid, vitamin B6, oral contraceptives and diuretics, but it was difficult to further evaluate the effect of these treatment options. The four PMS syndromes which were suggested are PMS-various, PMS-irritable and intolerant, PMS-bloat, and PMS-breast [131].

Han et al., (2006) conducted a research in order to find out the effect of aroma therapy on symptoms of dysmenorrheal and menstrual cramps. 67 female students were selected who had complaints related to menstrual cycle. The inclusion criteria were rating of menstrual cramps should be more than 6 on a visual analogue scale, no reproductive or systemic diseases, and no use of contraceptive drugs. Three groups were formed i.e. experimental, control and placebo group. Topical application of aroma oil was done in the females of

experimental group. This aroma oil was prepared using 1 drop rose (Rosa centifolia), a drop of clary sage (Salvia sclarea), and 2 drops lavender (Lavandula officinalis) in almond oil (5 cc). However, the placebo group received treatment with almond oil only whereas control group was not given any treatment. Visual analogue scale was used to assess the severity of menstrual cramps and multidimensional verbal scoring system was used to measure dysmenorrhea severity. It was revealed that experimental group suffered from significantly lesser menstrual cramps as compared to two other groups. It was concluded that menstrual cramps can be reduced by topical application of aroma oils consisting of rose, clary sage, and lavender. Therefore, aromatherapy can be a good alternative option for females who suffer from severe menstrual cramps and dysmenorrhea [132].

Derman et al., (2004) investigated the frequency of premenstrual syndrome (PMS) associated symptoms and effects of nutrition on PMS in adolescent girls. Patients and methods: One hundred and seventy-one adolescent girls who had menstrual cycles were included in this study. They were given a questionnaire on criteria for PMS, dysmenorrhea and regularity of menstrual cycle. Modified Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) criteria were used for the diagnosis of PMS. We also investigated which nutritional supplements affect the PMS-associated symptoms and signs. Results: One hundred and five adolescent girls out of 171 (61.4%) met DSM-IV criteria for PMS. There was an association between dysmenorrhea and PMS in 60 (57.1%). Half of the girls, i.e. 52 (49.5%) had mild, 39 (37.1%) had moderate and 14 (13.4%) had

severe PMS. The most common symptom of PMS was negative affect particularly in the form of stress (87.6%) and nervousness (87.6%). There was a statistically significant negative relationship between milk consumption and the following: abdominal bloating, cramps, craving for some foods and increased appetite. Conclusion: PMS and dysmenorrhea are frequently overlapping. We also found that PMS is associated with dietary habits [133].

Smith and Thomas (1996) conducted a study with the purpose to examine differences in locus of control and anger in college women with and without premenstrual syndrome (PMS). One hundred thirty-seven female undergraduates completed a biographical questionnaire, the Rotter Internal External Locus of Control (I-E) Scale, the Spielberger State Trait Anger Scale (STAS), the Framingham Anger Scale (FAS), and a women's health questionnaire. After 65 women who had had children or used hormonally based contraceptives or psychotropic medications were excluded, the remaining subjects were placed into a PMS (n = 48) or a non-PMS group (n = 24) according to whether they met DSM-IV criteria for Premenstrual Dysphoric Disorder (PMDD). After debriefing the sample, the women were asked if they believed they had PMS. Results of the study showed no significant differences between groups in locus of control or anger. Out of the 72 subjects in the final analysis, 64 (89%) believed they had PMS, and only 8 (or 11%) believed they did not. Self-diagnosis was not always correct; 16 (22%) of the women who believed they had PMS did not meet the DSM-IV criteria for the disorder. The DSM-IV criteria may need further refinement and validation [134].

McLean and Barr (2003) characterized associations of restraint with selected physical, lifestyle, personality and menstrual cycle characteristics in female university students. The survey instrument, distributed to 1350 women, included standardized questionnaires (Three-Factor Eating Questionnaire, Perceived Stress Scale and Rosenberg's Self-esteem Scale), and assessed weight and dieting history, exercise, lifestyle characteristics, menstrual cycle characteristics and whether participants were following vegetarian diets. Among the 596 respondents included in the analysis (44%), women with high (n=145), medium (n=262) or low (n=189) restraint had similar ages, heights and weights. Despite this, compared to women with low scores, those with high scores exercised more (4.6+/-5.3 vs. 3.2+/-3.5 h/wk), were more likely to be vegetarian (14.5 vs. 3.7%), have a history of eating disorders (13.7 vs. 1.2%), be currently trying to lose weight (80.3 vs. 15.3%), report irregular menstrual cycles (34.7 vs. 17.0%), and have scores reflecting lower self-esteem and higher perceived stress. Menstrual irregularity was an independent predictor of restraint score, and restraint score was the only variable to differentiate women with regular and irregular menstrual cycles. We conclude that women with high restraint may use a combination of behavioral strategies for weight control, and differ from women with low restraint scores in personality characteristics and weight history. Some of these behaviors or characteristics may influence menstrual function [135].

The purpose of this research conducted by Houston et al., (2006) was to determine: (1) The prevalence of dysmenorrhea, premenstrual symptoms and other menstrual disorders among adolescents who receive their health care at an urban

adolescent health center; (2) The attitudes and expectations adolescents have relating to their menstrual period; and (3) The relationship between teens' attitudes and expectations regarding menses and actual menstrual-related morbidities such as school absenteeism. A 35-item, survey was administered to post-menarcheal adolescents ages 12-21 years. Descriptive analysis of the prevalence of the menstrual disorders was completed. Chi-square testing was used to compare the prevalence of menstrual-related morbidities with the level of adolescents' expectations regarding menstruation. 91.5% of the respondents were African-American. Premenstrual syndrome (PMS) was the most prevalent reported menstrual disorder (84.3%) followed by dysmenorrhea (65%), abnormal cycle lengths (13.2%), and excessive uterine bleeding (8.6%). Only 2% of teens report receiving information about menstruation from their health care provider. Negative expectations regarding menstruation were associated with higher rates of school absenteeism and missed activities ($P = 0.0790$ and $P = 0.0297$ respectively). PMS and dysmenorrhea are prevalent medical disorders among urban adolescents. Morbidities, including school absenteeism, are higher among those with negative period expectations. Since only 2% of teens received information regarding menstruation from their health care provider, it is imperative that health care providers increase their anticipatory guidance regarding normal menstruation [136].

Premenstrual stress affects 75% of women of childbearing age and yoga has been found to be beneficial in many psycho-somatic disorders. Therefore, Kanojia et al., (2013) investigated the effect of integrated yoga on autonomic

parameters and psychological well-being during both pre and post phases of menstrual cycle in healthy young female subjects [137]. This investigation was a randomized control trial conducted in the Department of Physiology, Lady Hardinge Medical College, New Delhi, India. Fifty apparently healthy females in the age group of 18-20 years were randomized into two groups: Group I (n=25) consisted of subjects who practiced yoga 35-40 minutes per day, six times per week for the duration of three menstrual cycles. Training was given by qualified yoga instructor. Group II (n=25) subjects acted as controls. Following parameters were recorded at the beginning and after completion of three menstrual cycles in all the subjects: Height, weight (BW), Resting Heart Rate (HR), Resting Systolic (SBP) and Diastolic Blood Pressure (DBP), parasympathetic reactivity tests including Expiration Inspiration Ratio (E: I ratio) and 30:15 ratio, sympathetic reactivity tests including BP changes due to Isometric Hand Grip (IHG) exercise, and Cold Pressor Test (CPT). Assessment of psychological status was done by administering DIPAS (Defense Institute of Physiology and Allied Sciences) inventories of Anger self- report scale, Trait Anxiety, Sense of well-being and Depression scale. Intra-group comparison of physiological parameters was done by using paired 't' test, whereas intra-group comparison of non-parameteric data such as scores of anxiety, depression, anger and sense of well-being was done by Wilcoxon signed-rank test. Inter-group comparison of parameters was done by Students 't' test for parametric tests and Mann-Whitney 'U' test for non-parameteric tests. The results showed significantly higher BW, resting SBP, DBP, sympathetic activity and blunting of parasympathetic reactivity and also, significantly higher

scores of anger, depression, anxiety and decreased score of well-being in premenstrual phase as compared to postmenstrual phase in both the groups in initial cycle. There was significantly higher percentage decrease in BW, HR, SBP & DBP in yoga group as compared to control group in both the phases from initial to second and onwards between second and third menstrual cycle. Also, decrease in anger, depression and anxiety and increase in well-being score was significant in yoga group as compared to control group from initial to second and third cycle in premenstrual phase while the change was significant only in depression score in postmenstrual phase. In conclusion this study shows that there was significant alteration of autonomic functions and psychological status in premenstrual phase when compared with postmenstrual phase in young healthy females. Also, regular practice of yoga has beneficial effects on both phases of menstrual cycle by bringing parasympatho-dominance and psychological well-being probably by balancing neuro-endocrinal axis.

Woods et al., (1994) compared arousal levels and stress response across menstrual cycle phases in women with three perimenstrual symptom patterns. Women with low symptom severity (LS, N = 28), were compared with those with a premenstrual syndrome (PMS, N = 15) and premenstrual magnification (PMM, N = 19) pattern across post-menses and pre-menses phases. Each woman was assessed during relaxation and in response to mental task and symptom imaging stressors during a post-menses and pre-menses day. Results of baseline skin conductance (SCL), electromyogram (EMG), and finger temperature (T) demonstrated arousal pre-menses in women with the PMS pattern, but not in

women with the LS pattern. In addition, women with the PMS pattern experienced increased EMG and SCL response to stressors pre-menses. Women with the PMM pattern experienced a rise in finger temperature pre-menses, opposite the pattern of the women with LS or PMS. These results support development of symptom management strategies to reduce arousal and modulate stress response for women with PMS who seek help for their symptoms. In addition, the difference in arousal and stress response observed in women with PMS and PMM support development of different symptom management strategies for these two groups of women [138].

Jang and Lee (2004) assessed the effects of qi therapy on premenstrual symptoms in women with premenstrual syndrome (PMS). Thirtysix (36) college women with symptoms of PMS were selected for this investigation. After 2 months of screening, subjects with PMS were randomized to receive real qi therapy (18 subjects) or placebo (18 subjects). The subjects were informed that they would receive one of two types of treatment. They did not know which treatment they received. Each intervention was performed eight times during the second and third cycles with subjects completing a PMS diary. There were significant improvements in the symptoms of negative feeling, pain, water retention, and total PMS symptoms in subjects receiving qi therapy compared to placebo controls. Qi therapy may be an effective complementary therapy for managing the symptoms of PMS [139].

Nisar et al., conducted a observational study (2008) to determine the frequency and severity of Premenstrual Syndrome (PMS) in medical college

students and to evaluate the impact of the condition on the quality of life and find out the associated risk factors. This study was conducted at Isra University Hospital, Hyderabad, Sindh, Pakistan, from August to December 2006. Unmarried medical students aged 18-25 years with regular menstrual period for the last 06 months were recruited by convenience sampling. PMS related data was collected on daily record of severity of problems (DRSP) for two prospective cycles. Health-related quality of life data was collected on medical outcome study Short Form 36 (Sf - 36) after taking informed consent from participants. Descriptive and inferential analysis was done by two-tailed t-test and multivariate logistic regression analysis. Study participants (n=172) had mean age of 21.2 + 1.9 years. Eighty-nine (51%) girls met the criteria for PMS recording to ICD - 10, among them, 53 (59.5%) had mild PMS, 26 (29.2%) had moderate and 10 (11.2%) had severe PMS. Ten (5.8%) girls were found to have Premenstrual Dysphoric Disorder (PMDD) according to DSM - IV criteria. The order of frequency of symptoms were anger, irritability, anxiety, tiredness, difficult concentration, mood swings and physical symptoms like breast tenderness and general body discomfort with great impairment in social life / activities and work efficiency/productivity. Dysmenorrhea ($p=0.003$) and family history of premenstrual syndrome ($p < 0.001$) were significantly associated with premenstrual syndrome on univariate and multivariate analysis. Sf - 36 score on Mental Component Summary (MCS) and Physical Component Summary (PCS) were significantly lower in the affected group. Premenstrual syndrome is a common problem in young girls which adversely affects their educational performance and emotional well-being.

Strategies should be adopted for detection and management of PMS in young girls [140].

Tolossa and Bekele (2014) assessed the prevalence, impacts and medical managements of PMS on female medical students of Mekelle University College of Health Sciences. A cross-sectional study was conducted among systematically selected female students of Mekelle University College of Health Sciences, Mekelle town, northern Ethiopia from March to April 2013. A structured and pretested self-administered questionnaire was employed for data collection. The collected data were analyzed using the Statistical Package for the Social Sciences, SPSS Inc., Chicago, IL (SPSS version 16). The criteria proposed by the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV TR) were used to diagnose PMS. From the total population size of 608; a sample size of 258 was drawn. Age of the study participants ranged from 18 to 25 years, with mean age of 20.86 ± 1.913 years. Among the participants, 144(83.2%) have had at least one PM symptoms with their menstrual period. The prevalence of PMS according to DSM-IV was 37.0%. About 49(28.3%) reported frequent class missing, 17(9.8%) exam missing, 14(8.1%) low grade scoring and 3(1.7%) of them reported withdrawal from their learning associated with their PMS. Only 83(48.0%) participants sought medical treatment for their PMS. The treatment modalities used were pain killers, 63(36.4%), hot drinks like coffee and tea, 13(7.5%), and massage therapy and exercise, 7(4.0%). Binary logistic regression analysis revealed average length of one cycle of menstruation (COR = 0.20(0.070-0.569) and academic performance impairment (AOR = 0.345(0.183-0.653) were

significantly associated with the diagnosis of PMS and use of PMS treatments respectively. The study revealed a high prevalence and negative impact of PMS on students of Mekelle University. Therefore, health education, appropriate medical treatment and counseling services, as part of the overall health service, should be availed and provided to affected women [141].

Premenstrual syndrome (PMS) is a distressing group of symptoms related to menstrual cycle during reproductive age. Its substantial burden on daily function and quality of life, particularly on mental aspects, was to the impetus for this study with the aim of determining the effectiveness of a psycho-educational package on premenstrual syndrome and related symptoms. In a randomized clinical trial, conducted by Taghizadeh (2013) randomized 123 (17-19-year-old) adolescent girls with PMS to psychoeducational intervention (including 62 subjects) and control (including 61) groups. The participants completed a demographic questionnaire, premenstrual syndrome symptom daily record scale and the Symptom Checklist-90-Revised (SCL-90-R). A paired and two independent samples test and chi-squared test were used for analysing data using SPSS statistical package. At the end of the study there was statistically significant decrease in severity of total PMS in intervention compared with control group ($P < 0.001$). Also, a significant difference in somatization, anxiety and hostility was observed between two groups ($P < 0.05$). However, depression marginally decreased ($P < 0.1$) in intervention group, and interpersonal sensitivity was not statistically different between intervention and control groups. Intervention

alleviated the severity of PMS and related somatization, anxiety and hostility, yet it could not change the severity of depression and interpersonal sensitivity [142].

A review study was done by Stevinson Clare (2001) to find out whether there are enough evidences related to the effectiveness of alternative or complementary treatment in the form of clinical trials. Seven databases were searched in order to locate the trials and list of references were checked. In the review, randomized controlled studies that studied alternative/complementary treatments with respect to PMS were included. These studies were published in peer-reviewed journals. 27 studies which researched the effect of herbal medicine, dietary supplements, homeopathy, relaxation, reflexology, massage, biofeedback, and chiropractic were included in this review. In spite of some supportive findings, most of the evidences were not satisfactory for alternative and complementary therapies as there were many methodological restrictions. Based on these findings, it was concluded that alternative or complementary cannot be given for treatment of PMS [143].

In another study Schneider et al., (1999) studied menstrual function and premenstrual symptoms in a structured, rigorous military environment. A survey about high school menstrual and premenstrual function, and the Premenstrual Assessment Form (PAF), were completed by all 158 freshman female Cadets in July 1991. In May 1992, 83 participants completed a survey assessing menstrual and premenstrual symptoms, including interference with activities during the year. Participants reported menstrual patterns and premenstrual symptoms in high school similar to other females their age. Most (62%) predicted a change in

menstruation at the USMA, half were worried that physical symptoms would interfere with activities, one-fourth were worried that premenstrual symptoms would interfere with activities, and one-fourth were worried that obtaining and changing menstrual materials would interfere with activities. Almost all respondents (91%) reported changes in menstruation during the year, most commonly less regular, less frequent, shorter, lighter, and less crampy periods. Menstrual and premenstrual symptoms interfered with physical activities (66.2%, 61.4% respectively) more so than academic (50.6%, 45.7% respectively) or military activities (39.8%, 47.0% respectively). Female Cadets described significant difficulties with changing (62.6%), obtaining (51.8%), and disposing of (38.5%) menstrual materials. The data demonstrate major changes in menstrual function in over 90% of female Cadets; a significant perceived impact of menstrual and premenstrual symptoms on academic, physical, and military activities; and difficulties in obtaining, changing, and disposing of menstrual materials in a military setting. These findings have implications for females in the military, as well as for young women generally [144].

Yamamoto et al., (2009) examined the relationship between menses associated health problems of women, such as premenstrual symptoms, menstrual pain and irregular menstrual cycles, and psychosocial stress. A cross-sectional study was conducted among Japanese college students, measuring psychosocial stress levels by means of IMPS (The Inventory to Measure Psychosocial Stress). A total of 264 female students (mean age 19.4 years), who were invited to participate in the study in October 2007, completed the questionnaire, which dealt with

anthropometric data, lifestyle, menstrual history, and menstrual health status. Forty-three students were excluded due to missing data, and the remaining 221 were analyzed. The proportions of students who reported premenstrual symptoms, menstrual pain, and the experience of irregular menstrual cycles were 79%, 79%, and 63%, respectively. Students who reported premenstrual symptoms, menstrual pain, and the experience of irregular menstrual cycles had higher stress scores than those who did not. Multiple logistic regression analyses were used to identify independent factors associated with having premenstrual symptoms, menstrual pain, and the experience of irregular menstrual cycles. Stress score, heavy menstrual flow, and menstrual pain were significant predictors for premenstrual symptoms, while age at menarche and having premenstrual symptoms were significant predictors for menstrual pain. Both stress score and body mass index were found to be significant predictors for having experienced irregular menstrual cycles. The results suggest that psychosocial stress is independently associated with premenstrual symptoms and the experience of irregular menstrual cycles among college students, implying that changes in the functional potentiality of women as a result of stress are related with changes in their menstrual function [145].

Premenstrual syndrome is a term which includes a broad group of emotional, behavioral and physical symptoms that occur for several days before menses and subside following the menstrual period. Many women experience premenstrual syndrome symptoms, particularly physical ones such as breast tenderness and swelling. Approximately 5-10% women suffer from severe

premenstrual syndrome and another 30-40% have moderate symptoms. Premenstrual syndrome continues to be an unsolved problem. In this study, Ozisik et al., (2005) evaluated 24 premenstrual syndrome patients and 20 healthy women in the control group. The ages of the women were 2234 years (mean +/- SD: 25+/-3) for the premenstrual syndrome group and 2334 (25+/-3) for the control group [146]. The sympathetic skin response was recorded from the palms, soles and genital regions by using electrical stimuli to the median nerve at the wrist. The sympathetic skin response was recorded twice, in the follicular and late luteal phases of menstruation. The follicular and late luteal phase sympathetic skin response of the two groups were compared. The amplitudes and latency values of the late luteal and follicular phase sympathetic skin response from the premenstrual syndrome group and control group women were statistically similar. Further, there was not any latency or amplitude difference in the sympathetic skin response obtained from the three regions of the premenstrual syndrome patients and the control group. The investigators checked sympathetic skin response in the symptomatic (late luteal phase) and asymptomatic (follicular phase) periods of patients with premenstrual syndrome, a disorder known to have many autonomic symptoms, to determine whether there was sudomotor sympathetic involvement. The results of selected PMS patients indicate at the very least that there is no difference with the control subjects as regards peripheral sudomotor functions[146].

Kuczmierczyk and Adams (1986) compared eleven women with a clinical diagnosis of premenstrual syndrome (PMS) and ten non-PMS control women on

physiological measures in the intermenstrual and premenstrual phases of their menstrual cycle. Heart rate (HR) and skin conductance level (SCL) were monitored during baseline conditions and in response to a stressful laboratory procedure. Analyses for HR revealed a three-way interaction (groups X phase X tests) which approached significance indicating that the PMS group was generally lower during the intermenstrual testing but was higher in the premenstrual phase. No significant differences were observed on behavioral measures (pain threshold, pain tolerance) between the groups. Pain intensity ratings were found to be overall higher in the PMS group irrespective of menstrual cycle phase. The role of cognitive-perceptual processes is discussed in the context of the acquisition and maintenance of PMS symptomatology [147].

To investigate the comorbidity of premenstrual syndrome (PMS) and menstrual migraine, Facchinetti et al., (1993) administered the Menstrual Distress Questionnaire (MDQ) for two consecutive menstrual cycles to 22 patients with menstrual migraine, 12 cases with migraine without aura and 15 patients with PMS. MDQ scores varied throughout the menstrual cycle in each patient group, the wider changes being shown by patients with PMS. Fourteen menstrual migraine patients and 4 migraine without aura patients achieved diagnostic criteria for PMS over two menstrual cycles. In these patients MDQ scores did not differ from PMS sufferers at any stage of the menstrual cycle. The premenstrual increase of each cluster of PMS symptoms was identical in menstrual migraine and PMS subjects with the exception of negative affect. It was suggested that PMS

symptoms should be taken into account in the IHS diagnostic criteria for menstrual migraine [148].

Palmero and Choliz (1991) conducted a study on 64 undergraduate female students. During 3 consecutive months women answered a chart of daily report of symptoms, and finally, two groups were formed: women with premenstrual symptoms (PMS group) and women without premenstrual symptoms (NPMS group). Heart rates (HR) at rest were recorded throughout premenstrual, menstrual, postmenstrual, and ovulatory phases. In the premenstrual phase, PMS group showed significantly higher resting HR levels than NPMS group. With regard to resting HR levels across the four phases studied, significant differences within PMS group were observed. The results of this study are discussed from a psychophysiological point of view [149].

Groer and Ohnesorge (1993) investigated the effects of a program of relaxation and specific guided imagery on menstrual-cycle length and premenstrual distress. Thirty healthy college women with regular menstrual cycles were studied for 6 months. The subjects completed the Menstrual Distress Questionnaire (MDQ) at the beginning and end of the study and recorded their menstrual cycles for 3 months on an investigator-developed calendar recording sheet. Subjects were then given an audiotape with a progressive muscle relaxation exercise followed by guided imagery with a suggestive message focusing on lengthening the menstrual cycle and delaying the onset of menstrual bleeding. The 15 subjects who completed the entire study had significant increases in cycle lengths during the 3 months of imagery. The total premenstrual distress scores also

declined significantly, as did the subscales measuring behavior and negative affect. This study provides preliminary evidence that menstrual-cycle rhythmicity and premenstrual distress are amenable to the mind-body intervention of guided imagery and suggests that further investigation of this phenomena with larger sample size and careful controls for confounding variables be conducted [150].

The mood changes surrounding menstrual cycle mainly during luteal phase, known as premenstrual syndrome, have been described as early as the time of the ancient Greeks. Jasuja et al., (2014) studied psychological symptoms of anxiety and depression by using Beck Depression Inventory (BDI-II) and State Trait Anxiety Inventory (STAI). The main aim of this investigation was to study the psychological parameters and effects of PMR on females with premenstrual syndrome. Sixty participants aged between 18 and 40 years, volunteered for this study. Relaxation technique, PMR was given to the study group (Group A, Mean age 24.13±5.69) for one month and control group (Group B, Mean age 28.96±9.42) was evaluated without any intervention. Paired students t test. Alpha error was set at 1% level. PMR Group A showed significant decrease in Both BDI II and STAI scores ($p<0.001$), showing benefits of relaxation in reducing anxiety and depression. The study concluded that PMR helps to alleviate symptoms of premenstrual syndrome and decreases anxiety and depression as shown by changes in scores of both questionnaires [151].

An education program was developed by Chau and Chang (1999) and tested the efficacy in order to decrease the severe symptoms associated with PMS i.e. premenstrual syndrome and increasing the knowledge related to premenstrual

syndrome. The study participants were recruited from four schools aged 14-18 years in Hong Kong. 94 adolescent girls were assigned to either experimental group or control group. PMS knowledge questionnaire was administered to the experimental group immediately after giving the education program. Abraham's Menstrual Symptom Questionnaire's translated version was administered in order to measure total premenstrual syndrome scores. Whereas no such significant changes were found in the control group, suggesting that probably the education program was the reason for the decrease in premenstrual syndrome in young girls of experimental group [152].

Tabassum et al., (2005) conducted an observational study (2005) to find out the frequency of premenstrual syndrome (PMS) in young college girls and to describe the severity of emotional, physical and behavioural symptoms. The study was conducted at the Khyber Medical College, Peshawar by convenient sampling on 384 young girls. Data was collected over two cycles by filling a 29 items shortened premenstrual assessment form based on Moos Menstrual Distress Questionnaire after taking consent from medical students. Results were given according to both criteria i.e. ICD-10 and DSM-IV. The frequency of premenstrual syndrome was 53% according to ICD-10 criteria, among which 42% was mild, 18.2% moderate and 31.7% severe. A total of 64 girls (18.2%) met the DSM-IV criteria for severe PMS or Premenstrual Dysphoric disorder (PMDD). The order of frequency of symptoms occurring in PMS was general body discomfort, anxiety, backache,fatigue and depression. Most frequently reported symptoms in PMDD

group were anger, anxiety, stress, depression, fatigue and general body discomfort [153].

Frackiewicz and Shiovitz (2001) reviewed premenstrual disorders, their varied symptoms, possible etiology, and treatment options. Data Sources: Published articles identified through MEDLINE (1966-2001) using the search terms premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD) and the additional terms treatment and etiology. Additional references were identified from the bibliographies of the retrieved articles. PMS refers to a group of menstrually related disorders that are estimated to affect up to 40% of women of childbearing age. The varied symptoms of PMS include mood swings, tension, anger, irritability, headache, bloating, and increased appetite with food cravings. PMS symptoms occur during the luteal phase of the menstrual cycle and remit with the onset of menstruation or shortly afterward. Approximately 5% of women with PMS suffer from PMDD, a more disabling and severe form of PMS in which mood symptoms predominate. Because no tests can confirm PMS or PMDD, the diagnosis should be made on the basis of a patient-completed daily symptom calendar and the exclusion of other medical disorders. The causes of PMS and PMDD are uncertain, but are likely associated with aberrant responses to normal hormonal fluctuations during the menstrual cycle. For most women, symptoms can be relieved or reduced through lifestyle interventions, such as dietary changes and exercise, and drug therapy with hormonal or psychotropic agents. For PMDD, selective serotonin reuptake inhibitors have recently emerged as first-line therapy. Certain dietary supplements, including calcium, also may be

an option for some women. PMS and PMDD are complex but highly treatable disorders. Pharmacists can improve the recognition and management of these common conditions by providing patient education on premenstrual symptoms and counseling women on lifestyle interventions and pharmacotherapy to relieve their discomfort [154].

According to Abraham (1983) have reported 150 symptoms under the heading of premenstrual syndrome, in that more than 97% of women were experiences at least one of the symptoms. One of the important areas related to menstrual cycle is premenstrual syndrome that is related to the first part of menstrual cycle started after ovulation, increased its intensity during 3 to 5 days prior to the menstruation to first day of menstrual flow related to her physical change, mood, behavior and changes in social adjustment.

Anandhalakshmi, et al. (2011) SRM medical college hospital and research centre, conducted a cross sectional study to assess the prevalence of premenstrual syndrome among young college students. The study sample was 300 students, in that 96% of the students had at least one symptom of premenstrual syndrome and the prevalence of premenstrual syndrome was 67%. The finding shows that association between body mass index and premenstrual syndrome, they concluded that prevalence of premenstrual syndrome common in college students [155.].

Anderson and Johnson (2005) conducted a randomized controlled study to identify the use of complementary and alternative therapies for obstetrics and gynecological treatment and health promotion. Fifty four articles assessing a

variety of health modalities meeting the criteria were included. The study concluded that Complementary and Alternative medicine interventions have evidence of effectiveness for use in obstetrics and gynecological problems [156.].

Wang et al. (2012) investigated the prevalence of premenstrual syndrome and premenstrual dysphoric disorder among the age group of 18-45 years. For those who were consistent with premenstrual syndrome diagnostic criteria, the daily record of severity of problems assessed over two months. Participants were then categorized as having no perceived symptoms, mild premenstrual syndrome, and moderate premenstrual syndrome. Among them irritability 91%, breast tenderness 78%, depression 68 %, abdominal bloating 64% [157].

In the year 2012 Kitamura conducted a study to determine the relationship between premenstrual syndrome among adolescent girls, a total of 1,431 high school students were assessed. Out of them, 71.3% were classified with moderate to severe premenstrual syndrome and 30.2% with premenstrual dysphoric disorder and also 85% of the students had dysmenorrhoea. The rates of prevalence of premenstrual dysphoric disorder and moderate to severe premenstrual syndrome were increased according to the severity of dysmenorrhea [158].

A cross sectional study to assess the prevalence of premenstrual syndrome was conducted by Joshi et al. (2011), 107 samples were selected between the age group of 18-30 years by using simple random method, the findings shows that 26 (24.3%) persons did not reported any symptoms and 81 (75.7%) were reported the symptoms of premenstrual syndrome. Mastalgia was the most common symptom

(50.5%), followed by mood changes (46.7%), depression (7.5%) and anger attacks (6.5%) [159].

In Surya Fertility centre, Bhakti (2011) conducted a descriptive study to assess the prevalence of premenstrual syndrome among the reproductive age group. Among them 80% of them had mild to moderate premenstrual syndrome, it is estimated by including all women who experience any physical or emotional symptoms prior to menstruation. In that 30-40% of them had severe symptoms. Only 10% of them had more severe symptoms [160.].

Sharma et al. (2011) conducted a study to assess the type and frequency of problem related to menstruation in Maulana Azad medical college, New Delhi, 198 students had been studied. Data was collected by personal interviews using a pre-tested, semi structured questionnaire. Results showed that, dysmenorrhea (67.2%) was one of the problems and 63.1% had one or the other symptom of premenstrual syndrome. Daily routine of 60% of girl, was affected due to prolonged bed rest, missed social activities, disturbed sleep and decreased appetite. Study concluded that students had high prevalence of premenstrual syndrome and they need counseling services, relevant information on possible treatment options [161].

A cross sectional descriptive study was conducted to assess the prevalence and severity of premenstrual syndrome, with the objectives to rule out the problems related to menstruation in the last three cycles. Study was conducted in three medical collages at different states of India (Jagadalpur, Orissa and

madyapradesh). 107 female medical students were randomly chosen for this study. Results showed that the mean age at menarche was 12 years and premenstrual syndrome is the most common problem. In this study 6.32%, 30.37% and 63.2.9% participants were suffering from severe, moderate and mild level of premenstrual syndrome, respectively.

A descriptive study was conducted to determine the frequency and severity of Premenstrual Syndrome in medical college students to evaluate the impact of the condition on the quality of life and to find out the associated risk factors. Unmarried medical students aged between 18-25 years with regular menstrual period for the last six months were recruited by convenience sampling. Study participants (n=172) had mean age of 21 years. 89 (51%) of the girls met the criteria for Premenstrual syndrome, among them, 53 (59.5%) had mild symptoms, 26 (29.2%) had moderate symptoms and 10 (11.2%) had severe symptoms.10 (5.8%) of the girls were found to have Premenstrual Dysphoric Disorder. Dysmenorrhea ($p < 0.003$) and family history of premenstrual syndrome ($p < 0.001$) were significantly associated with premenstrual syndrome on univariate and multivariate analysis.

In the year (2009) cross-sectional study was carried out among college students of Zahedan University (Iran), aged between 18-27 years. Overall 300 participants were asked to complete an anonymous questionnaire assessing premenstrual symptoms. Out of the 300 participants, 98.2% reported at least one symptom. Most common symptoms were feeling of tiredness or lethargy (84%), depressed mood (72.3%), sudden feeling of sadness or tearfulness (70.3%),

anxiety (70%), backache (69%) and sleep problems (66%). The severity of symptoms was significantly higher for the younger women (18-24 years) compared to the older women (25-27 years). Preventive and treatment strategies for premenstrual syndrome are highly recommended. According to studies menstrual problems are common among young girls.

Thakra et al. (2008) conducted a study to find out the types and frequency of problems related to menstruation in adolescent girls and the effect of these problems on daily routine. 198 adolescent girls have been studied between the age group of 13-19 years. Data was collected by personal interviews on a pre-tested, semi-structured questionnaire. The questions covered menstrual problems. Dysmenorrhoea was the commonest problem is around 67% and 63.1% of the girls had one or the other symptoms of Pre-menstrual syndrome. Other related problems were present in 55% of study subjects. Among them 60% of girls were affected with daily routine due to prolonged bed rest, missed social activities/commitments, disturbed sleep and decreased appetite. 17% of them had absenteeism to school and 25% of them had abstained from work [162].

The study findings affirm the fact that premenstrual syndrome profoundly affects the academic activities of young female medical students [163].

A journal on alternative and complimentary medicine (2010), Kathryn, conducted a cross sectional study to explore the effect of aromatherapy on premenstrual syndrome among college students. The study was a randomized placebo-control trail. The sample size was 67 college students. The visual

analogue scale was used to assess their pain level with a verbal multidimensional scoring system. The menstrual cramps were significantly lowered in the aromatherapy group than in the other groups at both post-test points. The findings suggest that aromatherapy using topically applied lavender, clary sage, rose is effective in decreasing the severity of menstrual cramps. Aromatherapy can be offered as part of the nursing care to women experiencing menstrual cramps [164].

A study was conducted by Carroll (2011) among 80 students suffering from premenstrual syndrome. The students were randomly divided into two groups and received, either 10 drops of citrus essence or placebo drops, three times a day during the luteal phase for two cycles. The group on citrus essence witnessed a significant reduction of 46.08% in the symptoms compared to the group on placebo 14.21%, ($p<0.001$). After the intervention, there were also significant decreases in the severity of physical and psychological symptoms in both citrus essence respectively, 24.3% and 21.78% and placebo groups respectively, 2.07% and 9.21%, ($p<0.001$). The study showed that citrus essence could reduce the severity of premenstrual syndrome. The essence is suggested to be taken during the luteal phase in two consecutive cycles [165].

In the year 2010 Brush et al. conducted the study to evaluate the effectiveness of primrose oil on management of premenstrual syndrome, the sample size was 68 and they received 1-2gms of prime rose oil for 3 days before the onset of premenstrual symptoms until the first day of menstruation, based on self report scale the researcher concluded that among them 61% of them had

complete relief of premenstrual symptoms, 16% of them had partial relief of symptoms [166].

Dante (2010) conducted a meta analytical study to find out the use of natural oils for the management of premenstrual syndrome, the findings reported that vitex agnus castus and the evening primrose oil will be more effective in the management of premenstrual symptoms [167].

A study was conducted to evaluate the therapeutic effectiveness of evening primrose oil in the relief of 10 symptoms associated with premenstrual syndrome was studied in 38 women,. The prospective trial was randomized; double-blind and placebo controlled and was crossed over after three cycles. Although the result showed an improvement in symptoms of premenstrual syndrome during the trial, no significant difference in the scoring between the active and placebo groups were found over six cycles. No carry over effect of active medication was observed, the beneficial effect on all symptoms was rapid, the scoring decreasing in the first cycle but increasing slightly at the change-over period after the third cycle, irrespective of whether the active and placebo medication was next given. These findings indicate that the improvement by the women with moderate premenstrual syndrome was slowly a placebo effect. According to the report of George in the year 2007, more than 85% of the person will be getting relief of premenstrual syndrome with primrose oil massage. He selected the sample of 100 college students with premenstrual syndrome and the intervention given to the students with lavender oil massage for the duration of 15-20 minutes for three days [168].

Sampalis (2006) conducted a study to evaluate the effectiveness of Neptune Krill Oil for the management of premenstrual syndrome and dysmenorrhoea and to compare the effectiveness of Neptune krill oil for the management of premenstrual syndrome and dysmenorrhoea with that of omega-3 fish oil. Treatment period of three months with either Neptune krill oil or omega-3 fish oil. In 70 patients with complete data, a statistically significant improvement was demonstrated among baseline, intermittent, and final evaluations in the self assessment questionnaire ($p < 0.001$) within the Neptune krill oil group as well as between-group comparison to fish oil, after three cycles or 45 and 90 days of treatment. Data analysis showed that Neptune Krill Oil can significantly reduce dysmenorrhoea and the emotional symptoms of premenstrual syndrome and is shown to be significantly more effective for the complete management of premenstrual symptoms compared to omega-3 fish oil [169].

Kim et al. (2006) conducted a cross sectional study to explore the effect of aromatherapy on premenstrual syndrome among college students. The study was a randomized placebo-control trail. The sample size was 67 college students. The visual analogue scale was used to assess their pain level with a verbal multidimensional scoring system. The menstrual cramps were significantly lowered in the aromatherapy group than in the other groups at both post -test points. The findings suggest that aromatherapy using topically applied lavender, clay sage, rose is effective in decreasing the severity of menstrual cramps. Aromatherapy can be offered as part of the nursing care to women experiencing menstrual cramps. The study consisted of a double-blind, three-group

experimental pre-test and post-test design, and the results indicated that menstrual cramps were significantly lowered in the aromatherapy group than in the other two groups after the intervention [170].

A randomized placebo-controlled clinical trial on college students to assess the effect of aromatherapy upon menstrual cramps by Han et al. (2012). The students were randomized into three groups: (1) an experimental group who received aromatherapy, (2) a placebo group, and (3) a control group. Aromatherapy was applied topically to the experimental group in the form of an abdominal massage using two drops of clary sage and one drop of rose in 5 cc of almond oil. The placebo group received the same treatment but with almond oil only. The menstrual cramps were significantly lowered in the aromatherapy group then in the other two groups at both post-test time points [171].

Wang et al. (2012) conducted a cross sectional study to investigate the effect of self-aromatherapy massage on menstrual pain and anxiety among staff nurses. The subjects were 63 female nurses who rated their menstrual pain >5 on a 10-point visual analogue scale. Subjects were non-randomly allocated into three groups. Menstrual pain and anxiety levels were assessed using a visual analogue scale, and we assessed the menstrual pain 4 times during a short time period. The menstrual pain was significantly lower in the aromatherapy group than in the other two groups after 24 hours. Using multiple regression analysis, the use of aromatherapy was found to be associated with the changes in premenstrual symptoms [172].

In the year 2012 Taavoni conducted a randomized placebo-controlled clinical trial in a menopausal clinic at a gynecology hospital in Tehran. The study population comprised of 90 women who were assigned to an aromatherapy massage group, a placebo massage group, or a control group. Each participant in the aromatherapy massage group received 30-minute aromatherapy treatment sessions twice a week for 4 weeks with aroma oil, whereas participants in the placebo massage group received the same treatment with plain oil. When the aromatherapy massage and the placebo massage groups were compared, the menopausal score for the aromatherapy massage group was found to be significantly lower ($P < 0.001$) than for the placebo group. The results of the study demonstrate that both the placebo massage and aromatherapy massage were effective in reducing menopausal symptoms. However, aromatherapy massage was more effective than placebo massage [173].

Brent (2011) investigated the alleviating effects of aromatherapy massage and acetaminophen on menstrual pain among students subjects were divided into two groups: the aromatherapy massage group with the sample size of (n=32) and the acetaminophen group with the sample size of (n=32). Aromatherapy massage was performed on subjects in the treatment group. The abdomen was massaged once using clary sage, marjoram, cinnamon, ginger, and geranium in a base of almond oil. The level of menstrual pain was assessed using a visual analogue scale at baseline and twenty-four hours afterward. The reduction of menstrual pain was significantly higher in the aromatherapy group than in the acetaminophen group.

These finding suggest that aromatherapy massage provide effective treatment for menstrual pain among the students [174].

A randomized placebo- controlled clinical trial was conducted in Korea with the objective to explore the effect of aromatherapy on menstrual cramps and symptoms of dysmenorrhoea. The subjects were 67 college students. Subjects were randomized into three groups, an experimental group (n=25) who received aroma therapy, a placebo group (n=20) and a control group (n=22) Aromatherapy was applied topically to the experimental group in the form of an abdominal massage using two drops of lavender, one drop of clary sage and one drop of rose in 5cc almond oil. The placebo group almond oil only and the control group received no treatment. The menstrual cramps were assessed using a visual analogue scale. Menstrual cramps were significantly lowered in the aromatherapy group than in the other two groups [175].

4. MATERIALS AND METHODS

4.1 Subjects:

A total of 60 women volunteers who met the inclusion criteria with ages ranging between 18 to 35 years old participated in the study.

4.2 Source of subjects:

The study subject were women volunteers recruited from general population, students, the out-patient and In-patient department of Government Yoga and Naturopathy Medical College & hospital, Arumbakkam, Chennai-106. The subjects underwent medical examinations and completed a standardized PSST Questionnaire before inclusion into the study. None of the women were pregnant or reported taking oral contraceptives to control the menstrual cycle, however pregnancy tests were not performed and regular menstrual cycles resumed every month in all the subjects. Olfactory function tests were performed on subjects to assure that none had anosmia. subjects were given two sets of three bottles- two held distilled water and the third contained essential oil and were asked to choose the correct response in both trials.

4.3 Inclusion and Exclusion criteria:

4.3.1 Inclusion criteria:

The following inclusion criteria would be the basis for selecting the subjects:

- Age group: between 18-35 years.
- Women with premenstrual syndrome.

- Women who are not exposed to aromatherapy previously.
- Women who are willing to give their consent.

4.3.2 Exclusion criteria:

Participants will be excluded if they have systemic issue.

- Pre-menstrual dysphoric disorder.
- Below 18 years and above 35 years.
- Under medication.
- Chronic illness.
- Pregnancy and Lactation.
- Recently hospitalized.

4.4 Written Informed consent:

Subjects who fulfilled inclusion criteria received an explanation of the nature and purpose of the study; to investigate soothing effects of plant fragrance on symptoms of premenstrual syndrome and rights as research subjects. We did not, however inform subjects of which fragrance we would use for the experiments. Informed consent form was administered in English. Adequate time was given to each subject to go through the information sheet and their queries were answered. Their right to withdraw from the study and the need for willingness to participate voluntarily in the study was explained. All the subjects expressed their willingness to participate in the study by giving a signed informed consent. (A sample information sheet and consent form is enclosed in Annexure).

4.5 Study design:

Experimental study method. The total study duration of each patient is 3 months. Initial screening will be done to select the patients meeting the requirements of inclusion criteria and selected patients will be allotted for intervention.

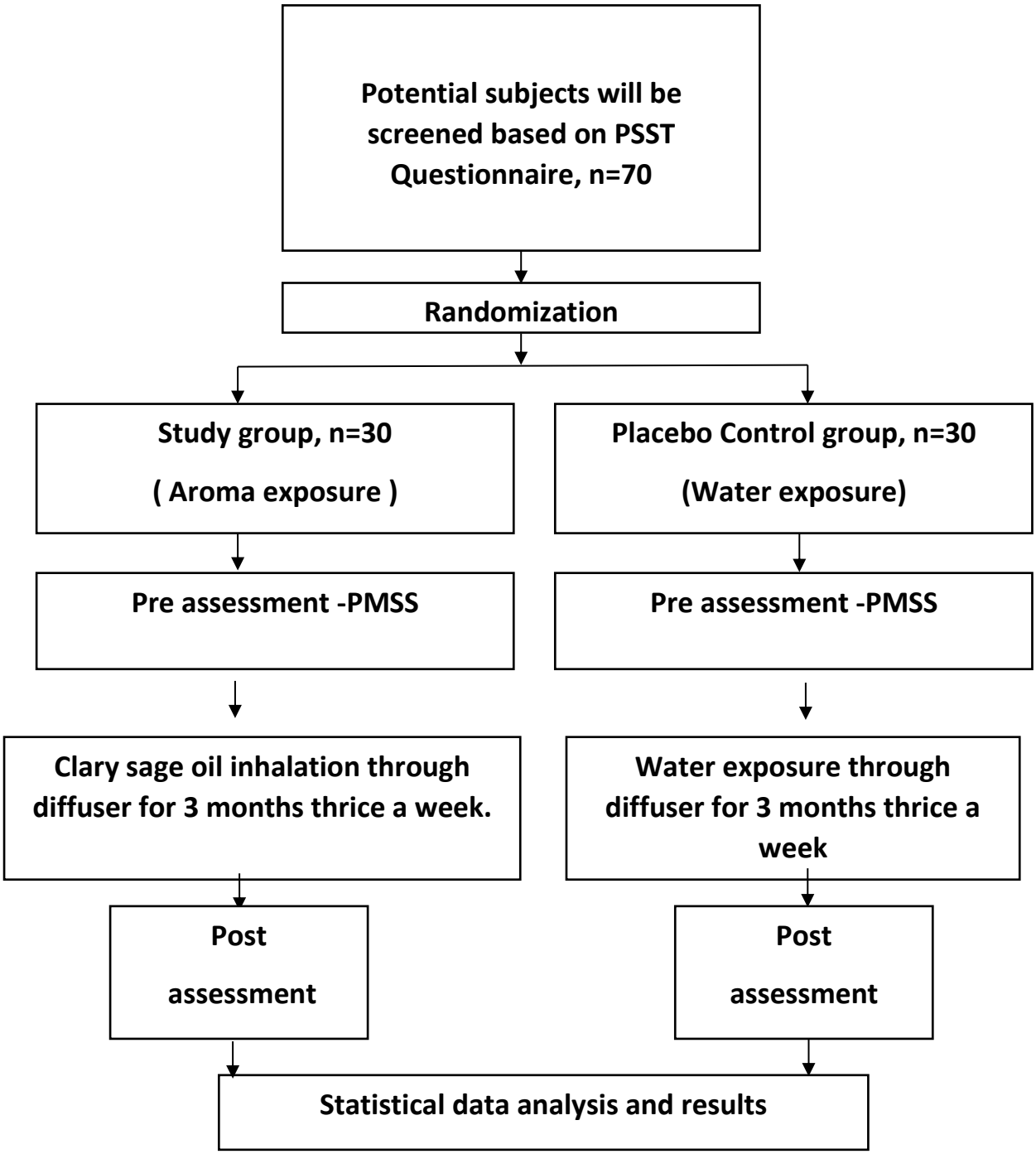
4.6 Ethical clearance:

Subjects who fulfilled the inclusion criteria were appraised about the purpose of the study and their rights as research subjects. Informed consent form was administered in local language i.e., Tamil and English as well. Adequate time was given to the participants to go thrugh the information sheet and their queries were answered. Their rights to withdraw anytime from the study and the need for willingness to participate voluntarily in the study were explained. All the subjects expressed their willingness to participate in the study by giving a signed informed consent. (A sample information sheet and consent form is enclosed as Annexure). Ethical clearance was obtained from the Institutional Ethical Committee prior to the start of the study and the approval for the same was granted.

4.7 Allocation of Subjects:

Subjects were randomly allocated in Study group (Aroma exposure group) and Placebo control group (Water exposure group) in 1:1 ratio. 70 Subjects were initially screened.60 subjects who met the inclusion and selection criteria were allocated in the study. Subjects were then randomly divided into 2 groups i.e., (n= 30) Study group and (n= 30) Placebo control group using lottery method.

4.8 Trial profile:



4.9 Intervention

4.9.1 Tools of Intervention:

4.9.1.1 PSST:

‘The Premenstrual Symptoms Screening tool’’ (PSST). The PSST reflects and ‘translates’ categorical DSM-IV criteria into a rating scale with degrees of severity. The results are in line with reported prevalence rates from several recent large prospective studies. We believe that the PSST applies a necessary degree of measure of severity and impact of premenstrual symptoms, establishes quickly if women qualify for PMDD, and is less time consuming and more practical than two cycles of prospective charting. This fast simple tool is an effective screening tool and an important starting point for further assessment.

4.9.1.2 PMSS:

Premenstrual syndrome scale (PMSS). The scale was to measure premenstrual symptoms, and validity and reliability analyses were performed. The premenstrual syndrome scale comprised 40 questions with three sub-scales (Physiological, Psychological and Behavioural symptoms). This 5-point Likert-type scale consisting of 40 items. The measurements on the scale are set according to the following scoring system: the response Never was scored as “1”, rarely as “2”, sometimes as “3”, very often as “4” and always as “5” points.

4.9.2 Study group:

30 subjects were randomly selected and exposed to clary sage aroma nasal diffuser for 10 minutes thrice a week for three months.

4.9.3 Procedure:

This experiment used two kinds of aroma stimulation – Clary sage(Salvia sclerae) and water as a control.10 µl of clary sage essential oil or water were pipetted into a small cotton pad designed for a diffuser(Aroma care diffuser).Air flow from the diffuser was placed near the subjects nostril using the diffusers 15 cm long circular cylinder fitted with a perforated funnel of diameter 3 cm for 10 minutes. The procedure was performed thrice a week for 3 months i.e 36 sessions after which the PMSS was repeated.

4.9.4 Placebo control group:

30 subjects were randomly selected and exposed to water through diffuser for 10 minutes thrice a week for three months.

4.9.5 Assessments:

The pre-intervention and post-intervention assessments were collected using Premenstrual Syndrome Scale questionnaire (PMSS). This a standardized, self-administered 40 item questionnaire to assess physiological, psychological and behavioral symptoms. Each symptom was rated on five points ranging from never to always. These added raw scores were then converted to T scores according to PMSS manual.

4.9.6 Data collection:

The baseline data was collected during the first month. After randomization and respective interventions post intervention data was collected at the end of three months using self-reported PMSS. Data were organized in Microsoft Excel sheets (version 2010)

5. RESULTS

All 60 participants successfully completed the study. Premenstrual Syndrome Scale questionnaire (PMSS) was used to assess the difference before and after intervention. PMSS is a self-reported scale consisting and assessing 3 components- physiological, psychological and behavioural. The normality of distribution was measured using Shapiro-wilks test. Comparisons between groups was measured using Mann whitney U-test and within group was measured using Wilcoxon signed rank test. At baseline, the mean physiological, psychological and behavioural components of the 60 participants were 65.07 (IQR 61, 69), 51.22 (IQR 48, 55.75) and 51.50 (IQR 47.25, 56) respectively (Table 1). Mean reduction in the physiological score was higher in the study group when compared to the placebo control group (30.60 ± 7.789 vs 8.87 ± 7.248). Similarly, better mean reduction in the psychological (19.43 ± 8.96 vs 4.23 ± 5.49) and behavioural (19.30 ± 7.3 vs 3.33 vs 4.097) scores was observed in the study group in comparison to the control group (Table 2).

The results are also expressed in terms of median due to a wider range and standard deviation observed, especially in the control group. A statistically significant reduction in all three physiological, psychological and behavioural scores ($p<0.0001$) was observed in the intervention group when compared to the control group (Table 3). Interestingly, within group analysis showed a statistically significant reduction in the control group similar to that of the intervention group (both $p<0.001$). However, the difference in reduction in the control group was not as ‘clinically’ significant or relevant as in the intervention group in the physiological (7.50 vs 32.50), psychological (6.0 vs

19.50) and behavioural (2.50 vs 20.0) scores. Therefore, the results shows a high level of statistical and clinical significance and highly favours the intervention group in the reduction of all 3 components of the PMSS when compared to the placebo-controlled group.

Table 1: Summary of Study characteristics (n=60)

	Physiological Pre score	Physiological Post score	Physiological Difference score	Psychological Pre score	Psychological Post score	Psychological Difference score	Behavioural Pre score	Behavioural Post score	Behavioural Difference score
N	60	60	60	60	60	60	60	60	60
Mean	65.07	45.33	19.73	51.22	39.38	11.83	51.50	40.18	11.32
Median	65.50	45.00	21.00	51.50	42.50	10.00	52.00	38.50	7.50
SD	7.346	16.628	13.256	5.149	10.235	10.633	5.500	9.663	9.963
Minimum	50	21	0	41	21	-5	41	22	0
Maximum	80	72	44	60	56	36	60	59	32
IQR	(61.00 , 69.00)	(28.25 , 61.00)	(8.00 , 30.75)	(48.00 , 55.75)	(31.25 , 46.00)	(3.00 , 21.00)	(47.25 , 56.00)	(32.00 , 50.00)	(2.00 , 20.00)

Table 2: Summary of study characteristics by group

Group		Physiological Pre score	Physiological Post score	Physiological Difference score	Psychological Pre score	Psychological Post score	Psychological Difference score	Behavioural Pre score	Behavioural Post score	Behavioural Difference score
Control	N	30	30	30	30	30	30	30	30	30
	Mean	69.77	60.90	8.87	52.07	47.83	4.23	51.83	48.50	3.33
	Median	68.50	61.00	8.00	52.00	46.00	3.50	52.50	50.00	2.00
	SD	5.488	5.215	7.248	4.417	4.450	5.494	5.427	5.859	4.097
	Minimum	61	51	0	43	44	-5	41	39	0
	Maximum	80	72	27	60	56	16	60	59	20
	IQR	(65.75 , 74.25)	(56.75 , 64.25)	(2.75 , 12.00)	(48.75 , 56.00)	(44.75 , 54.00)	(-.25 , 8.00)	(47.75 , 56.25)	(41.75 , 53.00)	(1.00 , 4.00)
Study	N	30	30	30	30	30	30	30	30	30
	Mean	60.37	29.77	30.60	50.37	30.93	19.43	51.17	31.87	19.30
	Median	61.00	28.50	30.50	51.00	31.50	21.00	52.00	32.00	19.50
	SD	5.828	5.829	7.789	5.738	6.751	8.962	5.645	3.540	7.302
	Minimum	50	21	14	41	21	3	41	22	3
	Maximum	70	39	44	60	41	36	60	38	32
	IQR	(55.75 , 65.25)	(24.75 , 35.25)	23.75 , 37.00)	(45.00 , 55.25)	(23.75 , 37.00)	(12.00 , 26.25)	(46.75 , 55.25)	(29.75 , 35.00)	(14.75 , 24.00)

Figure 3: Histogram of Physiological symptom score difference

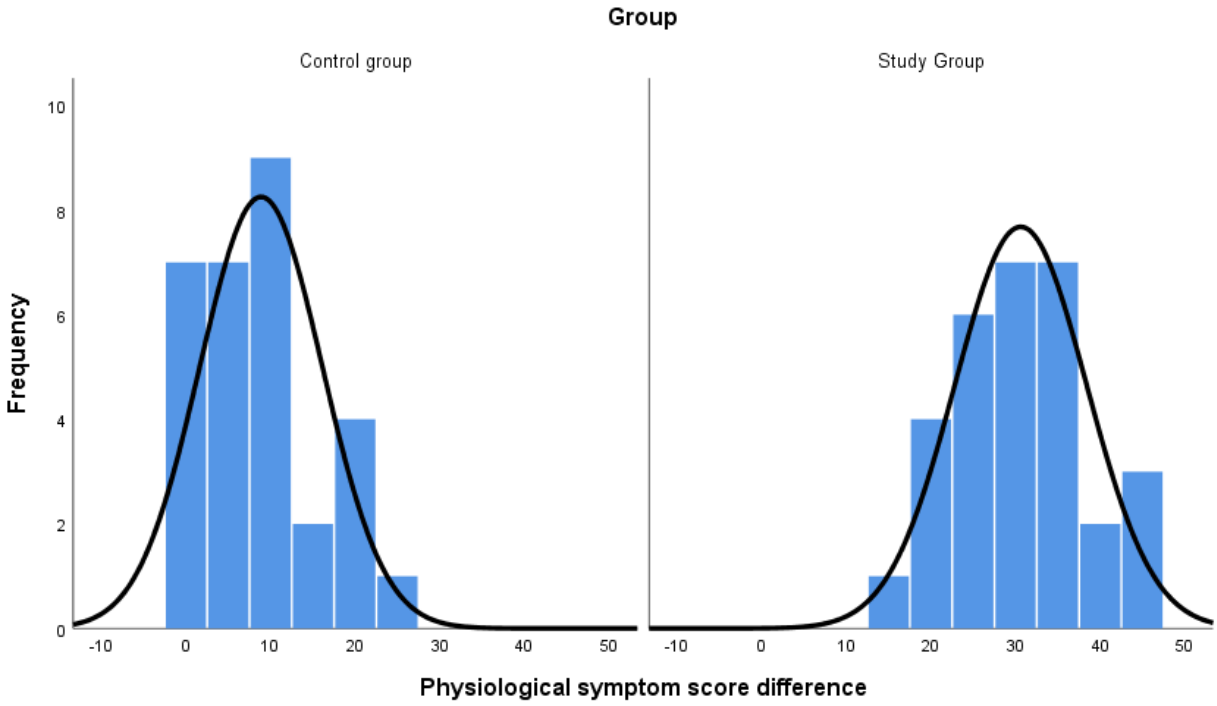


Figure 4: Histogram of Psychological symptom score difference

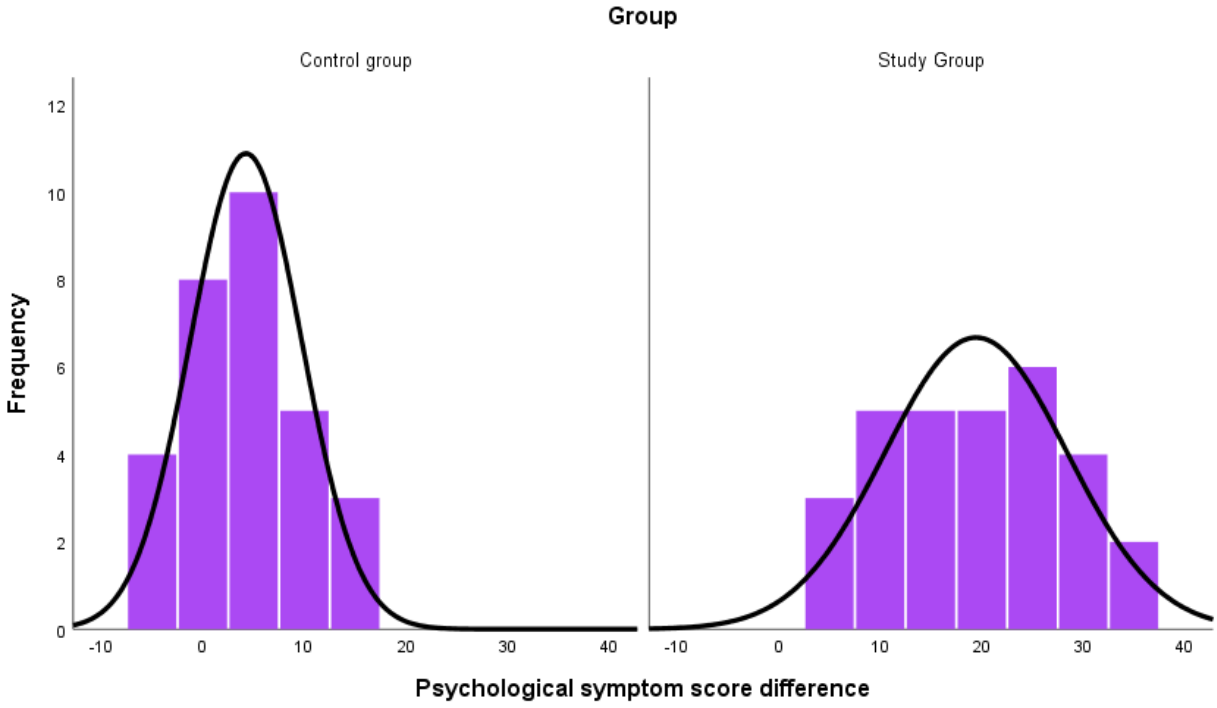


Figure 5: Histogram of Behavioural symptom score difference

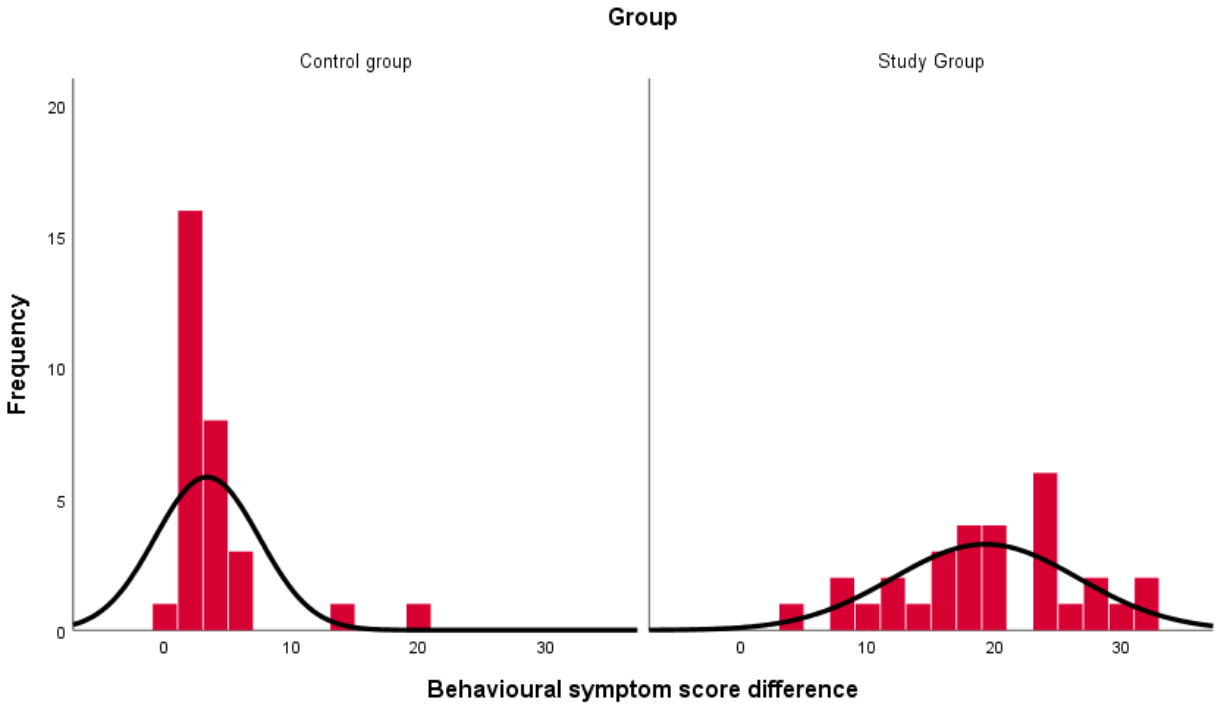


Table 3: Comparison on Physiological, Psychological and Behavioural symptom score between groups using Mann Whitney test

	Control Group		Study group		P value
	N	Median(IQR)	N	Median(IQR)	
Physiological Pre score	30	68.50 (65.75 , 74.25)	30	61.00 (55.75 , 65.25)	-
Physiological Post score	30	61.00 (56.75 , 64.25)	30	29.77 (24.75 , 35.25)	-
Physiological Difference score	30	08.00 (2.75 , 12.00)	30	30.50 (23.75 , 37.00)	<0.0001
Psychological Pre score	30	52.00 (48.75 , 56.00)	30	50.37 (45.00 , 55.25)	-
Psychological Post score	30	46.00 (44.75 , 54.00)	30	31.50 (23.75 , 37.00)	-
Psychological Difference score	30	03.50 (-0.25 , 8.00)	30	21.00 (12.00 , 26.25)	<0.0001
Behavioural Pre score	30	52.50 (47.75 , 56.25)	30	52.00 (46.75 , 55.25)	-
Behavioural Post score	30	50.00 (41.75 , 53.00)	30	32.00 (29.75 , 35.00)	-
Behavioural Difference score	30	02.00 (1.00 , 4.00)	30	19.50 (14.75 , 24.00)	<0.0001

Interpretation: There is an evidence to show that statistically significant (all 3 parameters change p = <0.0001) difference between groups on their change of Physiological, Psychological and Behavioural symptom score.

Table 4: Analysis of with in group comparison using Wilcoxon signed Rank test

Group		Physiological Pre score	Physiological Post score	Physiological Difference score	Psychological Pre score	Psychological Post score	Psychological Difference score	Behavioural Pre score	Behavioural Post score	Behavioural Difference score
Control	N	30	30	30	30	30	30	30	30	30
	Median	68.50	61.00	7.50	52.00	46.00	6.00	52.50	50.00	2.50
	IQR	(65.75 , 74.25)	(56.75 , 64.25)	(2.75 , 12.00)	(48.75 , 56.00)	(44.75 , 54.00)	(-.25 , 8.00)	(47.75 , 56.25)	(41.75 , 53.00)	(1.00 , 4.00)
	P value	-	-	<0.0001	-	-	0.001	-	-	<0.0001
Study	N	30	30	30	30	30	30	30	30	30
	Median	61.00	28.50	32.50	51.00	31.50	19.50	52.00	32.00	20.00
	IQR	(55.75 , 65.25)	(24.75 , 35.25)	23.75 , 37.00)	(45.00 , 55.25)	(23.75 , 37.00)	(12.00 , 26.25)	(46.75 , 55.25)	(29.75 , 35.00)	(14.75 , 24.00)
	P value	-	-	<0.0001	-	-	<0.0001	-	-	<0.0001

Interpretation: There is an evidence to show that statistically significant difference between pre and post of Physiological, Psychological and Behavioural symptom score in the study group (p = <0.0001). Also the same significant difference observed in the control group.

6. DISCUSSION

Comparisons between groups was measured using Mann whitney U-test and within group was measured using Wilcoxon signed rank test. In this study, the severity of PMS physical and mental symptoms in all participants who had received thirty six sessions of intervention had a significant reduction compared to the Placebo-control group; however, the reduction was higher in the aroma exposure group than in the Placebo-control group. Reviewing articles showed many studies on aromatherapy, but very little research has been done on aromatherapy nasal exposure particularly its effects on PMS. Lavender oil research investigated the effects of aromatherapy on PMS emotional symptoms, and their study showed that aromatherapy inhalation reduced PMS emotional symptoms [129]. The book "Ayurveda and Aromatherapy" mentions that "Clary sage has a rejuvenating effect on the endocrine system. It balances the pituitary and is especially effective at feeding estrogen directly into the skin." [100]. In this case we have studied the effects of clary sage oil through nasal exposure and its effects on physiological, psychological and behavioural symptoms. This study also showed that the severity of physiological symptoms such as breast tenderness and swelling, abdominal bloating, weight gain, headache, dizziness/fainting, fatigue, palpitation, pelvic discomfort and pain, abdominal cramps, change in bowel habits, increased appetite, generalized aches and pain, food craving(sugar/salt), skin changes, rashes and pimples, nausea/vomiting, muscle and joint pain; psychological symptoms such as irritability, anxiety, tension, mood swings, loss of concentration, depression, forgetfulness, easy crying/crying spells, sleep changes, insomnia/hypersomnia,

confusion, aggression, hopelessness; behavioural symptoms such as social withdrawal, restlessness, lack of self-control, feeling guilty, clumpsiness, lack of interest in usual activities, poor judgement, impaired work performance, obsessional thoughts, compulsive behavior, irrational thoughts, being over-sensitive decreased more in the study group than in the placebo-control group. Since this research is the first study involving clary sage oil in the field of aromatherapy on PMS, in that case positive results have been obtained, hence further studies are recommended to confirm the findings.

7. CONCLUSION

The present study indicated Clary sage aromatherapy as a potential therapeutic modality, is attributable to the improvement of physiological, psychological and behavioural symptoms. This study further implies that Clary sage helps to relieve premenstrual symptoms, and ultimately, support the mind and body health of women.

8. BIBLIOGRAPHY

1. RCOG. RCOG Green-top Guideline No.48: Management of Premenstrual Syndrome. London: Royal College of Obstetricians and Gynaecologists, 2007:1–16.

2.Campbell E, Peterkin D, O'Grady K, Sanson-Fisher R. Premenstrual symptoms in general practice: prevalence and treatment. J Reprod Med 1997;42:637–46.PubMed | CAS | Web of Science® Times Cited: 51

3.Borenstein J, Chiou CF, Dean B, Wong J, Wade S. Estimating direct and indirect costs of premenstrual syndrome. J Occup Environ Med 2005;47:26–33.PubMed | Web of Science® Times Cited: 25

4. Biggs WS, Demuth RH. Premenstrual syndrome and premenstrual dysphoric disorder. Am Fam Physician. 2011; 84(8):918-24.

5. Baker LJ, O'Brien PM. Premenstrual syndrome (PMS): a peri-menopausal perspective. Maturitas. 2012; 72(2):121-5.

6. Ashraf Direkvand-Moghadam,1 Kourosh Sayehmiri,2 Ali Delpisheh,3 and Satar Kaikhavandicorresponding author4.Epidemiology of Premenstrual Syndrome (PMS)-A Systematic Review and Meta-Analysis Study.J Clin Diagn Res. 2014 Feb; 8(2): 106–109.

7. Yonkers KA, O'Brien PMS, Eriksson E. Premenstrual syndrome.Lancet. 2008;371(9619):1200–1210.

8. Perkonigg A, Yonkers KA, Pfister H, Lieb R, Wittchen HU. Risk factorsfor premenstrual dysphoric disorder in a community sample of youngwomen: the role of traumatic events and posttraumatic stress disorder.J Clin Psychiatry. 2004;65(10):1314–1322.

9. Ossewaarde L, van Wingen GA, Ripkema M, et al. Menstrual cyclerelated changes in amygdale morphology are associated with changes in stress sensitivity. Hum Brain Mapp. 2013;34(5):1187–1193.

10. Olson KC, Carroll HA, Lustyk MK. Psychophysiological stress reactivity relationships across the menstrual cycle. J Horm. 2015;2015:1–5.

11. Biggs WS, Demuth RH. Premenstrual syndrome and premenstrual dysphoric disorder. Am Fam Physician. 2011; 84(8):918-24.

12. O'Brien PM. Helping women with premenstrual syndrome. BMJ 1993;307:1471–1475.

13. Chrousos GP, Torpy DJ, Gold PW. Interactions between the hypothalamic-pituitary-adrenal axis and the female reproductive system: clinical implications. Ann Intern Med 1998;129:229–240.

14. A. L. D. S. Teixeira,´E. C. M. Oliveira, and M. R. C. Dias, "Relationship between the level of physical activity and premenstrual syndrome incidence," Revista Brasileira de Ginecologia e Obstetricia,vol.35,no.5,pp.210–214,2013.

15. J.Borenstein,C.-F.Chiou,B.Dean,J.Wong,andS.Wade,"Estimating direct and indirect costs of premenstrual syndrome," JournalofOccupationalandEnvironmentalMedicine,vol.47,no. 1,pp.26–33,2005.

16. De Yuan Wang. Acupuncture And Premenstrual Syndrome. Thesis. VictoriaUniversity Of Technology, 1998.

17. O'Brien PM. (1993). Helping Women with premenstmal syndrome. British Medical Joumal. 307 (6917); 1471-5

18.Sadler D. A GP's Perspective of PMS. NAPS. 31:4 . Summer 2000.

19. Steiner M. Premenstrual syndromes. Annual Review in Medicine. 48: 447-445.1997.

20. Mahesh , A., Zubair, S., Tirmizi, A., Ali, S.S. "Frequency and associated factors of premenstrual syndrome in medical college girls", Med Channel ,2011; 17(1):34-38.

21. Samia, T., Bilqis, A., Zahid, A., Wajeeha, T. "Premenstrual syndrome: "Frequency and severity in young college girls, Journal of Pakistan Medical Association", 2005; 55(12): 546-549.

22. Nour, M. B., Mahnaz, M., Golbahar, K. "Prevalence and severity of premenstrual symptoms among Iranian female university students", Journal of Pakistan Medical Association, 2009; 51(4):205-8.

23. Kroll, A. R. "Recreational physical activity and premenstrual syndrome in college-aged women", Masters Theses, UMASS, AMHERST. 2009. available at http://scholarworks.umass.edu/theses/428,accessed on 2011.

24. Zegeye, D.T., Megabiaw, B., Mulu, A. "Age at menarche and the menstrual pattern of secondary school adolescents in northwest Ethiopia", Biomed Central Women's Health, 2009: 9-29.

25. Andrea, J. R.& Sharon, A.W. "Premenstrual syndrome and premenstrual dysphoric disorder: quality of life and burden of illness", Gynecological Endocrinology, 2008; 24 (11):659-62.

26. Paula K. B. "Mini-Review: Premenstrual syndrome and premenstrual dysphoric disorder", Journal of Pediatric and Adolescent Gynecology", 2007; 20:3-12.

27. Ziba, T., Maryam, S., Mohammad, A., Abbas, M. “The effect of premenstrual syndrome on quality of life in adolescent girls”, Iranian Journal of Psychiatry, 2008; 3:105-109.

28. Preeti, K., Archana, A. “Pre-menstrual syndrome: awareness, incidence and prescription pattern in a random female population of dehradun”, The African Journal Of Pharmaceutical Sciences and Pharmacy, 2011; 2(1): 104-113.

29. Freeman, E.W., Halberstadt, S.M., Rickels, K., Legler, J.M., Lin, H., Sammel, M.D. “Core symptoms that discriminate premenstrual syndrome”, J Womens Health, 2011; 20:29-35.

30. Rosseinsky DR, Debonnel PG. An evolutionary theory of premenstrual tension. Lancet. 1974; 2:1024. [PubMed: 4138262]

31. Rapkin AJ, Pollack DB, Raleigh MJ, Stone B, McGuire MT. Menstrual cycle and social behavior in vervet monkeys. Psychoneuroendocrinology. 1995; 20:289–97. [PubMed: 7777657]

32. Hyde J, Sawyer TF. Estrous cycle fluctuations in aggressiveness of house mice. Horm Behav. 1977; 9:290–95. [PubMed: 565333]

33. Ba ¨ckstro ¨m T, Sanders D, Leask RM, Davidson D, Warner P, Bancroft J. Mood, sexuality, hormones and the menstrual cycle. II. Hormone levels and their relationship to premenstrual syndrome. Psychosom Med 1983;45:503–7

34. Hammarba ¨ck S, Ekholm UB, Ba ¨ckstro ¨m T. Spontaneous anovulation causing disappearance of cyclical symptoms in women with the premenstrual syndrome. Acta Endocrinol 1991;125:132–7

35.Andreen L, Sundstro ¨m-Poromaa I, Bixo M, Andersson A, Nyberg S, Ba ¨ckstro ¨m T. Relationship between allopregnanolone and negative mood in postmenopausal women taking sequential hormone replacement therapy with vaginal progesterone. Psychoneuroendocrinology 2005;30:212–

36. Oinonen K, Mazmanian D. To what extent do oral contraceptives influence mood and affect? J Affect Disord 2002;70:229–40

37. Chan AF, Mortola JF, Wood SH, Yen SS. Persistence of premenstrual syndrome during low-dose administration of the progesterone antagonist RU 486. Obsret Gynecol 1994;84:1001–5

38. Sampson GA. Premenstrual syndrome: a double-blind controlled trial of progesterone and placebo. Br J Psychiatry 1979;135:209–15

39. Hammarba ¨ck S, Damber JE, Ba ¨ckstro ¨m T. Relationship between symptom severity and hormone changes in patients with premenstrual syndrome. J Clin Endocrinol Metab 1989;68:125–30

40. Schmidt PJ, Nieman LK, Danaceau MA, Adams LF, Rubinow DR. Differential behavioral effects of gonadal steroids in women with and in those without premenstrual syndrome. N Engl J Med 1998;338:209–16

41. Rupprecht R. Neuroactive steroids: mechanisms of action and neuropsycho-pharmacological properties. Psychoneuroendocrinology 2003;28:139–68

42. Uzunova V, Sheline Y, Davis JM, et al. Increase in the cerebrospinal fluid content of neurosteroids in patients with unipolar major depression who are receiving fluoxetine or fluvoxamine. Proc Natl Acad Sci USA 1998;95:3239–44

43. Rapkin AJ, Morgan M, Goldman L, Brann DW, Simone D, Mehesh VB. Progesterone metabolite allopregnanolone in women with premenstrual syndrome. Obstet Gynecol 1997;90:709–14

44. Wang M, Ba ¨ckstro ¨m T, Sundstro ¨m PI, et al. Neuroactive steroids and central nervous system disorders. Int Rev Neurobiol 2001;46:421–59

45. Smith SS, Gong QH, Li X, et al. Withdrawal from 3alpha-OH-5alpha-pregnan-20-One using a pseudopregnancy model alters the kinetics of hippocampal GABAA-gated current and increases the GABAA receptor alpha4 subunit in association with increased anxiety. J Neurosci 1998:18:5257–84

46. Follesa P, Porcu P, Sogliano C, et al. Changes in GABAA receptor gamma 2 subunit gene expression induced by long-term administration of oral contraceptives in rats. Neuropharmacology 2002;42:325–36

47. Maguire JL, Stell BM, Rafizadeh M, Mody I. Ovarian cycle-linked changes in GABA(A) receptors mediating tonic inhibition alter seizure susceptibility and anxiety. Nat Neurosci 2005;8:797–804

48.Sundstro ¨m PI, Smith S, Gulinello M. GABA receptors, progesterone and premenstrual dysphoric disorder. Arch Womens Ment Health 2003;6:23–41

49. Sundstro ¨m I, Ba ¨ckstro ¨m T. Citalopram increases pregnanolone sensitivity in patients with premenstrual syndrome: an open trial. Psychoneuroendocrinology 1998;23:73–88

50. Rapkin AJ. The role of serotonin in premenstrual syndrome. Clin Obstet Gynecol 1992;35:629–36

51. Ashby CR, Carr LA, Cook CL, Steptoe MM, Franks DD. Alteration of platelet serotonergic mechanisms and monoamine oxidase activity in premenstrual syndrome. Biol Psychiatry 1988;24:225–33

52. Rapkin AJ, Edelmuth E, Chang LC, Reading AE, McGuire MT, Su TP. Whole-blood serotonin in premenstrual syndrome.Obstet Gynecol 1987b;70:533–7

53. Biegon A, McEwen BS. Modulation by estradiol of serotonin receptors in brain. J Neurosci 1982;2:199–205

54. Berman KF, Schmidt PJ, Rubinow DR, et al. Modulation of cognition-specific cortical activity by gonadal steroids: a positron-emission tomography study in women. Proc Natl Acad Sci USA 1997;94:8836–41

55. Epperson CN, Haga K, Mason GF, et al. Cortical gamma-aminobutyric acid levels across the menstrual cycle in healthy women and those with premenstrual dysphoric disorder: a proton magnetic resonance spectroscopy study. Arch Gen Psychiatry 2002;59:851–8

56. Jovanovic H, Cerin A, Karlsson P, Lundber J, Halldin C, Nordstro ¨m AL. A PET study of 5-HT1A receptors at different phases of the menstrual cycle in women with premenstrual dysphoria. Psychiatry Res 2006;148:185–93

57. Protopopescu X, Tuescher O, Pan H, et al. Toward a functional neuroanatomy of premenstrual dysphoric disorder. J affect Disord 2008;108:87–94

58. Rapkin AJ, Berman SM, Mandelkern MA, Silverman DHS, Morgan M, London ED. Neuroimaging evidence of cerebellar involvement in premenstrual dysphoric disorder. Biol Psychiatry 2011;69:374–80

59. Sigmon ST, Dorhofer DM, Rohan KJ, Boulard NE. The impact of anxiety sensitivity, bodily expectations, and cultural beliefs on menstrual symptom reporting: a test of the menstrual reactivity hypothesis. J Anxiety Disord. 2000;14(6):615–633.

60. Sigmon ST, Schartel JG, Herman BA, Cassel AG, Thorpe GL. The relationship between premenstrual distress and anxiety sensitivity: the mediating role of rumination. J Rat Emo Cognitive Behav Ther. 2009; 27:188–200

61. Schmelzer K1, Ditzen B2, Weise C3,4, Andersson G4,5, Hiller W1, Kleinstäuber M3.Clinical Profiles of Premenstrual Experiences Among Women Having Premenstrual Syndrome (PMS): Affective Changes Predominate and Relate to Social and Occupational Functioning.Health Care Women Int. 2015;36(10):1104-23. doi: 10.1080/07399332.2014.954701. Epub 2014 Nov 3.

62. Rebecca Ryser & Leslie L. Feinauer.Premenstrual syndrome and the marital relationship.Journal The American Journal of Family Therapy Volume 20, 1992 - Issue 2

63. Heinemann LA1, Minh TD, Filonenko A, Uhl-Hochgräber K.Explorative evaluation of the impact of severe premenstrual disorders on work absenteeism and productivity.Womens Health Issues. 2010 Jan-Feb;20(1):58-65. doi: 10.1016/j.whi.2009.09.005.

64. Limosin F1, Ades J.Psychiatric and psychological aspects of premenstrual syndrome.Encephale. 2001 Nov-Dec;27(6):501-8.

65. İlhan G1, Verit Atmaca FV1, Kurek Eken M2, Akyol H1.Premenstrual Syndrome Is Associated With a Higher Frequency of Female Sexual Difficulty and Sexual Distress.J Sex Marital Ther. 2017 Nov 17;43(8):811-821. doi: 10.1080/0092623X.2017.1305030. Epub 2017 Mar 13.

66. Nowosielski K1, Drosdzol A, Skrzypulec V, Plinta R.Sexual satisfaction in females with premenstrual symptoms.J Sex Med. 2010 Nov;7(11):3589-97. doi: 10.1111/j.1743-6109.2010.01927.x.

67. Nobles CJ1,2, Thomas JJ2,3, Valentine SE1,2, Gerber MW1, Vaewsorn AS1, Marques L1,2.Association of premenstrual syndrome and premenstrual dysphoric disorder with bulimia nervosa and binge-eating disorder in a nationally representative epidemiological sample.Int J Eat Disord. 2016 Jul;49(7):641-50. doi: 10.1002/eat.22539. Epub 2016 May 20.

68. Déborah Ducasse , Isabelle Jaussent, Emilie Olié, Sébastien Guillaume, Jorge Lopez-Castroman, Philippe Courtet.Personality Traits of Suicidality Are Associated with Premenstrual Syndrome and Premenstrual Dysphoric Disorder in a Suicidal Women Sample.February 10, 2016 https://doi.org/10.1371/journal.pone.0148653

69. E.R. Bertone-Johnson A.G. Ronnenberg S.C. Houghton C. Nobles S.E. Zagarins B.B. Takashima-Uebelhoer J.L. Faraj B.W. Whitcomb. Association of inflammation markers with menstrual symptom severity and premenstrual syndrome in young women.Human Reproduction, Volume 29, Issue 9, 1 September 2014, Pages 1987–1994,

70. Melissa M. ButtnerEmail authorSarah L. MottTeri PearlsteinScott StuartCaron ZlotnickMichael W. O'Hara.Examination of premenstrual symptoms as a risk factor for depression in postpartum women.Archives of Women's Mental Health June 2013, Volume 16, Issue 3, pp 219–225

71. Bertone-Johnson ER1, Houghton SC1, Whitcomb BW1, Sievert LL2, Zagarins SE1, Ronnenberg AG3.Association of Premenstrual Syndrome with Blood Pressure in Young Adult Women.J Womens Health (Larchmt). 2016 Nov;25(11):1122-1128. Epub 2016 Jul 15.

72. Seyed Saeed Sadr, MD,1 Seyed Mehdi Samimi Ardestani, MD,•,2 Katayoon Razjouyan, MD,3 Mahboobeh Daneshvari, MD,4 and Ghazal Zahed, MD5.Premenstrual Syndrome and Comorbid Depression Among Medical Students in the Internship Stage: A Descriptive Study.Iran J Psychiatry Behav Sci. 2014 Winter; 8(4): 74–79.

73. Paula K. B. "Mini-Review: Premenstrual syndrome and premenstrual dysphoric disorder", Journal of Pediatric and Adolescent Gynecology", 2007; 20:3-12.

74. Biggs, W.S., Demuth, R.H. "Premenstrual syndrome and premenstrual dysphoric disorder", Am Fam Physician, 2011; 84:918-924.

75. Rizk, D.E., Mosallam, M., Alyan, S., Nagelkerke, N. “Prevalence and impact of premenstrual syndrome in adolescent schoolgirls in the United Arab Emirates”. Acta Obstet Gynecol Scand, 2006; 85:589-598.

76. Rapkin, A.J., Winer, S.A. “Premenstrual syndrome and premenstrual dysphoric disorder: quality of Life and burden of illness”, Expert Review of Pharmacoeconomics & Outcomes Research, 2009; 9:157-170.

77. Heinemann, L.A.J., Minh, T.D., Filonenko, A., Uhl-Hochgrber, K . “Explorative evaluation of the impact of premenstrual disorder on daily functioning and quality of Life”, Patient Centered Outcomes Research, 2010; 3:125-132.

78. Prior JC, Vigna Y, Sciarretta D, Alojado N, Schulzer M. Conditioning exercise decreases premenstrual symptoms: a prospective, controlled 6-month trial. Fertil Steril 1987; 47: 402–408.

79. Girman A, Lee R, Kligler B. An integrative medicine approach to premenstrual syndrome. Am J Obstet Gynecol 2003; 188 (5 Suppl.): S56–S65.

80. Kleijnen J, Ter Riet G, Knipschild P. Vitamin B6 in the treatment of premenstrual syndrome – a review. Br J Obstet Gynaecol 1990; 97: 847–852.

81. Wyatt K, Dimmock P, Jones P, O’Brien P. Efficacy of vitamin B-6 in the treatment of premenstrual syndrome: systematic review. BMJ 1999; 318: 1375–1381.

82. Facchinetti F, Borella P, Sances G, Fioroni L, Nappi RE, Genazzani AR. Oral magnesium successfully relieves premenstrual mood changes. Obstet Gynecol 1991; 78: 177–181.

83. Walker AF, De Souza MC, Vickers MF, Abeyasekera S, Collins ML, Trinca LA. Magnesium supplementation alleviates premenstrual symptoms of fluid retention. J Womens Health 1998; 7: 1157–1165.

84. De Souza MC, Walker AF, Robinson PA, Bolland K. A synergistic effect of a daily supplement for 1 month of 200 mg magnesium plus 50 mg vitamin B6 for the relief of anxiety related premenstrual symptoms: a randomized, double-blind, crossover study. J Womens Health Gender Based Med 2000; 9: 131–139.

85. Bertone-Johnson ER, Hankinson SE, Bendich A, Johnson SR, Willett WC, Manson JE. Calcium and vitamin D intake and risk of incident premenstrual syndrome.Arch Intern Med 2005; 165: 1246–1252.

86. Alvir JM, Thys-Jacobs S. Premenstrual and menstrual symptom clusters and response to calcium treatment. Psychopharmacol Bull 1991; 27: 145–148.

87. Thys-Jacobs S, Ceccarelli S, Bierman A, Weisman H, Cohen MA, Alvir J. Calcium supplementation in premenstrual syndrome: a randomized crossover trial. J Gen Intern Med 1989; 4: 183–189.

88. Thys-Jacobs S, Starkey P, Bernstein D, Tian J. Calcium carbonate and the premenstrual syndrome: effects on premenstrual and menstrual symptoms. Premenstrual Syndrome Study Group. Am J Obstet Gynecol 1998; 179: 444–452.

89. Burke BE, Olson RD, Cusack BJ. Randomized, controlled trial of phytoestrogen in the prophylactic treatment of menstrual migraine. Biomed Pharm 2002; 56: 283–288.

90. Taher S, Cahill A, Eliahoo J, Calvin M, Rothon C, Panay N. Randomised placebo controlled pilot study comparing red clover (P-07) versus placebo for the treatment of premenstrual syndrome. Maturitas 2009; 63: S114–S115.

91. Schellenberg R. Treatment for the premenstrual syndrome with agnus castus fruit extract: prospective, randomised, placebocontrolled study. BMJ 2001; 322: 134–137.

92. Lauritzen C, Reuter HD, Repges R, et al. Treatment of premenstrual tension syndrome with Vitex agnus castus. Controlled, double-blind study versus pyridoxine. Phytomedicine 1997; 4: 183–189.

93. He Z, Chen R, Zhou Y, Geng L, Zhang Z, Chen S, et al. Treatment for premenstrual syndrome with Vitex agnus castus: a prospective, randomized, multi-center placebo controlled study in China. Maturitas 2009; 6 March [Epub ahead of print].

94. Stevinson C, Ernst E. Apilot study of Hypericum perforatum (St John's Wort) for the treatment of premenstrual syndrome. Br J Obstet Gynaecol 2000; 107: 870–876.

95. Huang KL, Tsai SJ. St. John's wort (Hypericum perforatum) as a treatment for premenstrual dysphoric disorder: case report. Int J Psychiatry Med 2003; 33: 295–297.

96. Khoo SK, Munro C, Battistutta D. Evening primrose oil and treatment of premenstrual syndrome. Med J Aust 1990; 153: 189–192.

97. Budieri D, Li-Wan Po A, Dornan JC. Is evening primrose oil of value in the treatment of premenstrual syndrome? Control Clin Trials 1996; 17: 60–68.

98. Cheung KL. Management of cyclical mastalgia in oriental women: pioneer experience of using gamolenic acid (Efamast) in Asia. Aust N Z J Surg 1999; 69: 492–494.

99. Bruce Kessel. Premenstrual Syndrome. Advances in Diagnosis and Treatment. Obstetrics and Gynecology Clinics. (2000): 27(3)

100. Ayurvedha &Aromatherapy-The Earth Essential Guide to Ancient Wisdom and Modern Healing.Dr.Light Miller and Dr.Bryan Miller.ISBN CODE:81-208-1593-99788120815933

101. Posadzki P, Watson LK, Alotaibi A, Ernst E. Prevalence of use of complementary and alternative medicine (CAM) by patients/consumers in the UK: systematic review of surveys. Clin Med. 2013;13:126–31.

102. Ernst E. Prevalence of use of complementary/alternative medicine: a systematic review. Bull World Health Organ. 2000;78:252–7.

103. Maddocks-Jennings W, Wilkinson JM. Aromatherapy practice in nursing: literature review. J Adv Nurs. 2004;48:93–103.

104. Boryensko, op. cit., p. 151.

105. Alexander, M. (2001) How Aromatherapy Works, Vol. 1: Principle Mechanisms in Olfaction. Odessa, FL: Whole Spectrum Books, p. 293.

106. W. B. Saunders Company (2001) Dorland's Pocket Medical Dictionary. Edition 25, Philadelphia, PA: W. B. Saunders Company, p. 506.

107. Boryensko, op. cit., p. 53.

108. ibid., pp. 53

109. Tisserand, R. 1977. The Art of Aromatherapy. C.W. Daniel, Essex.

110. Andreassi, J.L. 2000. Psychophysiology: Human behavior & Physiological Response, Lawrence Erlbaum Associated, New Jersey.

111. Stern, R.M., Ray, W.J., and Quigley, K.S. 2001. Psychopyhsiological recording, Oxford University Press, New York.

112. Kh. K. Dzumayev , I. A. Tsibulskaya , I. G. Zenkevich , K. G. Tkachenko & I. F. Satzyperova.Essential Oils of Salvia sclarea L. Produced from Plants Grown in Southern Uzbekistan. Southern Uzbekistan.Pages 597-604 | Received 01 Sep 1994, Published online: 09 Dec 2011

113. Tisserand M. Aromatherapy for Woman, A Practical Guide to Essential Oils for Health and Beauty. Rochester, VT: Healing Arts Press, 1996.

114. Cole A, Shanley E. Complementary therapies as a means of developing the scope of professional nursing practice. J Adv Nurs 1998;27:1171–1176.

115. Buckle J. Clinical Aromatherapy. New York: Churchill Livingstone, 2003.

116. Halcon L. Aromatherapy: therapeutic application of plant essential oils. Minn Med 2002;42–44.

117. Seol, G. H., Lee, Y. H., Kang, P., You, J. H., Park, M., & Min, S. S. (2013). Randomized controlled trial for Salvia sclarea or Lavandula angustifolia: differential effects on blood pressure in female patients with urinary incontinence undergoing urodynamic examination. Journal of Alternative and Complementary Medicine (New York, N.Y.), 19(7), 664–70. http://doi.org/10.1089/acm.2012.0148

118. Toda, M., & Morimoto, K. (2008). Effect of lavender aroma on salivary endocrinological stress markers. Archives of Oral Biology, 53(10), 964–968. http://doi.org/10.1016/j.archoralbio.2008.04.002

119. Lee, K.B.; Cho, E.; Kang, Y.S. Changes in 5-hydroxytryptamine and cortisol plasma levels in menopausal women after inhalation of clary sage oil. Phytother. Res. 2014, 28, 1599–1605. [CrossRef] [PubMed]

120. Seol, G.H.; Shim, H.S.; Kim, P.J.; Moon, H.K.; Lee, K.H.; Shim, I.; Suh, S.H.; Min, S.S. Antidepressant-like effect of Salvia sclarea is explained by modulation of dopamine activities in rats. J. Ethnopharmacol. 2010, 130, 187–190. [CrossRef] [PubMed]

121. Komori, T.; Fujiwara, R.; Tanida, M.; Nomura, J.; Yokoyama, M.M. Effects of citrus fragrance on immune function and depressive states. Neuroimmunomodulation 1995, 2, 174–180

122. Guzmán-Gutiérrez, S.L.; Gómez-Cansino, R.; García-Zebadúa, J.C.; Jiménez-Pérez, N.C.; Reyes-Chilpa, R. Antidepressant activity of Litsea glaucescens essential oil: Identification of β-pinene and linalool as active principles. J. Ethnopharmacol. 2012, 143, 673–679.

123. Guzmán-Gutiérrez,S.L.;Bonilla-Jaime,H.;Gómez-Cansino,R.; Reyes Chilpa, R. Linalool and β-pinene exert their antidepressant-like activity through the monoaminergic pathway. Life Sci. 2015, 128, 24–29. [CrossRef] [PubMed]

124. Coelho, V.; Mazzardo-Martins, L.; Martins, D.F.; Santos, A.R.; da Silva Brum, L.F.; Picada, J.N.; Pereira, P. Neurobehavioral and genotoxic evaluation of (-)-linalool in mice. J. Nat. Med. 2013, 67, 876–880. [CrossRef] [PubMed]

125. Deng, X.Y.; Xue, J.S.; Li, H.Y.; Ma, Z.Q.; Fu, Q.; Qu, R.; Ma, S.P. Geraniol produces antidepressant-like effects in a chronic unpredictable mild stress mice model. Physiol. Behav. 2015, 152, 264–271. [CrossRef] [PubMed]

126. Irie, Y.; Itokazu, N.; Anjiki, N.; Ishige, A.; Watanabe, K.; Keung, W.M. Eugenol exhibits antidepressant-like activity in mice and induces expression of metallothionein- III in the hippocampus. Brain Res. 2004, 1011, 243–246. [CrossRef] [PubMed]

127. Tao, G.; Irie, Y.; Li, D.J.; Keung, W.M. Eugenol and its structural analogs inhibit monoamine oxidase A and exhibit antidepressant-like activity. Bioorg. Med. Chem. 2005, 13, 4777–4788.

128. Lakusic´, B.; Lakusic´, D.; Ristic´, M.; Marcetic´, M.; Slavkovska, V. Seasonal variations in the composition of the essential oils of Lavandula angustifolia (Lamiacae). Nat. Prod. Commun. 2014, 9, 859–862

129. Biopsychosoc Med. 2013 May 31;7:12. doi: 10.1186/1751-0759-7-12. eCollection 2013.Does lavender aromatherapy alleviate premenstrual emotional symptoms?: a randomized crossover trial.Matsumoto T1, Asakura H2, Hayashi T3.

130. Indian J Physiol Pharmacol. 2008 Jan-Mar;52(1):69-76. Effect of '61-points relaxation technique' on stress parameters in premenstrual syndrome. Dvivedi J1, Dvivedi S, Mahajan KK, Mittal S, Singhal A.

131. Pullon, S. R., Reinken, J. A., & Sparrow, M. J. (1989). Treatment of premenstrual symptoms in Wellington women. N Z Med J., 102, 862, 72-74

132. Han, S. H., Hur, M. H., Buckle, J., Choi, J., & Lee, M. S. (2006). Effect of aromatherapy on symptoms of dysmenorrhea in college students: A randomized placebo-controlled clinical trial. J Altern Complement Med., 12(6), 535-541.

133. Derman, O., Kanbur, N. O., Tokur, T. E., & Kutluk, T. (2004). Premenstrual syndrome and associated symptoms in adolescent girls. European Journal of Obstetrics Gynecology & Reproduction Biology, 116(2), 201- 206.

134. Smith, H., & Thomas, S. P. (1996). Anger and locus of control in young women with and without premenstrual syndrome. Issues in Mental Health & Nursing, 17(4), 289-305

135. McLean, J. A., & Barr, S. I. (2003). Cognitive dietary restraint is associated with eating behaviors, lifestyle practices, personality characteristics and menstrual irregularity in college women. Appetite, 40(2), 185-192

136. Houston, A. M., Abraham, A., Huang, Z., & D'Angelo, L. J. (2006). Knowledge, attitudes, and consequences of menstrual health in urban adolescent females. J Pediatr Adolesc Gynecol., 19(4), 271-275.

137. Kanojia, S., Sharma, V. K., Gandhi, A., Kapoor, R., Kukreja, A., & Subramanian, S. K. (2013). Effect of yoga on autonomic functions and psychological status during both phases of menstrual cycle in young healthy females. J Clin Diagn Res., 7(10), 2133-2139.

138. Woods, N. F., Lentz, M. J., Mitchell, E. S., & Kogan, H. (1994). Arousal and stress response across the menstrual cycle in women with three perimenstrual symptom patterns. Res Nurs Health., 17(2), 99-110.

139. Jang, H. S., & Lee, M. S. (2004). Effects of qi therapy (external qigong) on premenstrual syndrome: a randomized placebo-controlled study. J Altern Complement Med., 10(3), 456-462.

140. Nisar, N., Zehra, N., Haider, G., Munir, A. A., & Sohoo, N. A. (2008). Frequency, intensity and impact of premenstrual syndrome in medical students. J Coll Physicians Surg Pak., 18(8), 481-484.

141. Tolossa, F. W., & Bekele, M. K. (2014). Prevalence, impacts and medical managements of premenstrual syndrome among female students: cross-sectional study in College of Health Sciences, Mekelle University, Mekelle, Northern Ethiopia. BMC Womens Health, 29, 14- 52

142. Taghizadeh, Z., Shirmohammadi, M., Feizi, A., & Arbabi, M. (2013). The effect of cognitive behavioural psycho-education on premenstrual syndrome and related symptoms. J Psychiatr Ment Health Nurs., 20(8), 705-713.

143. Stevinson, C. (2001). Complementary/alternative therapies for premenstrual syndrome: A systematic review of randomized controlled trials. American Journal of Obstetrics & Gynecology, 185(1), 227-235.

144. Schneider, M. B., Fisher, M., Friedman, S. B., Bijur, P. E., & Toffler, C. P. (1999). Menstrual and premenstrual issues in female military cadets: a unique population with significant concerns. J Pediatr Adolesc Gynecol., 12(4), 195-201

145. Yamamoto, K., Okazaki, A., Sakamoto, Y., & Funatsu, M. (2009). The relationship between premenstrual symptoms, menstrual pain, irregular menstrual cycles, and psychosocial stress among Japanese college students. J Physiol Anthropol., 28(3), 129-136

146. Ozisik, H., Kamisli, O., Karlidag, R., Kizkin, S., & Ozcan, C. (2005). Sympathetic skin response in premenstrual syndrome. Clin Auton Res., 15(3), 233-237.

147. Kuczmierczyk, A. R., & Adams, H. E. (1986). Autonomic arousal and pain sensitivity in women with premenstrual syndrome at different phases of the menstrual cycle. J Psychosom Res., 30(4), 421-428

148. Facchinetti, F., Neri, I., Martignoni, E., Fioroni, L., Nappi, G., & Genazzani, A. R. (1993). The association of menstrual migraine with the premenstrual syndrome. Cephalalgia, 13(6), 422-425.

149. Palmero, F., & Choliz, M. (1991). Resting heart rate (HR) in women with and without premenstrual symptoms (PMS). J Behav Med., 14(2), 125-139.

150. Groer, M., & Ohnesorge, C. (1993). Menstrual-cycle lengthening and reduction in premenstrual distress through guided imagery. J Holist Nurs., 11(3), 286-294.

151. Jasuja, V., Purohit, G., Mendpara, S., & Palan, B. M. (2014). Evaluation of psychological symptoms in premenstrual syndrome using pmr technique. J Clin Diagn Res., 8(4), 1-3.

152. Chau, J. P., & Chang, A. M. (1999). Effects of an educational programme on adolescents with premenstrual syndrome. Health Educ Res., 14(6), 817-830.

153. Tabassum, S., Afridi, B., Aman, Z., Tabassum, W., & Durrani, R. (2005). Premenstrual syndrome: frequency and severity in young college girls. J Pak Med Assoc., 55(12), 546-549.

154. Frackiewicz, E. J., & Shiovitz, T. M. (2001). Evaluation and management of premenstrual syndrome and premenstrual dysphoric disorder. J Am Pharm Assoc, 41(3), 437-447.

155. Anandhalakshmi , et al.(2011). Prevalence of Premenstrual Syndrome, SRM University, Journal on Health Quality Outcome. 8(16), 213 – 216.

156. Anderson, F.W., & Johnson, C.T. (2005). Complementary and Alternative Medicine In Obstetrics & Gynecology. An International Journal of Obstetrics & Gynecology, 91(2), 116 – 24.

157. Wang, et al. (2011).Prevalence of Premenstrual Syndrome Among Reproductive Age Group, Retrieved on Oct 15, 2012 from http://www.scribd.com.

158. Kitamura, M. (2012). Effect of Premenstrual Syndrome. Asian Journal of B.Sc Nursing Practice, 2(39), 110 – 115.

159. Josi, et al. (2011).Prevalence of Premenstrual Syndrome. Journal on Midlife Health, 1(14), 203 – 205.

160. Bhakti, R. (2011). Prevalence of premenstrual syndrome. Surya Fertility Centre. Retrieved on Oct 14, 2012 from http://www.yogapoint.com

161. Sharma, A. et al. (2012). Problems Related to Menstruation. Asian Journal of Public Health, 1(24), 136 – 150.

162. Indian J Pediatr. 2008 Feb;75(2):125-9.Problems related to menstruation amongst adolescent girls.Sharma P1, Malhotra C, Taneja DK, Saha R.

163. Hashim ET AL. PREMENSTRUAL SYNDROME: MESSES WITH MY ACADEMIC PERFORMANCE. Vol 64 No 2 (2014):

164. Kathryn, E. (2010).Effect of Aromatherapy. A Journal on Alternative and Complementary Medicine, 9(4), 534 – 545.

165. Carroll, D. (2011). Effect of Aromatherapy on Menstrual Discomfort. Journal on Complementary Therapy, 92(10), 105 – 110.

166. Brush, et al. (2010). Management of Premenstrual Syndrome. American Journal of Obstetrics and Gynecology, 150(2), 363 – 369.

167. Dante.G., & Facchinetti,F. (2010). Management of Premenstrual Syndrome. Asian Journal of B.Sc Nursing Practice, 2(39), 110 – 115.

168. George,F. (2007). Effect of Prime Rose Oil. Bandolier Journal on Complementary Medicine, 4(15), 116 – 120.

169. Sampalis, F. (2006). Effect of Neptune Krill Oil on Premenstrual Syndrome. Journal on Alternative and Complementary Medicine, 12(3), 207 – 227.

170. Kim, J.et al. (2008). Effect of Aromatherapy. Journal of Alternative and Complementary Medicine. 6(10), 95 – 101.

171. Han, S.H. et al. (2012). Effect of Aromatherapy Upon Menstrual Cramps.International Journal of B.Sc Nursing Practice, 110 – 114.

172. Wang, et al. (2011).Prevalence of Premenstrual Syndrome Among Reproductive Age Group, Retrieved on Oct 15, 2012 from http://www.scribd.com.

173. Taavoni. (2012).Effect of Aromatherapy Massage Retrieved on Oct 15, 2012 from http://www.pubmed.com

174. Brent, B.A. (2011). Effects of Aromatherapy, Retrieved on June 6, 2012 from http://www.americanscienceorg.

175. SUN-HEE HAN. The Journal Of Alternative And Complementary Medicine. Volume 12, Number 6, 2006, pp. 535–541 © Mary Ann Liebert, Inc. Effect of Aromatherapy on Symptoms of Dysmenorrhea in College Students: A Randomized Placebo-Controlled Clinical Trial.

9. ANNEXURES

INFORMATION SHEET

We are conducting a study **"Efficacy of Clary sage oil on Pre-Menstrual Syndrome (PMS) – A Controlled Trial"** at Government Yoga and Naturopathy Medical College Hospital, Chennai – 106.

The purpose of this study is to evaluate the efficacy of aromatherapy in relieving the symptoms of premenstrual syndrome.

We need your participation in this study. There is no invasive investigation for the study.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefit to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of investigator:

Signature of participant:

Date:

INFORMED CONSENT FORM

Title of the study:

"Efficacy of Clary sage oil on Pre-Menstrual Syndrome (PMS) – A Controlled Trial"

Name of the Participant:

Name of the Principal Investigator: Dr. Geethanjali.S

Name of the Institution: Government Yoga & Naturopathy Medical College,

Chennai – 600 106.

Documentation of the informed consent

I _____ have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent to be included as a participant in **"Efficacy of Clary sage oil on Pre-Menstrual Syndrome (PMS) – A Controlled Trial"**

1. I have read and understood this consent form and the information provided to me.

2. I have had the consent document explained to me.

3. I have been explained about the nature of the study.

4. I have been explained about my rights and responsibilities by the investigator.

5. I have been informed the investigator of all the treatments I am taking or have taken in the past _____ months including any native (alternative) treatment.

6. I have been advised about the risks associated with my participation in this study.

7. I agree to cooperate with the investigator and I will inform him/her immediately if I suffer unusual symptoms.

8. I have not participated in any research study within the past _____month(s).

9. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.

10. I am also aware that the investigator may terminate my participation in the study at any time, for any reason, without my consent.

12. I hereby give permission to the investigators to release the information obtained from me as result of participation in this study to the sponsors, regulatory authorities, Govt. agencies, and IEC. I understand that they are publicly presented.

13. I have understood that my identity will be kept confidential if my data are publicly presented.

14. I have had my questions answered to my satisfaction.

15. I have decided to be in the research study.

I am aware that if I have any question during this study, I should contact the investigator. By signing this consent form I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

Name and signature / thumb impression of the participant

Name _____ Signature_____

Date_____

Name and Signature of the investigator or his representative obtaining consent:

Name _____ Signature_____

Date_____

INFORMATION TO PARTICIPANTS

Investigator: Dr. Geethanjlali. S

Name of Participant:

Title:

"Efficacy of Clary sage oil on Pre-Menstrual Syndrome (PMS) – A Controlled Trial"

You are invited to take part in this research/ study /procedures. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns. You are being asked to participate in this study being conducted in **Government Yoga & Naturopathy Medical College, Chennai – 600 106**

What is the Purpose of the Research?

The purpose of this study is to evaluate the efficacy of aromatherapy in relieving the symptoms of Pre-menstrual syndrome

The Study Design:

60 patients are exposed to clary sage oil inhalation through diffuser.

Study Procedures:

Patients are initially screened to rule out depression and Pre-menstrual Dysphoric disorder with questionnaires before and at the end of intervention. They will be asked to maintain a symptoms diary to throughout the study.

Possible Risks to you : nil

Possible benefits to you:

Aromatherapy exposure helps you in coping up with the Pre-menstrual symptoms you experience every month.

Possible benefits to other people:

The result of the research may provide benefits to the society in terms of advancement of medical knowledge and/or therapeutic benefits to future patients.

Confidentiality of the information obtained from you

You have the right to confidentiality regarding the privacy of your medical information (personal details, results of physical examinations, investigations, and your medical history). By signing this document, you will be allowing the research team investigators, other study personnel, sponsors, IEC and any person or agency required by law like the Drug Controller General of India to view your data, if required.

The information from this study, if published in scientific journals or presented at scientific meetings, will not reveal your identity.

How will your decision to not participate in the study affect you?

Your decisions to not to participate in this research study will not affect your medical care or your relationship with investigator or the institution. Your doctor will still take care of you and you will not lose any benefits to which you are entitled.

Can you decide to stop participating in the study once you start?

The participation in this research is purely voluntary and you have the right to withdraw from this study at any time during course of the study without giving any reasons. However, it is advisable that you talk to the research team prior to stopping the treatment.

REMARKS OF THE GUIDE

This work undertaken / to be done by **Dr. Geethanjali. S** titled **"Efficacy of Clary sage oil on Pre-Menstrual Syndrome (PMS) – A Controlled Trial"** at Government Yoga and Naturopathy Medical College Hospital, will be under my supervision and I ensure that the candidate will abide by the rules of the Institutional Ethics Committee.

Dr. N. Mangaiarkarasi B.N.Y.S, M.Sc. (psy), PGDHAN,

H.O.D

Dept. of Acupuncture And Energy Medicine,

Government Yoga and Naturopathy Medical College, Chennai– 600106

Date:

The premenstrual symptoms screening tool (PSST)

(please mark an "X" in the appropriate box)

Do you experience some or any of the following premenstrual symptoms which start before your period and stop within a few days of bleeding?

Symptom	Not at all	Mild	Moderate	Severe
1.Anger / irritability				
2. Anxiety / tension				
3.Tearful/Increased sensitivity to rejection				
4.Depressed mood/hopelessness				
5.Decreased interest in work activities				
6. Decreased interest in home activities				
7. Decreased interest in social activities				
8.Difficulty concentrating				
9.Fatigue / lack of energy				
10.Overeating / food cravings				
11.Insomnia				
12.Hypersomnia (needing more sleep)				
13.Feeling overwhelmed or out of control				
14.Physical symptoms: breast tenderness, headaches, joint/muscle pain, bloating, weight gain				

Have your symptoms, as listed above, interfered with:

	Not at all	Mild	Moderate	Severe
A. Your work efficiency or productivity				
B. Your relationship with co-workers				
C. Your relationships with your family				
D. Your social life activities				
E. Your home responsibilities				

Scoring

The following criteria must be present for a diagnosis of **PMDD**

1. At least one #1, #2, #3, #4 is **severe**
2. In addition at least four of #1 to #14 are **moderate to severe**
3. At least one of A, B, C, D, E is **severe**

The following criteria must be present for a diagnosis of **moderate to severe PMS**

1. At least one #1, #2, #3, #4 is **moderate to severe**
2. In addition at least four of #1 to #14 are **moderate to severe**
3. At least one of A, B, C, D, E is **moderate to severe**

PREMENSTRUAL SYNDROME SCALE

		SCORES				
		Never (1)	**Rarely (2)**	**Sometimes (3)**	**Very often (4)**	**Always (5)**
	Physiological symptoms					
1	Breast tenderness and swelling					
2	Abdominal bloating					
3	weight gain					
4	Headache					
5	Dizziness/fainting.					
6	Fatigue					
7	Palpitations					
8	Pelvic discomfort and pain					
9	Abdominal cramps					
10	Change in bowel habits					
11	Increased appetite					
12	Generalized aches and pains					
13	Food cravings (Sugar/ Salt)					
14	Skin changes, rashes, pimples					
15	Nausea/vomiting					
16	Muscle and Joint pain					
	Psychological symptoms					
17	Irritability					
18	Anxiety					
19	Tension					
20	Mood swings					
21	Loss of concentration					
22	Depression					
23	Forgetfulness					
24	Easy crying/ Crying spells					
25	Sleep changes (Insomnia/ hypersomnia)					
26	Confusion					
27	Aggression					
28	Hopelessness					
	Behavioural symptoms					
29	Social withdrawal					
30	Restlessness					
31	Lack of self control					
32	Feeling guilty					
33	Clumsiness					
34	Lack of interest in usual activities					
35	Poor judgment					
36	Impaired work performance					
37	Obsessional thoughts					
38	Compulsive behavior					
39	Irrational thoughts					
40	Being over sensitive					

Level of symptoms		**Actual Scores**	**Percentage of Scores**
No symptoms		1- 40	< 20
Mild symptoms	- only slightly apparent	41 - 80	21 -40
Moderate symptoms	- aware of symptom, but it doesn't affect daily activity at all	81 – 120	41 60
Severe	- continuously bothered by symptoms	121 - 160	61 -80
very severe	- symptom is overwhelming and /or interferes with daily activity	161 -200	> 80

In addition, the total score obtained from the sub-scales established the "PMSS total score." The scale's lowest score is 40 and highest score is 200. If the scale's total score reached 80 points or above, this indicates the occurrence of PMS. Increases in the scores indicate an increase in PMS severity.

SCORING PROCEDURE:

Based on the percentage of scores the levels of premenstrual symptoms were graded in four categories. They are "No symptoms", "Mild", "Moderate" "severe" and very severe symptoms.