International Journal of Chemical and Biochemical Sciences
(ISSN 2226-9614)

Journal Home page: www.iscientific.org/Journal.html

Traditional herbal interventions for premenstrual syndrome management: A comprehensive literature review

Md Abul Hasan Roni [1,2], Md Abu Bakar Siddique Jami [3,4], Rezwana Sultana [3,4], Prethula Areefin [5], Safayet Hossain [6], Sahadat Hossen [7], Rozina [8], Mohd Yusri Bin Mohd Yunus [1*]*

[1] *Faculty of Chemical and Process Engineering, Technology, Universiti Malaysia Pahang Al-Sultan Abdullah (UMPSA), Gambang, Malaysia.*

[2] *Bangladesh Army International University of Science and Technology, Cumilla, Bangladesh.*

[3] *Department of Pharmacy, East West University, Dhaka, Bangladesh.*

[4] *Department of Pharmacy, Faculty of Life and Earth Sciences, Jagannath University, Dhaka, Bangladesh.*

[5] *Department of Pharmacy, Stamford University Bangladesh, Dhaka, Bangladesh.*

[6] *Institute of Pharmaceutical Sciences, Kurukshetra University, Thanesar, Haryana, India.*

[7] *Young Women's College Preparatory Academy, Science Department, Houston, Texas, USA.*

[8] *Mainamoti Medical College and Hospital, Cumilla, Bangladesh.*

Abstract

Premenstrual syndrome (PMS) causes severe physical and emotional health problems in many women. Due to concerns regarding the potentially harmful effects of conventional treatments, there has been an increased interest in exploring alternative medicines, mainly traditional herbal remedies. This comprehensive literature review employed a rigorous methodology involving extensive data collection from databases such as Scopus®, Web of Science®, and PubMed®, as well as respected publishers like Oxford University Press, Elsevier, Springer Nature, and others. The study examines the properties and potential benefits of *Cyperus rotundus*, *Curcuma longa* (turmeric), *Aloe vera*, *Angelica sinensis* (Dong Quai), *Zingiber officinale* (ginger), *Crocus sativus* (saffron), and *Withania somnifera* (Ashwagandha) in the context of PMS management. It is important to note that these traditional herbs offer diverse therapeutic properties, which can effectively address both the physical and emotional symptoms of PMS. These herbal interventions have notable analgesic and anti-inflammatory effects, as well as mood-enhancing and adaptogenic qualities. As promising and versatile alternatives to conventional medications, it is essential to conduct further research to prove their efficacy, safety, and ideal use fully. This calls for extensive clinical trials, mechanistic analyses to reveal their mechanisms of action, the creation of standardized formulations, and the adoption of a patient-centered strategy that considers unique preferences and needs. It is possible to significantly improve the holistic approach to PMS management by realizing the full potential of these conventional herbal treatments. This study highlights the vital importance of these herbal interventions in PMS management, ultimately providing women with safer options for PMS relief and an enhanced quality of life.

Keywords: Premenstrual Syndrome, PMS, Dysmenorrhea, Herbal, Traditional medicine.

Full length article **Corresponding Author*, e-mail: yusri@ump.edu.my, roni_chem@baiust.edu.bd

1. Introduction

Every healthy woman of reproductive age has menstruation regularly, and it is essential for the uterine lining to regenerate to get ready for conception. Premenstrual syndrome (PMS) typically presents as a mix of physical, behavioral, and emotional symptoms during the final week of the luteal phase, frequently the week before menstruation, which is when it typically manifests [1]. The American

College of Obstetricians and Gynecologists (ACOG) defined PMS as a clinical disorder marked by the cyclic presence of physical and emotional symptoms that appear in each of the three previous menstrual cycles five days before menstruation and disappear within four days of the start of menstruation. These symptoms don't reappear until at least cycle day thirteen [2]. The severe form of PMS is termed premenstrual dysphoric disorder (PMDD). PMS and PMDD are clinically extreme conditions and can severely impact a woman's quality of life [3]. Even though 50–80% of women of reproductive age report having at least mild premenstrual symptoms, 30–40% report symptoms requiring medical attention, and 3-8% of women experience PMDD and fulfill the demanding DSM–IV criteria. However, the majority of premenstrual symptomatic women suppress their symptoms without receiving any proper diagnosis or treatment [4]. Though it is unsure what the actual prevalence of PMS is, it has been estimated that between 70-90% of menstruating women face some symptoms before their period [5]. Many conventional treatment methods are available for treating these symptoms, with which women often self-medicate themselves. While traditional medicine offers a range of treatments to alleviate PMS symptoms, the choice to self-medicate raises essential considerations, especially in underdeveloped countries [6]. However, traditional herbal interventions have been studied for the management of Premenstrual Syndrome (PMS) alongside conventional medicinal treatment. It has been demonstrated that several traditional and complementary therapies, including herbal therapy, significantly reduce PMS symptoms [7].

1.1. Etiology and Symptoms

The exact etiology of premenstrual syndrome (PMS) has not been established, but various theories have been proposed involving alterations in neurotransmitters, hormones, and neuroendocrine pathways [8]. However, prior research has revealed that there may be some significant elements underlying PMS, such as hormonal changes, specific chemical changes, body weight, inadequate physical activity, mental stress, food, postpartum depression, and other things [9,10]. We have listed different etiological factors; their short explanations are depicted in Table 1. However, there still needs to be a clear pathophysiological explanation for PMS in the literature. These theories need more rigorous investigation and empirical evidence to establish a definitive understanding [11-18]. In terms of symptoms, PMS symptoms can vary widely among individuals [19-25]. PMS's severity and recurrent nature have contributed to its prevalence in women, impacting their everyday activities, interpersonal relationships, and jobs and income [26-30]. A patent was found that proposed treatments for various PMS and PMDD symptoms. This invention listed symptoms like muscle aches, bloating, cramping, acne, tender breasts, bloating, fatigue, difficulty concentrating, decreased impulse control, irritability, anxiety, tension, anger, depression, insomnia, and rapid mood changes (mood swings), among others [31]. According to an article from Hofmeister and Bodden, PMS is a disorder marked by recurring physical and psychological symptoms that happen in a cycle one to two weeks before a woman's menstruation. Therefore, PMS can be categorized into physical and emotional symptoms [32-36]. We have listed some of the significant physical and emotional symptoms of PMS found in the literature and their short explanations in Table 2 [37-42].

1.2. Current Strategies for PMS Management

Current conventional strategies for managing different premenstrual symptoms include both pharmacological and non-pharmacological approaches [43-50]. Cardiovascular exercise [51-55], dietary adjustments, and cognitive-behavioral therapy are examples of common non-pharmacological treatments [56-61]. For pain and cramps, nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen can help relieve pain and reduce cramping. Over-the-counter pain relievers like NSAIDs can help alleviate headaches [62]. Wearing supportive clothing, undergarments, and NSAIDs can alleviate breast discomfort [63]. Reducing salt intake, increasing water consumption, and avoiding gas-producing foods may help manage bloating problems [64,65]. Mood swings can be controlled by daily exercise, stress reduction methods (such as yoga and meditation), and lifestyle adjustments [66]. Selective serotonin reuptake inhibitors (SSRIs) like fluoxetine and sertraline, benzodiazepines like alprazolam, and gonadotropin-releasing hormone (GnRH) agonists are among the medications used to treat behavioral and emotional premenstrual symptoms [67,68]. If symptoms are severe, a doctor may prescribe antidepressants or recommend therapy. Maintaining a healthy diet, getting adequate sleep, and exercising frequently can all help to control lethargy and its accompanying symptoms [69]. Eating a balanced diet and managing stress can help control cravings for unhealthy foods [70]. Practicing good time management, getting sufficient sleep, and using organizational tools can aid in managing concentration difficulties [71]. Sleep quality can be improved by keeping a regular sleep schedule, refraining from coffee and electronic gadgets before bed, and developing a relaxing bedtime routine [72,73]. However, some people may require prescription medications. Skin issues like acne can be controlled using over-the-counter or prescribed topical medications containing benzoyl peroxide, salicylic acid, or retinoids [74,75]. Maintaining a high-fiber diet, staying hydrated, managing stress, and drugs like domperidone can help regulate bowel movements [76–78]. Historically, oral contraceptives (OCs) have had limited data to support their efficacy. However, recent research has demonstrated that OC containing the progestin drospirenone helps lower premenstrual discomfort [79]. The management of premenstrual symptoms often combines pharmacological and non-pharmacological methods. The advantages of traditional herbal treatments for treating these symptoms are not entirely understood, however. The potential adverse effects of medications like NSAIDs and SSRIs should be noted [80–82]. Managing PMS symptoms is crucial, and while conventional medication may be an option, it can come with potential risks of several side effects. Traditional herbal interventions, on the other hand, offer a potentially safer alternative. However, their efficacy and safety need further investigation, and there is limited literature on these traditional herbals and their potential PMS management activities. Therefore, this study aims to bridge this knowledge gap by conducting a thorough exploration of the literature on using conventional herbal substances to manage PMS symptoms.

2. Methodology

This review article uses a meticulous and comprehensive approach to examine the effectiveness of herbal remedies in treating Premenstrual Symptoms. The data is collected by carefully selecting primary sources, including well-known databases such as SciVerse, Scopus®, Web of Science®, and PubMed®. Additionally, the study includes data from famous publishers such as Cambridge University Press, Oxford University Press, Springer Nature, Routledge, Elsevier, Peter Lang, Thomson Reuters, Blackwell, Sage, MDPI, Frontiers, Wiley Online, and PLOS ONE, both in their online and printed versions. The search criteria comprises of various aspects related to Premenstrual Symptoms and herbal remedies. It includes their local and scientific names such as *Cyperus rotundus* (Nagarmotha/Motha), *Withania somnifera* (Ashwagandha), *Curcuma longa* (Turmeric), *Aloe vera* (Ghrit Kumari), *Angelica sinensis* (Dong quai/Female Ginseng), *Zingiber officinale* (Ginger), and *Crocus sativus* (Saffron). The study excludes non-English articles to maintain focus. The selection rigor is ensured by thoroughly reviewing the full manuscripts of relevant articles, including titles, abstracts, and conclusive remarks, to verify their suitability for inclusion in the study. This approach ensures the paper's comprehensiveness in addressing the research objectives.

3. Traditional herbal remedies for PMS symptom management

3.1. *Cyperus rotundus* (Nagarmotha / Nut Grass)

Cyperus rotundus, which is locally also called "Nut Grass," "Nagarmotha," or "Motha," is a well-known medicinal plant that is utilized worldwide [83]. Traditionally, people used it in many countries to treat disease conditions such as diarrhea, pyresis, diabetes, inflammation, stomach and bowel disorders, and malaria [84]. However, little direct research has been done on this herb regarding its ability to cure PMS and its associated symptoms. Volatile oil from this plant contains the crucial ingredients b-pinene, cyperene, a-cyperone, b-cyperone, and acyperol. Triterpenes, flavonoids, and alkaloids are also present. Its volatile oil has a somewhat estrogenic effect, which may aid in treating menopause, premenstrual syndrome (PMS), mood swings, depression, and convulsions (Figure 1) [85].

3.1.1. Antispasmodic, antidiarrheal, anti-inflammatory activity of Cyperus rotundus

A substance with antispastic, antidiarrheal, and anti-inflammatory properties relieve physical symptoms like abdominal bloating, cramps, and muscle pain during PMS. Its effectiveness can also address emotional symptoms such as mood swings, irritability, and anxiety, contributing to overall relief from a range of PMS-related discomforts. A direct relaxing activity on the smooth muscle was demonstrated by the ethanol extract of *Cyperus rotundus*, which relaxed the rabbit ileum and had a spasmolytic effect against contractions brought on by acetylcholine, barium chloride, and 5-hydroxytryptamine [86]. An aqueous extract of *C. rotundus* was tested by Shamkuwar et al. (2012) for its ability to treat mice with castor oil-induced diarrhea. At doses of 125 mg/kg, 250 mg/kg, and 500 mg/kg, *C. rotundus* extract showed 30.36%, 37.90%, and 45.45% inhibition of diarrhea, while Loperamide (a widely prescribed drug to reduce the frequency of diarrhea) at dose of 2 mg/kg showed 92.45% inhibition of diarrhea. Researchers concluded that an antisecretory mechanism was responsible for its antidiarrheal effects [87]. In a different study, mice with castor oil-induced diarrhea responded significantly to the oral administration of *C. rotundus* rhizome methanol extract. The total number of wet feces in 4 hours was 3.00 ± 0.55 and 1.8 ± 0.37, respectively, for dosages of 250 and 500 mg/kg body weight ($P < 0.01$) [88]. In another study, the methanolic extract of *C. rotundus* rhizome effectively decreased castor oil-induced diarrhea in mice when given orally at 250 and 500 mg/kg body weight dosages. Several in vitro investigations assessed free radicals, reactive oxygen species, and IC50 values of *C. rotundus* rhizomes extract. The rhizome extract scavenges superoxide anion radicals, hydroxyl radicals, nitric oxide radicals, and hydrogen peroxide, chelating and reducing abilities in a concentration-dependent manner [83]. There are 45 µg/g of chlorogenic acid in the ethanol extract of *C. rotundus*. Topical administration of *C. rotundus* extract lowered cellular infiltration and edema in acute and chronic skin inflammation models. These results demonstrate *C. rotundus* extract's topical anti-inflammatory and antiproliferative action for the first time, suggesting that the extract may someday be used as a cutting-edge therapeutic strategy for the treatment of inflammatory skin problems, which may demonstrate its effectiveness for PMS-related acne and other skin problems [89]. Anti-inflammatory compounds have been studied for their potential role in managing symptoms such as pain and discomfort [90]. A review article by Bhaskar Das et al. (2015) reported that, in another animal model study, *C. rotundus* tuber extract was used to assess the anti-inflammatory efficacy in adult albino Wistar rats. Three equal amounts of the powder were extracted and given to the test group in ether, ethanol, and distilled water. The findings showed that the extract significantly reduced inflammation when applied to carrageenan-induced rat paw edema in mice [91].

3.1.2. Analgesic, sedative, tranquilizing activity of Cyperus rotundus

Herbal substances with analgesic, soothing, and tranquilizing activities can be crucial for alleviating physical symptoms such as headaches, cramps, muscle pain, and joint pain during PMS. Additionally, its effectiveness in promoting relaxation and reducing irritability can address emotional symptoms like mood swings, anxiety, and social withdrawal, enhancing overall relief from PMS-related distress. In previous research, the tail-flick technique was used on mice to assess the crude extract of *C. rotundus*' analgesic effectiveness. Compared to the control and conventional medications, the natural extract at 300 mg/kg body weight (dissolved in 0.9 percent saline solution) showed a substantial and noticeable change in reaction time (5s ± 0.45) [84]. Imam and Sumi conducted research using a *C. rotundus* hydro-methanol extract and discovered that it had antinociceptive ability against chemical- and heat-induced nociception. The hydro-methanol extract demonstrated a substantial, fast, and persistent antinociceptive action at 100 and 200 mg/kg doses [92]. In a previous study, an acetic acid writhing test indicated analgesic effects from the whole decocts of *C. rotundus* rhizomes. Both the plant's essential oil and petroleum ether extract have been shown to have analgesic properties. Additionally, research on the sesquiterpene isocurcumenol, which was isolated from the *C. rotundus*

plant, has shown that it functions as a benzodiazepine receptor agonist, favorably modulating GABAergic neurotransmission by enhancing GABA's interaction with its receptor in animals. An essential part of the GABA receptor complex is the benzodiazepine receptor. These findings offer a pharmacological rationale for using *C. rotundus* as a sedative because GABA is an inhibitory neurotransmitter [93]. The ethanolic extract of *C. rotundus* had strong sedative effects in several experiments, including those that focused on how it affected motor coordination, potentiated pentobarbital narcosis, and reduced mice's spontaneous muscle movements [94]. In a 2012 study, researchers employed the forced swimming test (FST) and the tail suspension test (TST), two traditional behavioral models for antidepressant screening, to assess the antidepressant effects of the iridoid glycosides isolated from *C. rotundus*. Few of them have been shown to possess intense antidepressant activity, according to the research findings [95]. FST and TST were utilized by Hao et al. (2017) to investigate the antidepressant effect of CR extract and discovered that *C. rotundus* extract drastically reduced Monoamine Oxidize A (MAO) activity across the rat's whole brain. The findings showed that MAO inhibitory activity may dependently be dependent on the antidepressant effect of *C. rotundus* extract in the rat. However, the study only looked at the animal level, not the clinical level or the intracellular process [95,96]. Intense and persistent menstrual cramps are known as Dysmenorrhea [43]. Anti-dysmenorrhea effects of a substance are vital in reducing menstrual cramps and abdominal pain during PMS. An article by Prof. Dr Ali Esmail Al-Snafi reviewed some lab trials. Mice were used to investigate the anti-dysmenorrhea effects of the essential oil from the rhizome of *C. rotundus* (EOC). Four groups of mice were created: Group 1 acted as the control group, while groups 2, 3, and 4 received low, intermediate, and high dosages of EOC (0.01g/kg, 0.02g/kg, and 0.1g/kg, respectively). To generate an animal model of dysmenorrhea, the mice were initially intragastrically administered diethylstilbestrol for 12 straight days (2 mg/kg/day). Over the last three days, each group's mice received a different dose of EOC and equivalent saline. The mice were intraperitoneally treated with 0.1 ml of oxytocin injection 30 minutes after the last medication treatment, and distortions were noted and recorded after 15 and 30 minutes. *Cyperus rotundus* rhizome-derived EOC was treated to column chromatography for fractionation, yielding six fractions, denoted by F1–F6. After intraperitoneal oxytocin administration, distortion durations were significantly decreased by EOC and its fractions F2 through F6, with F4 performing the best as it contains spathulenol, β-caryophyllene oxide, and isoaromadendrene oxide, according to GC-MS analyses. As a result, substantial anti-dysmenorrhea was seen in EOC and its fractions F2 through F6. The results of the GC-MS analysis of EOC and its fractions F2 to F6 indicated that more than one component was responsible for the anti-dysmenorrhea effect [97].

3.2. Curcuma longa (Turmeric / Haldi)

Turmeric is produced by the perennial plant *Curcuma longa*, a member of the ginger family. The yellowish hue of turmeric is caused by curcumin. The primary active component of turmeric is curcumin, a yellow polyphenol with the chemical name diferuloylmethane. Curcumin has potent analgesic, anti-inflammatory, and antioxidant properties. Vitamins E and C and curcumin have similar antioxidant properties. Prostaglandins are inhibited by curcumin [98]. Both the pathways, cyclooxygenase (COX) and lipooxygenase (LOX), are the mechanisms that make up the metabolism of arachidonic acid. The primary enzyme is cyclooxygenase, which transforms arachidonic acid into prostaglandins in the COX pathway (COX1 and COX2). Curcumin prevents the synthesis of these prostaglandins [99]. By interfering with Nuclear factor kappa B (NF-B), the inflammatory response of human endothelial cells that TNF-α has activated is reduced by curcumin. It prevents the synthesis of these inflammatory cytokines. Curcumin also can suppress platelet-derived growth factors. In addition to alleviating physical discomforts associated with PMS, its efficacy can also treat mental symptoms like mood changes, impatience, and anxiety (Figure 2) [100,101].

3.2.1. Analgesic, antioxidant & anti-inflammatory activity of Curcuma longa

A double-anonymized, randomized, controlled clinical trial was conducted by Tabari et al. They underwent a two-month screening process during which participants' demographic information, menstrual features, and the severity of dysmenorrhea were documented. Verbal Multi-Dimensional Scoring was employed to evaluate the severity of dysmenorrhea after the two cycles. According to the questionnaire, participants were classified as having grade 2 dysmenorrhea and randomly assigned to one of two treatment groups: the curcumin group and a placebo group. 500 mg of curcumin-containing drug was given for three days with food throughout the first three menstrual cycle days. In both successive cycles, the students used a visual analog scale (VAS) to record their pain severity and duration before and three hours after the intervention. Before taking the medication, the average pain level in the drug group was 5.408 ± 3.001. However, three hours after taking the medication, it was -5.017 ± 2.294. Therefore, this study shows that curcumin can effectively reduce PMS-related discomfort in terms of duration and severity of pain [102]. Another study was conducted by Arabnezhad et al. to observe the effect of curcumin on PMS. This triple-blinded, placebo-controlled, randomized study created a control group and an experimental group of PMS and dysmenorrhea-afflicted women. One capsule (500 mg of curcuminoid plus 5 mg of piperine or placebo) was given to the test group daily during three consecutive menstrual cycles, from approximately seven days before menstruation to 3 days after menstruation. The severity of menstrual cramps was assessed based on the PSST questionnaire, ranging from 0 (no cramps) to 3 (severe cramps). It was found that after taking this medication, the severity of menstrual cramps reduced from 3 to 2 (moderate) and 2 to 1 (mild), showing evidence of curcumin's analgesic effect. Again, when compared to the placebo, curcumin significantly raised average (IQR) serum levels of vitamin D from 18.6 ng/ml (2.2-26.8) to 21.3 ng/ml (5.2-27.1; P = 0.017), up from 12.8 ng/ml (7.0-24.6) to 16.2 ng/ml (6.4-28.8). A considerable increase in vitamin D levels was seen after taking curcumin supplements by PMS and dysmenorrhea-afflicted women [103]. According to another pertinent study, the curcumin group's physical, behavioral, and emotional scores were significantly lower following the intervention than before. After the intervention, the mean physical score in the placebo group considerably dropped

from 46.7 ± 26.8 to 38.50 ± 20.27 (p=0.0425). However, the average scores for behavioral and mood following the intervention did not differ substantially from the values before the intervention. The total PMS score fell considerably in the curcumin group from 102.06 ± 39.64 to 42.47 ± 16.37 (p<0.0001), although the same score in the placebo group did not change significantly from (106.06 ± 44.12 to 91.60 ± 43.56, p=0.058) following the intervention [104]. A previous study Talebpour et al. conducted a triple-blind, placebo-controlled clinical trial with 76 young women experiencing PMS and dysmenorrhea. Daily oral curcumin administration for three consecutive menstrual cycles significantly reduced high-sensitivity C-reactive protein (hsCRP) levels (an inflammatory marker) compared to a placebo, with no significant impact on iron profile. The median hsCRP levels reduced in the curcumin group, with a p-value of 0.041, from 0.30 mg/L (0.0-1.10) to 0.20 mg/L (0.0-1.3). Comparing the curcumin-treated group to the placebo group shows a statistically significant decrease in hsCRP levels. As a result, curcumin may help with PMS-associated inflammation [105].

3.3. Aloe vera (Ghrit Kumari)

Ghrit Kumari is a crucial herb used as a medicinal plant, *Aloe vera* (Linn.) Burm. F. of the Liliaceae family, also known as Aloe barbadensis Mill. (Liliaceae), has a variety of effects on the human body. *Aloe vera*'s stemless plant has rosettes of highly thick, meaty leaves [106]. A, C, and E vitamins are present in this plant. As lipid peroxidation is decreased, it gains antioxidant capabilities as well. Salicylic acid, nutrients and minerals, enzymes, tannins, and several polysaccharides are all present in *Aloe vera* (Figure 3) [107].

3.3.1. Analgesic activity of Aloe vera

An earlier study Sardashti et al. sought to ascertain whether oral *Aloe vera* gel supplementation impacted menstrual pain intensity. One hundred fifty single students between the ages of 20 and 26 who had menstruation pain participated in a randomized, single-blind clinical intervention. With the help of the COX Menstrual Symptom Scale (CMSC), the severity of the pain was assessed. There were 60 participants in each group, and aloe vera gel pills were distributed randomly to each participant. Until the pain level was one or lower, the initial trial group consumed 10 mg of *Aloe vera* gel four times daily. Three pills were given orally three times per day to the control group. Participants' pain intensity and duration changes in both groups were assessed in the first and second months. It was found that the average pain score in the *Aloe vera* group lowered from 2.81 ± 0.65 to 2.02 ± 0.34. The two groups' pain levels in the second month of the trial were alike. Therefore, menstrual discomfort can be effectively treated with *Aloe vera* gel pills, an alternative natural pain reliever with no side effects [108]. An earlier study Khazaiyan et al. conducted a double-blind clinical experiment with 80 female students who had primary dysmenorrhea. The subjects in the control group received a bottle containing 120 cc of placebos. In contrast, the intervention group members received a bottle containing 120 cc of *Aloe vera* gels each cycle. Beginning two days before menstruation and continuing for the first three days after the start of the menstrual cycle, the patients took the prescribed medication every day for two cycles. Using a verbal multidimensional grading system, the effects of drugs on the severity of dysmenorrhea were evaluated. Results revealed a significant difference in the amount of bleeding, analgesic application, and pain severity between the *Aloe vera* and placebo groups (P < 0.05); however, no significant differences were seen in the side effects (P > 0.05) [109].

3.4. Angelica sinensis (Dong quai / Dang Gui / Female Ginseng)

The Chinese Pharmacopoeia describes the dried root of *Angelica sinensis* (Oliv.) Diels *as Angelica sinensis.* (110), which is a member of the family Umbelliferae. It is a perennial with a height of 1 m (3ft. 3in.) and a width of 0.7 m (2ft. 4in.). It is also known as Dong Quai, Danggui, or Female Ginseng, and this herb is found in mainland China, Japan, and Korea. The famous Chinese herbal remedy *A. sinensis* has been used for centuries as a feeding and hematological agent in treating gynecological issues [111]. *A. sinensis* has several pharmacological properties, including heart protection, immunological function enhancement, anti-arrhythmic, anti-atherosclerotic, and myocardial infarction prevention [112]. N-butylidenephthalide, ligustilide, n-butyl-phthalide, ferulic acid, nicotinic acid, and succinic acid are the main therapeutic ingredients of *A. sinensis* (Figure 4) [113].

3.4.1. Antidepressant activity of Angelica sinensis

In a study involving 60 male Sprague-Dawley rats, researchers investigated the potential antidepressant effects of *A. sinensis* using a chronic unexpected mild stress (CUMS) model. After one-week incubation, rat models were divided into five different groups randomly: control (NS), model (MS), positive control venlafaxine (VLF), high-dosage group of *A. sinensis* (HAS), and low-dosage group of *A. sinensis* (LAS). The HAS and LAS groups received 15 g and 7.5 g herb/kg of *A. sinensis*, respectively, for 28 days, based on established efficacious dosages. The VLF group received 35 mg/kg of venlafaxine. Venlafaxine was mixed with water at 3.5 mg/ml, while *A. sinensis* was diluted at concentrations of 0.72 and 0.36 g/ml. Results showed that *A. sinensis* had a more potent antidepressant effect in the rat model of CUMS-induced depression, probably due to activation of the BDNF signaling pathway and increased expression of BDNF, phosphorylated ERK 1/2, and CREB proteins in the hippocampus tissue [114]. In a metabonomic study, treatment with *A. sinensis* was found to regulate 26 biomarkers associated with depression potentially. Among these biomarkers, eight were previously linked to sphingolipid and amino acid metabolic pathways, suggesting that *A. sinensis* may also modulate energy metabolism in an anemic model. *A. sinensis* appeared to alter energy metabolism in depression by suppressing lactate dehydrogenase A (LDHA) and pyruvate dehydrogenase lipoamide kinase isozyme 1 (PDK-1) activities. These findings indicate that *A. sinensis*'s antidepressant effects may be attributed, in part, to its regulation of the blood system [115].

3.4.2. Anti-fatigue activity of Angelica sinensis

In a study by Yeh et al., mice models were divided into four groups: (1) vehicle control, (2) exercise control, (3) exercise control with *A. sinensis* therapy at 0.41 g/kg/day (ExAS1), and (4) vehicle control with 2.05 g/kg/day (ExAS5). The vehicle and *A. sinensis* were given oral administration for six weeks. Forelimb grip strength, serum lactate, exhausting swimming time, glucose, ammonia, and

creatine kinase (CK) levels after a 15-minute swim were used to measure the ergogenic and anti-fatigue effects. *A. sinensis* treatment increased swimming endurance and blood glucose levels while decreasing serum lactate, CK, and ammonia levels, with the ExAS1 and ExAS5 groups showing significant reductions in blood lactate by 14.5% ($p = 0.0171$) and 23.6% ($p = 0.0002$), respectively. In addition, serum ammonia levels in the ExAS1 and ExAS5 groups were lower than those in the exercise control group by 19.3% and 26.1%, respectively ($p < 0.0001$). *A. sinensis* supplementation mitigated oxidative stress induced by exercise, supported blood glucose utilization for energy during physical activity, and enhanced glycogen deposition in the liver and muscles, ultimately improving exercise performance. These findings indicate that *A. sinensis* has anti-fatigue properties in mice by modulating blood lactate and ammonia levels, promoting glycogen storage, and enhancing physical endurance [116]. Another study investigated the anti-fatigue effects of *A. sinensis* polysaccharides (APS) in mice. Four groups were tested: standard control, low-dose APS (LAT), medium-dose APS (MAT), and high-dose APS (HAT). APS was administered orally for 28 days. APS-treated groups showed significantly higher exhaustive swimming times ($p < 0.05$) than the regular control group. Post-swimming, APS-treated groups had significantly lower blood lactic acid and serum urea nitrogen levels ($p < 0.05$). APS-treated groups also exhibited higher liver glycogen levels (LAT, MAT, and HAT) and muscle glycogen levels (MAT and HAT) compared to the regular control group ($p < 0.05$). The study used dried Dong quai (the root of *A. sinensis*) and demonstrated APS's anti-fatigue effects [117].

3.4.3 Hormonal and Physiological Functions Regulation of Angelica sinensis

A standardized ethanol extract of *Angelica sinensis* root was administered orally to female Wistar rats (200 ± 21 g) at 100 and 300 mg/kg daily for seven days. The estradiol benzoate was given subcutaneously at 0.1 µg/rat for seven days. Controls received the vehicle alone. After the last dose, the rats were weighed and killed, and blood samples were collected for LH and FSH measurement. The 300 mg/kg dose of *A. sinensis* extract significantly modified vaginal smear in 67% of treated rats. It stimulated uterine histoarchitecture, induced vaginal epithelial cornification, and reduced serum LH levels, indicating its estrogenic nature. This research suggests that *A. sinensis* may exhibit positive estrogenic activity, which could be explored for alleviating PMS symptoms. Additionally, it has been shown that *A. sinensis* contains anti-inflammatory activities that can help inhibit excessive antibody response, lower allergies, and lessen inflammation, all of which may help relieve several PMS symptoms [118]. *A. Sinensis* contains volatile oil, organic acid, polysaccharides, coumarin, and amino acids. It is responsible for its extensive pharmacological activities, including regulating the vascular system and blood flow, hepatoprotective activity, anti-inflammatory effects, antioxidant effects, and neurological protection [119].

3.5 *Zingiber officinale (Ginger)*

Zingiber officinale Roscoe, the scientific name for ginger, is a member of the Zingiberaceae family. It is a tropical plant that originates in Southeast Asia and grows to a height of 1 meter. *Z. officinale* has traditionally been used to treat a wide range of illnesses, including nausea, vomiting, asthma, coughing, palpitations, inflammation, dyspepsia, lack of appetite, constipation, indigestion, and pain in Ayurveda, Siddha, Chinese, Arabian, African, and Caribbean medical systems, among many others [120]. Ginger has been reported to have biological properties, including anti-inflammatory, antibacterial, antioxidant, and anticancer properties [121]. Ginger has a high amount of phytochemical components. Ginger is a promising herbal medicine to treat many chronic conditions, such as PMS, menopausal symptoms, and dysmenorrhea (Figure 5) [122].

3.5.1 Clinical trials on PMS management activity of Zingiber officinale

In a three-month double-anonymized clinical study conducted by Khayat et al., 70 participants with PMS were identified through a daily record scale questionnaire over two menstrual cycles. They were randomly divided into two groups (n = 35 each). The first group received 250 mg of ginger capsules every 12 hours, while the second group received placebo capsules. Both treatments were given from 7 days before to 3 days after the start of menstrual bleeding. The severity of symptoms was assessed using a daily record scale questionnaire for three cycles. After one month of intervention, ginger significantly reduced the total PMS score, mood severity, and somatic and behavioral symptoms. This suggests that ginger can be a safe and effective remedy for PMS symptoms [122]. In a 2013 double-blinded, placebo-controlled study on 70 female students, daily record questionnaires were used to diagnose PMS based on DSM-IV criteria. Participants with PMS were randomly assigned to receive either ginger capsules (250 mg every 12 hours for seven days before and three days after menstruation) or placebos. After one month, ginger significantly reduced total PMS scores ($p < 0.001$) compared to placebo, with pre-intervention scores being almost similar (ginger: 106.7 ± 44.65, placebo: 110.2 ± 30.77) [122].

3.5.2. Activity for abdominal discomfort of Zingiber officinale

Zingiber officinale has been studied in several clinical trials to treat abdominal bloating. In a double-blind, randomized controlled trial of 106 patients with functional bloating, those who received KAASER, a supplement containing ginger, three times a day for two weeks showed significant improvements compared to the placebo and dimethicone treatment groups. KAASER demonstrated marked reductions in bloating frequency and severity ($P < 0.001$) as well as improvements in the frequencies of defecation, eructation, and borborygmus ($P = 0.03$) across all phases of follow-up among the patients who completed the study [123]. Another clinical trial was conducted to compare the effectiveness of a ginger and artichoke supplement with a placebo in treating functional dyspepsia (FD) in adult male and female patients. The study found that the group receiving the ginger supplement showed a significant improvement in their symptoms, including nausea ($P<0.001$), epigastric fullness ($P<0.001$), epigastric pain ($P=0.002$), and bloating ($P=0.017$), compared to the placebo group [124]. After a cesarean section surgery, a ginger supplement was found to be more effective than a placebo in reducing abdominal distention severity in a randomized, double-blind, placebo-controlled trial. In comparison to the placebo group, the

ginger group performed better in terms of effectiveness in reducing abdominal distention (91% vs 65.2%, $p < 0.001$). In terms of quality of life, more patients in the ginger group were able to eat than in the placebo group (59.6% vs. 43.8%, $p = 0.035$) [125]. Furthermore, a study evaluated the efficacy of a traditional Japanese herbal medicine containing ginger called Daikenchuto (DKT). Face scale measurements of the intensity of the abdominal pain and bloating showed a substantial reduction ($P = 0.039$ and $P = 0.008$, respectively). The quality of life for individuals with persistent constipation was enhanced with DKT therapy [126]. Overall, these studies suggest that ginger, alone or in combination with other ingredients, may effectively reduce abdominal bloating, a prominent physical PMS symptom. One of the primary signs of premenstrual syndrome is dysmenorrhea. Primary dysmenorrhea is initiated by an excess of prostaglandins produced by endometrial tissue, and prostaglandin inhibitors can alleviate 80% of instances of dysmenorrhea. Changes in the prostaglandin system have been suggested as one of the causes of premenstrual syndrome. The metabolism of cyclooxygenase and lipoxygenase is inhibited by ginger, which stops the formation of prostaglandins [113].

3.5.3. Pain relieving activity of Zingiber officinale

In two double-masked, placebo-controlled, randomized trials, Black et al. investigated the effects of ginger supplementation on muscular pain. Study 1 involved 34 participants, while study 2 had 40 participants. During two studies, participants consumed either 2 grams of raw or heated ginger or a placebo for 11 days. Participants then underwent 18 eccentric elbow flexor motions to induce inflammation or discomfort, and the results showed that raw ginger (25% reduction, -0.78 SD, $P = 0.041$) and heated ginger (23% reduction, -0.57 SD, $P = 0.049$) significantly reduced pain intensity compared to the placebo 24 hours after exercise. Raw ginger reduced pain intensity by 25% (9.3 VAS units), while heated ginger reduced it by 23% (8.6 VAS units). Ginger's action involves desensitizing TRPV1 receptors, implicated in pain processing and nociception, by compounds such as gingerols, shogaols, and zingerone. This suggests that ginger supplementation may effectively reduce muscular pain intensity, which may be associated with PMS [127]. In a 2012 study by Rahnama et al., a double-blind, placebo-controlled, and parallel-group trial with balanced randomization (1:1) was conducted on 120 female dormitory students in Iran aged over 18. There were two equal groups: one received 500 mg of ginger thrice daily or a placebo. Both groups were given two different treatment protocols at monthly intervals. The study indicates that ginger may be a safe and effective therapy for easing the pain in women with primary dysmenorrhea. The treatment should be administered at the onset of menstruation and three days prior to it [128]. Another placebo-controlled randomized trial was conducted by Kashefi et al. with 150 high school students aged 15 to 18 in Iran. In this study, participants were randomly assigned to one of three groups: zinc sulfate (n=48), ginger (n=56), or placebo (n=46). The capsules provided to each group contained either 250mg of ginger powder for the ginger group, 220mg of zinc sulfate for the zinc sulfate group, or lactose for the placebo group. The results showed that both the ginger and zinc sulfate groups reported significant pain relief ($p<0.05$) during the study compared to the placebo group. Overall, the ginger and zinc sulfate groups showed a significant reduction in primary dysmenorrheal pain for young women [129].

3.6. Crocus sativus (Saffron)

For many years, especially in Asian countries, saffron, or *Crocus sativus* L. (C. sativus), has been used extensively as a food ingredient and a curative agent in traditional medicine. Picrocrocin, safranal, and crocin are three bioactive components in this spice that have therapeutic effects on various illnesses, including cardiovascular, pulmonary, gastrointestinal, neurological, mental, and female-specific diseases. This herbal compound is said to have anti-nociceptive, anti-inflammatory, and anti-oxidative properties. Additionally, several studies have focused on the potential function of saffron in modulating the serotonergic system, which may help treat certain diseases that affect women specifically, such as PMS, PPD, postmenopausal symptoms, and sexual dysfunction [130]. Additionally, saffron includes more than 150 volatile and aroma-producing compounds and several non-volatile active substances such as polysaccharides and carotenoids like zeaxanthin, lycopene, and beta-carotene [131]. Because of the potential properties of this valuable substrate, several patent products or pharmaceutical formulations are now available in drug shops in some countries as supplements (Figure 6) [132].

3.6.1. Clinical trials on PMS management activity of Crocus sativus

A study on the impact of saffron on PMS symptoms was carried out in 2007 by Agha-Hosseini et al. The study involved women aged between 20 and 45 who had regular menstrual cycles and had been experiencing PMS symptoms for at least six months. One group of women received saffron supplements, while the other group received a placebo. After taking 15 mg of saffron orally twice daily for two menstrual cycles, 75% of participants reported a 50% decrease in the severity of their PMS symptoms. Furthermore, 60% of those in the saffron group reported a 50% decrease in their depressive symptoms. Based on these findings, saffron may work well as a complementary medicine for PMS [134]. In a study conducted by Fukui et al., the effects of saffron odor on premenstrual syndrome, dysmenorrhea, and irregular menstruation were investigated. The study involved 35 women with an average sense of smell who were exposed to saffron odor for 20 minutes. The results showed that saffron odor had both physiological and psychological effects on women, including an increase in cortisol levels, a decrease in 17-beta estradiol levels, and a decrease in the STAI score (State-Trait Anxiety Inventory) during both the follicular and luteal phases. The findings suggest that saffron odor may help alleviate menstruation discomfort, particularly for PMS, dysmenorrhea, and irregular menstruation. This study is the first of its kind to demonstrate the potential benefits of saffron odor for menstrual health [135]. In a 2013 randomized, triple-blind controlled study by S. Pirdadeh Beiranvand et al. involving 78 female students, saffron capsules (30 mg/day) were administered to one group for two menstrual cycles, while another group received placebos. Initially, both groups had similar PMS severity ($P = 0.81$). However, at the study's conclusion, the mean PMS severity significantly decreased in both groups ($P = 0.001$ for the intervention group and $P = 0.04$ for the control group). The difference in PMS severity changes between the two groups was substantial ($P < 0.001$).

This suggests that saffron may reduce PMS symptoms, but further research is needed to confirm its efficacy [136].

3.6.2. Antidepressant, anxiolytic, pain-relieving activity of Crocus sativus

Two clinical studies have shown that taking saffron capsules can be just as effective as taking fluoxetine capsules in treating mild to moderate depression. The first study, conducted by Noorbala et al., found that taking 30 mg of saffron capsules for six weeks was as beneficial as taking 20 mg of fluoxetine capsules ($F = 0.13$, d.f. = 1, $P = 0.71$) [137]. The second study, conducted by Akhoundzadeh et al., compared the efficacy of saffron capsules with fluoxetine in treating depressed patients in an 8-week pilot double-blind randomized trial. The results showed that taking 30-mg saffron capsules for six weeks was more effective than taking a placebo in treating mild to moderate depression ($F= 0.03$, d.f.= 1, $P=0.84$) [138]. In a 12-week double-blind, placebo-controlled study, researchers assessed the effects of saffron extract on anxiety and depression in 60 adult patients. At the end of the 12 weeks, the group that received saffron supplements had significantly better psychiatric scores ($p < 0.001$), as measured by the Beck Anxiety Inventory and the Beck Depression Inventory, compared to the group that received placebo. These results suggest that saffron may be an effective treatment for anxiety and depression disorders. However, more research is needed to assess the potential side effects of saffron supplementation. [139]. Another study combined saffron with two other herbal components to treat primary dysmenorrhea. Each test capsule contained 500 mg of SCA (saffron, celery seed, and anise extracts). One hundred eighty individuals were randomly assigned to one of three test groups: mefenamic acid (250 mg), placebo, or both. For three cycles, all participants took one related capsule every 8 hours from the first onset of menstruation or pain. At months 2 and 3, the subjects' pain severity and duration were assessed using a visual analog pain intensity scale. These findings indicate that SCA is a safe and effective treatment for primary dysmenorrhea, although the researchers recommended more clinical trials [140].

3.7. Withania somnifera (Ashwagandha)

For many years, ashwagandha has been recognized as a beautiful rejuvenator, a general health tonic, and a treatment for various conditions. It has sedative, diuretic, and anti-inflammatory properties and is well-known for increasing energy endurance and acting as an adaptogen with potent immunostimulatory and anti-stress effects [141]. Ashwagandha has been the subject of numerous pharmacological research to confirm its efficacy as a multifunctional therapeutic agent [142]. According to the Indian Herbal System (Ayurveda), Ashwagandha is one of the most significant herbs and the finest adaptogenic. Cuseohygrine, anhydride, tropine, and anaferine are among its constituents, as are glycosides, withanolide, starches, and amino acids [141]. It has been used for an extended period for all age groups, both sexes, and even during pregnancy, with no adverse effects. Recently, WS has been utilized to prevent the development of tolerance and reliance on certain psychiatric medicines when administered chronically (Figure 7) [143].

3.7.1. Clinical trials on PMS management activity of Withania somnifera

A clinical pilot study was conducted in India to assess the effectiveness of a combination of ‘Ashwagandha Vati’ and ‘Satvavajaya Chikitsa’ in managing premenstrual syndrome. Ashwagandha Vati is a formulation prepared from *Withania somnifera*, which aims to mitigate lousy digestion, bloating, and constipation. Satvavajaya Chikitsa is a structured ayurvedic psychotherapy that seeks to restructure the mind. The study involved 30 female volunteers at a tertiary Ayurveda hospital in a South Indian city. The research participants experienced more psychological symptoms than physical ones. They took two Ashwagandha Vati (500 mg) orally twice daily with milk and underwent four Satvavajaya Chikitsa sessions over a month (1 menstrual cycle). After the combination treatment, there was a significant improvement ($P < 0.001$) in cognitive, affective/psychological, and behavioral symptoms. The study concluded that the combination of Ashwagandha Vati and Satvavajaya Chikitsa effectively managed PMS symptoms [144]. A previous study Akhila M et al. conducted an interventional study with 20 females aged 20-35 years experiencing PMS. They were treated with ‘Punarnavadi Kashayam’ (48 mL two times a day) and ‘Aswagandha Choorna’ (3 grams two times a day) for three consecutive menstrual cycles. The medications were administered 14 days before menstruation and continued until the fourth day of menstruation. Both treatments effectively improved depressive symptoms, anxiety, exhaustion, irritability, pain, sleep changes, and bloating, as measured by the premenstrual scale. Additionally, the medications restored serum sodium and potassium levels to normal. The study concluded that Punarnavadi Kashayam and Aswagandha Choorna are highly beneficial in treating PMS [145]. An open-label exploratory clinical study was conducted with 35 participants who met diagnostic criteria for PMS. The participants received Ashwagandha Vati (500mg twice daily with milk) and Satvavajaya Chikitsa (counseling, relaxation, yoga, and pranayama). After treatment, significant improvements were observed in various domains, including negative affect, concentration, behavioral changes, arousal, control, hydration retention, and autonomic response. The combined therapy's efficacy may be attributed to Ashwagandha's anxiolytic and adaptogenic properties, along with the calming effects of Satvavajaya chikitsa. The lasting effect of Satvavajaya, particularly the relaxation response and positive recommendations, may have contributed to the sustained benefits even after treatment cessation [146].

3.7.2. Anti-oxidant, anti-stress, anxiolytic activity of Withania somnifera

A study conducted by the Institute of Basic Medical Sciences at Calcutta University investigated the impact of Ashwagandha on chronic stress in animals. The animals were subjected to mild electric shocks on their feet for 21 days, causing hyperglycemia, glucose intolerance, a rise in plasma corticosterone levels, stomach ulcers, male sexual dysfunction, cognitive impairment, immunosuppression, and depression. Researchers found that mice given Ashwagandha one hour before the foot shock experienced a considerably lower stress level. These findings suggest that Ashwagandha has a significant anti-stress adaptogenic impact. [147]. In a prospective, randomized, double-blind, placebo-controlled

trial, Ashwagandha root extract was tested for its stress-relieving effects on 60 stressed healthy individuals. They were divided into three groups: Ashwagandha extract 125 mg, Ashwagandha extract 300 mg, and placebo, taken twice daily for eight weeks. Both 250 mg and 600 mg Ashwagandha doses significantly reduced stress levels ($P < 0.05$ and $P < 0.001$, respectively) and lowered serum cortisol levels ($P < 0.0001$). Participants who received Ashwagandha reported improved sleep quality. The study concluded that supplementing with Ashwagandha root extract for eight weeks significantly reduced stress levels and improved overall quality of life [148].

4. Discussion and future recommendations

The comprehensive literature review thoroughly investigated the potential use of traditional herbal interventions for managing Premenstrual Syndrome (PMS). These reviews underscore the rich historical significance, intricate botanical characteristics, and bioactive compounds of the herbs, which collectively contribute to their potential therapeutic effects on the multifaceted symptoms associated with PMS. *Cyperus rotundus* (Nagarmotha / Nut Grass) demonstrates a multifaceted range of activities that can potentially alleviate various symptoms associated with PMS. Its antispasmodic, anti-diarrheal and anti-inflammatory properties hold promise in addressing physical discomfort, including abdominal bloating, cramps, muscle pain, and joint discomfort, frequently experienced during PMS. Moreover, these properties extend to emotional well-being by potentially reducing mood swings, irritability, and anxiety. The herb's ability to relax smooth muscles and relieve digestive issues further positions it as a natural remedy for PMS. Its analgesic, sedative, and tranquilizing effects add to its potential in managing headaches, muscle pain, and mood-related symptoms like anxiety and irritability. Turmeric, also known by its scientific name *Curcuma longa*, has much promise for reducing PMS symptoms. Curcumin, its main active ingredient, has potent analgesic, anti-inflammatory, and antioxidant effects. Its efficiency in lowering the duration and intensity of pain brought on by dysmenorrhea has been demonstrated in clinical studies. Furthermore, curcumin has the potential to lessen inflammation in women with PMS and dysmenorrhea due to its capacity to raise serum vitamin D levels and lower high-sensitivity C-reactive protein (hsCRP) levels. *Aloe vera*, also known as Ghrit Kumari, has been recognized for its potential to ease menstrual pain that comes with PMS. It is rich in vitamins and bioactive compounds, which provide antioxidant properties and analgesic effects. Research studies have revealed that ingesting *Aloe vera* gel can effectively reduce the intensity of menstrual pain in young women, making it a natural and side-effect-free solution for managing menstrual discomfort related to PMS. Additionally, it also helps to maintain hormonal balance and have skin protection activity by lessening acne. *Angelica sinensis*, commonly known as Dong Quai or Female Ginseng, is a versatile medicinal herb that shows great potential for managing PMS symptoms. Its unique properties offer a multifaceted approach to addressing both the emotional and hormonal aspects of PMS. The herb's antidepressant properties, anti-fatigue effects, and estrogenic properties make it a valuable tool for combating mood swings, fatigue, and hormonal imbalances. Additionally, its anti-inflammatory attributes may help reduce excessive antibody production and alleviate inflammatory reactions, contributing to the relief of various PMS symptoms. Ginger, or *Zingiber officinale* as it is named scientifically, is another treatment option for PMS and its symptoms. Clinical studies have demonstrated that ginger can successfully lessen the intensity of PMS symptoms, including mood swings and physical pain. Due to its anti-inflammatory and prostaglandin-inhibiting qualities, ginger is an effective treatment for dysmenorrhea, a painful condition that many women experience during their period. Additionally, ginger can ease bloating and abdominal discomfort, which are typical physical signs of PMS. Ginger can provide relief to those looking for a holistic method of treating PMS symptoms because it is a natural and secure treatment. Saffron, also known as *Crocus sativus*, has been found to be effective in treating PMS and its related symptoms. Clinical trials have demonstrated that saffron can significantly reduce the severity of PMS symptoms, particularly those related to depression. Its anti-depressant, anti-anxiety, and pain-relieving properties make it a versatile herbal solution for mood disorders and discomfort. Additionally, its impact on regulating hormones, primarily cortisol and estradiol levels, highlights its potential in alleviating PMS and menstrual irregularities. *Withania somnifera* (Ashwagandha) emerges as a valuable candidate for managing PMS, addressing psychological and physical manifestations. Combining Ashwagandha with structured Ayurvedic psychotherapy has successfully managed cognitive, affective, and behavioral symptoms. Furthermore, Ashwagandha's anti-stress and anxiolytic effects provide relief from stress-related conditions. Its adaptogenic qualities and role in regulating hormonal responses position it as a holistic approach to PMS management. Future recommendations include the need for larger-scale clinical trials to establish efficacy, determine optimal dosages, and assess long-term safety profiles conclusively. Mechanistic studies are necessary to elucidate the underlying action pathways, and standardized formulations would enhance consistency and reproducibility. Exploring combination therapies and patient-centered approaches tailored to individual preferences will optimize PMS management.

Table 1: Etiological factors of PMS

Etiological Factors	Explanation	References
Hormonal Imbalances	PMS can result from fluctuations in estrogen and progesterone levels during the menstrual cycle.	(12–14)
Serotonin Levels	Changes in serotonin levels in the brain may contribute to mood swings and emotional symptoms.	(15,16)
Chemical Changes	Altered sensitivity to neurotransmitters and chemicals in the brain can influence PMS symptoms.	(17,18)
Genetic Predisposition	A family history of PMS or mood disorders may increase the likelihood of experiencing PMS.	(19–21)
Lifestyle Factors	Poor diet, lack of exercise, and high stress can exacerbate PMS symptoms.	(22,23)
Environmental Factors	Exposure to environmental toxins or pollutants may play a role in PMS development.	(24–26)
Psychological Factors	Depression and anxiety are prevalent mental health conditions that might exacerbate PMS symptoms.	(27,28)
Neuroendocrine Factors	The interplay between the nervous and endocrine systems can affect PMS symptoms.	(14,29)

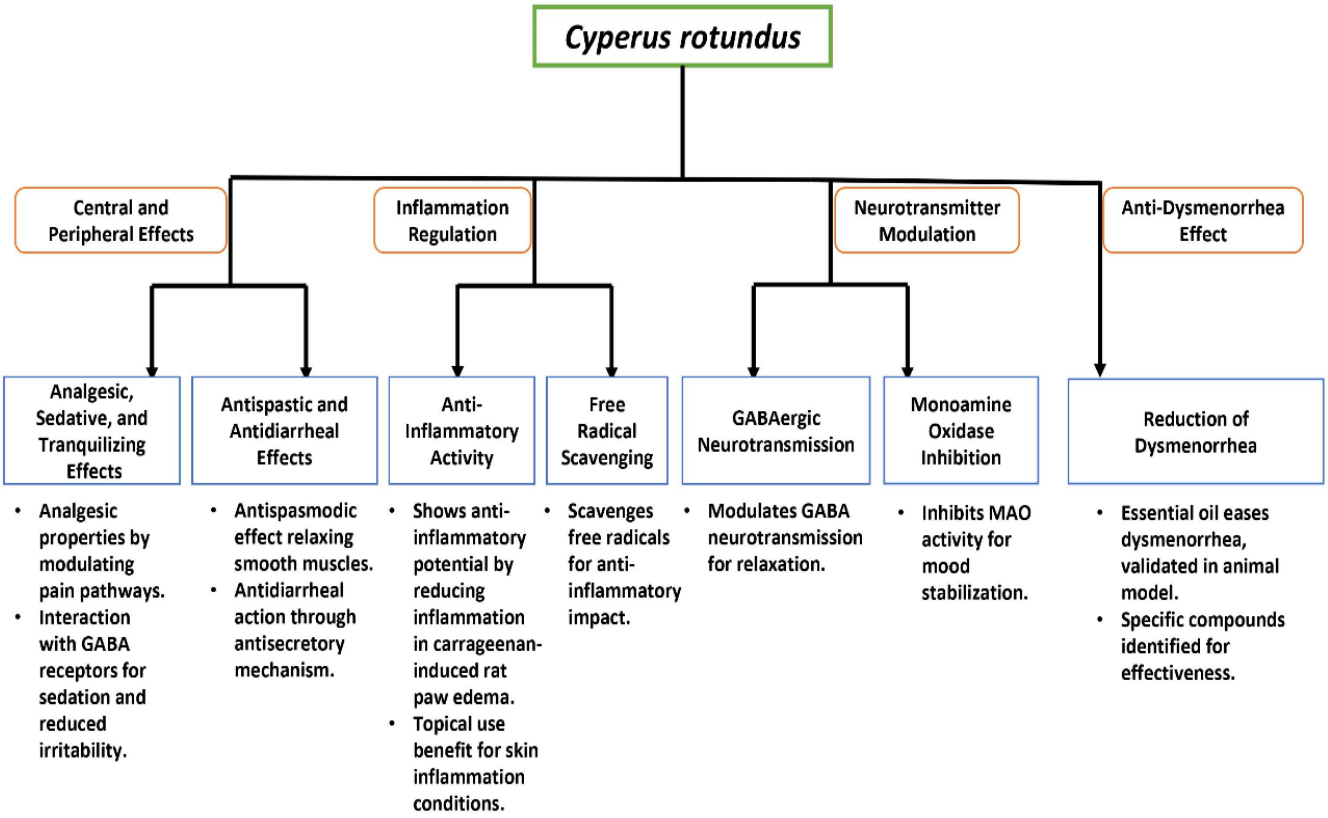

Figure 1: Effectiveness of *Cyperus rotundus* for Premenstrual Syndrome.

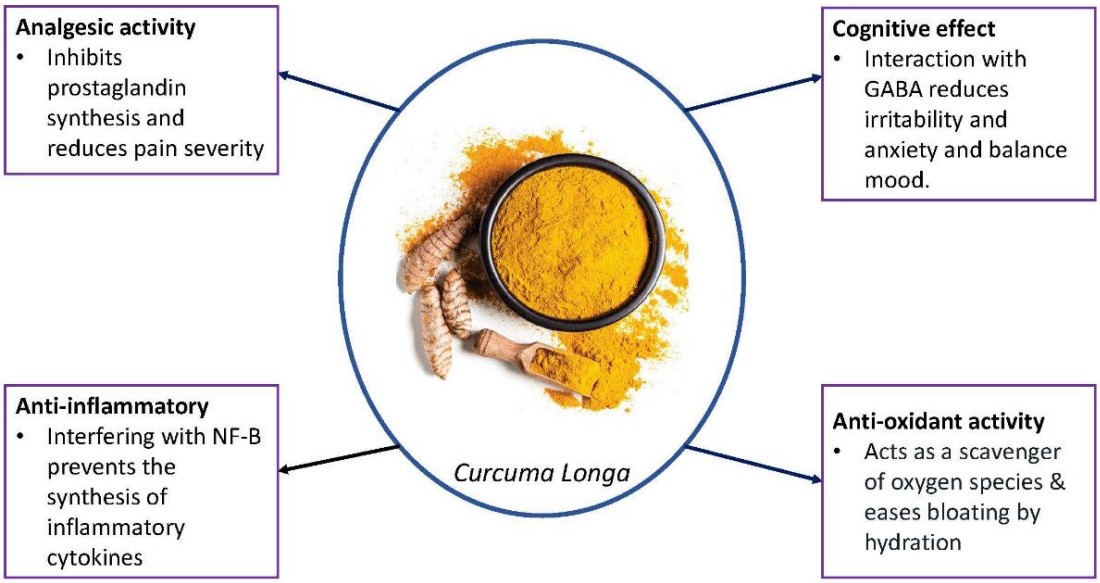

Figure 2: Biological effects of *Curcuma longa* in PMS management.

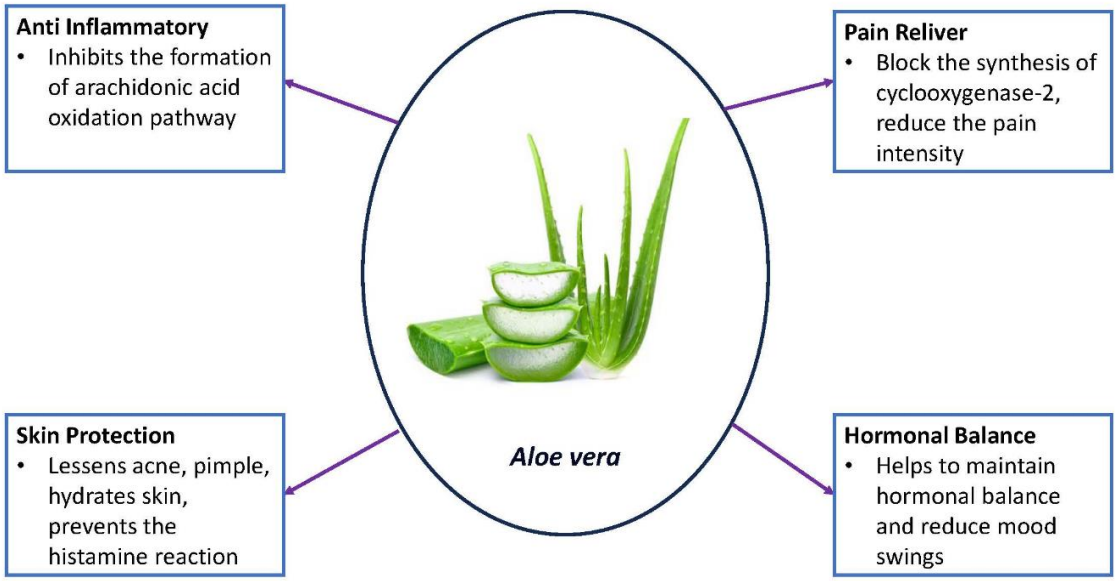

Figure 3: Biological effects of *Aloe vera* in PMS management.

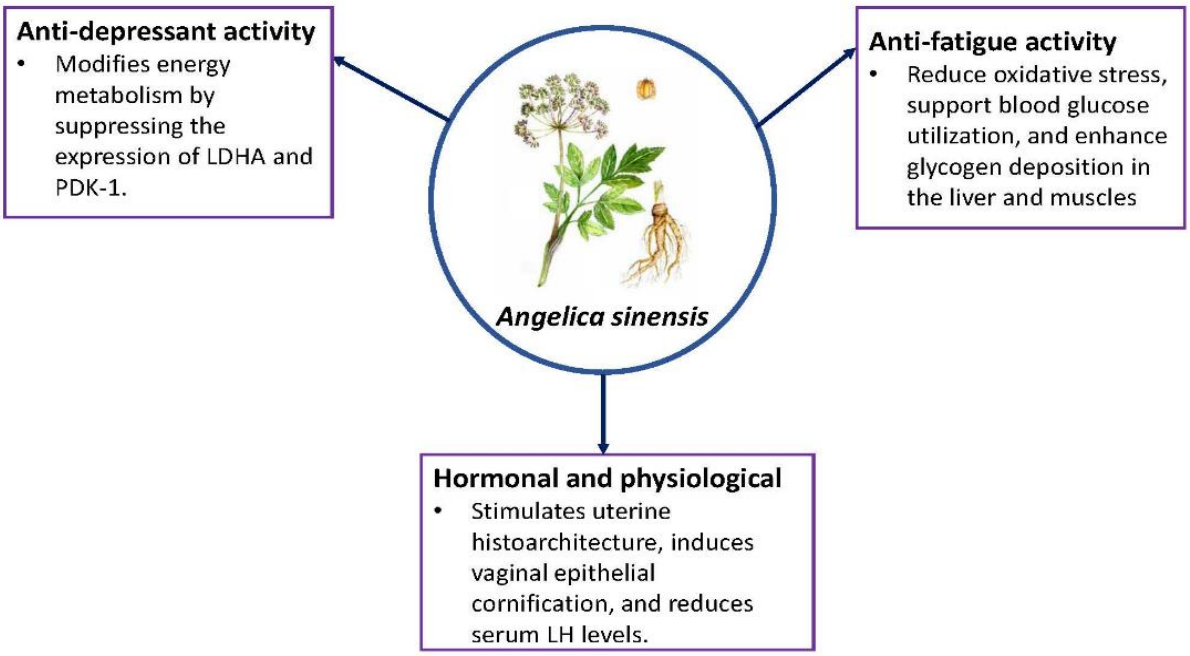

Figure 4: Biological effects of *Angelica sinensis* in PMS management.

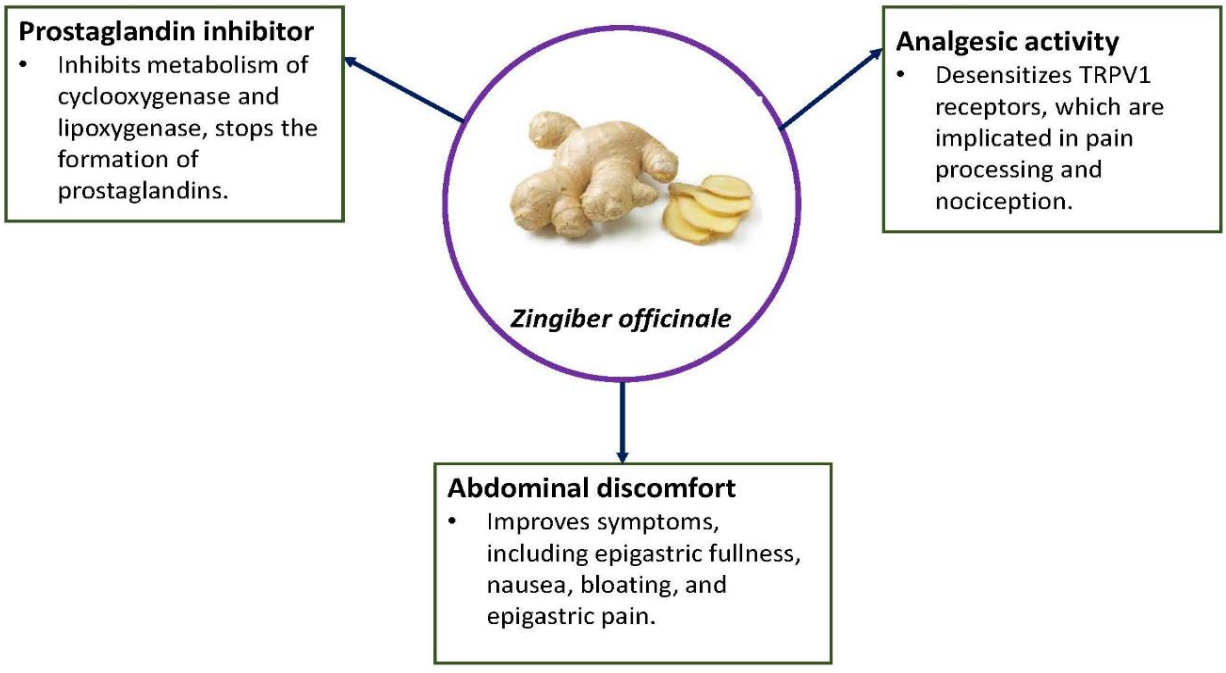

Figure 5: Biological effects of *Zingiber officinale* in PMS management.

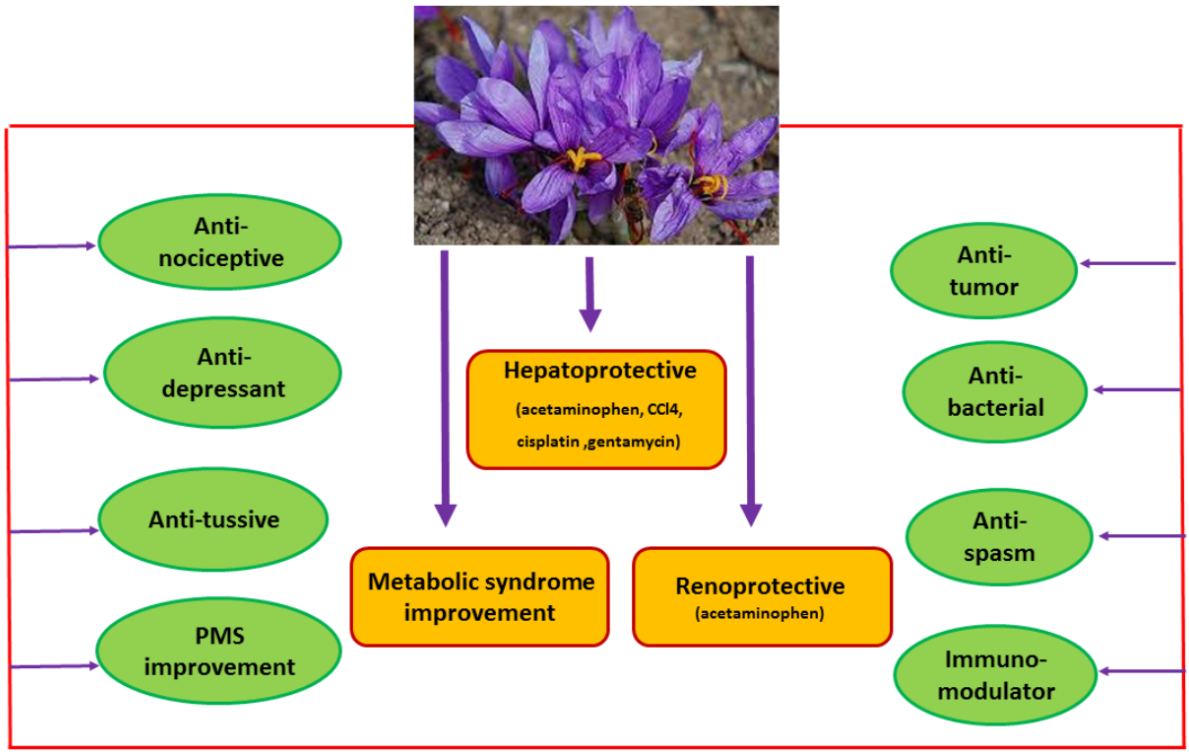

Figure 6: Pharmacological benefits of saffron (*Crocus sativus*) (133).

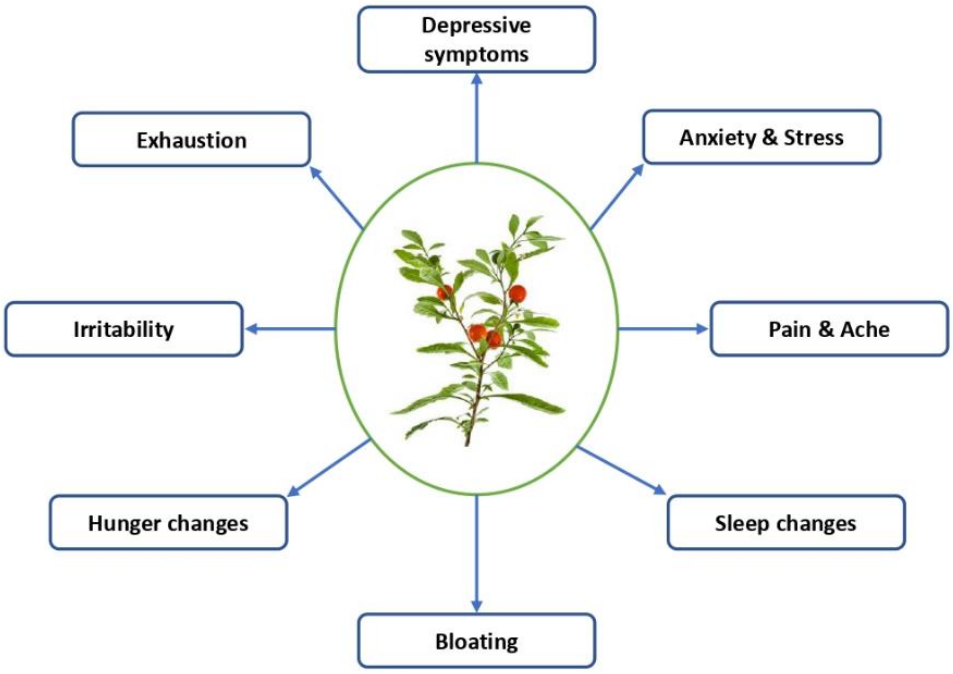

Figure 7: Ashwagandha (*Withania somnifera*) benefits for different PMS symptoms.

Table 2: Symptoms of PMS

Physical Symptoms	**Explanation**	**References**
Breast Tenderness	Swelling and tenderness in the breasts.	(33–35)
Abdominal Bloating	The feeling of fullness and bloating in the lower abdomen.	(36,37)
Headache	Mild to severe headaches may occur.	(38–40)
Fatigue	Persistent tiredness and lack of energy.	(3,9,41)
Cramp and Muscle Pain	Muscle aches and pains, sometimes resembling mild flu-like symptoms.	(42–44)
Joint Pain	Pain and discomfort in the joints.	(3,5,44)
Skin Issues	Acne breakouts or other skin problems may worsen.	(36,37,45)
Sleep Disturbances	Insomnia or disrupted sleep patterns.	(41,46)
Emotional Symptoms	**Explanation**	
Mood Swings	Rapid and extreme changes in mood.	(16,37,47)
Irritability	Increased sensitivity and irritability.	(27,35,47)
Anxiety	Feelings of nervousness or tension.	(27,48,49)
Depression	Feeling sad, hopeless, or experiencing a lack of interest in activities.	(27,50,51)
Crying Spells	Uncontrollable crying or heightened emotional response.	(3,36,52)
Difficulty Concentrating	Reduced ability to focus and concentrate.	(50,53,54)
Changes in Appetite	Food cravings or loss of appetite.	(55–57)
Social Withdrawal	Avoiding social interactions or isolating oneself.	(58–60)

A comprehensive and multidisciplinary approach, including rigorous research and standardized protocols, is essential to unlock the full potential of traditional herbal interventions in PMS management.

5. Conclusions

This comprehensive literature review has shed light on the potential of traditional herbal interventions as promising approaches for managing the complex array of symptoms associated with Premenstrual Syndrome (PMS). These herbs, including *Cyperus rotundus*, *Curcuma longa* (turmeric), *Aloe vera*, *Angelica sinensis* (Dong Quai), *Zingiber officinale* (ginger), *Crocus sativus* (saffron), and *Withania somnifera* (Ashwagandha), each offer unique therapeutic attributes that address both physical and emotional manifestations of PMS. From analgesic and anti-inflammatory properties to mood-enhancing and adaptogenic effects, these herbal remedies present potential alternatives to conventional medications, which may carry side effects. However, it's essential to emphasize the need for further research, including large-scale clinical trials, mechanistic investigations, standardized formulations, and consideration of individual patient preferences. These steps are crucial in establishing these herbal interventions' efficacy, safety, and optimal usage, ultimately providing women with diverse and potentially safer options for managing PMS symptoms. In doing so, we can unlock the full potential of traditional herbal remedies and enhance the holistic approach to PMS management.

Funding Information

This study received no specific grant from any funding agency, commercial or not-for-profit sectors.

Competing Interest

The authors declare that they have no competing interest.

References

[1] R. Abu Alwafa, M. Badrasawi, R. Haj Hamad. (2021). Prevalence of premenstrual syndrome and its association with psychosocial and lifestyle variables: a cross-sectional study from Palestine. BMC Women's Health. 21(1): 233.

[2] N. Buddhabunyakan, S. Kaewrudee, C. Chongsomchai, S. Soontrapa, W. Somboonporn, J. Sothornwit. (2017). Premenstrual syndrome (PMS) among high school students. International journal of women's health. 501-505.

[3] R.F. Casper, W.F. Crowley Jr, Patient education: Premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD)(Beyond the Basics). In 2019.
Available from: https://www.uptodate.com/contents/premenstrual-syndrome-pms-and-premenstrual-dysphoric-disorder-pmdd-beyond-the-basics/print?search=sindrome premenstrual&source=search_result&selectedTitle=5~150&usage_type=default&display_rank=5.

[4] A. Ryu, T.-H. Kim. (2015). Premenstrual syndrome: A mini review. Maturitas. 82(4): 436-440.
Available from: https://www.sciencedirect.com/science/article/pii/S0378512215300451.

[5] M. Zaka, K.T. Mahmood. (2012). Pre-menstrual syndrome- A review. Journal of Pharmaceutical Sciences and Research. 2012;4(1):1684–91.
Available from: https://www.jpsr.pharmainfo.in/Documents/Volumes/vol4Issue01/jpsr 04120109.pdf.

[6] M.A.B.S. Jami, K. Biswas. (2023). A cross-sectional study regarding the knowledge, attitude and awareness about self-medication among

Bangladeshi people. Health Policy and Technology. 100715.
Available from: https://www.sciencedirect.com/science/article/pii/S2211883722001228.

[7] C.L. Vandeleur, S. Rothen, Y. Lustenberger, J. Glaus, E. Castelao, M. Preisig. (2017). Ayurvedic Management Of Premenstrual Syndrome: A Case Study. International Journal of Ayurveda and Pharma Research. Volume 8:119–21.

[8] B.L. True, S.M. Goodner, E.A. Burns. (1985). Review of the etiology and treatment of premenstrual syndrome. Drug intelligence & clinical pharmacy. 19(10): 714-722.
Available from: https://doi.org/10.1177/106002808501901003.

[9] A. Mishra, G. Banwari, P. Yadav. (2015). Premenstrual dysphoric disorder in medical students residing in hostel and its association with lifestyle factors. Industrial psychiatry journal. 24(2): 150.

[10] Women's Health Concern. (2015). Premenstrual Syndrome (PMS) [Internet].
Available from: https://www.womens-health-concern.org/wpcontent/uploads/2015/02/WHC_FS_PMS.pdf.

[11] S. Walsh, E. Ismaili, B. Naheed, S. O'Brien. (2015). Diagnosis, pathophysiology and management of premenstrual syndrome. The Obstetrician & Gynaecologist. 17(2): 99-104.

[12] C. Roomruangwong, A.F. Carvalho, F. Comhaire, M. Maes. (2019). Lowered plasma steady-state levels of progesterone combined with declining progesterone levels during the luteal phase predict peri-menstrual syndrome and its major subdomains. Frontiers in psychology. 10: 2446.

[13] R. Hamidpour, L. Rashan. (2017). An Herbal Preparation that Relieves Symptoms of Premenstrual Syndrome. Translational Biomedicine. 8(3): 126.

[14] E.M. Mulligan, B.D. Nelson, Z.P. Infantolino, K.R. Luking, R. Sharma, G. Hajcak. (2018). Effects of menstrual cycle phase on electrocortical response to reward and depressive symptoms in women. Psychophysiology. 55(12): e13268.

[15] J.G. Hensler. (2010). Serotonin in mood and emotion. In Handbook of behavioral neuroscience, Elsevier: 2010; Vol. 21, pp 367-378. Available from: https://www.sciencedirect.com/science/article/pii/S1569733910700904.

[16] K.G. Commons, Serotonin system function, organization, and feedback. In Handbook of Behavioral Neuroscience, Elsevier: 2020; Vol. 31, pp 41-48.
Available from: https://www.sciencedirect.com/science/article/pii/B9780444641250000037.

[17] E. Bannister. (2019). There is increasing evidence to suggest that brain inflammation could play a key role in the aetiology of psychiatric illness. Could inflammation be a cause of the premenstrual syndromes PMS and PMDD? Post Reproductive Health. 25(3): 157-161.
Available from: https://doi.org/10.1177/2053369119875386.

[18] P. Liu, Y. Wei, Y. Fan, R. Li, Y. Liu, G. Wang, Y. Wei, Y. Pang, D. Deng, W. Qin. (2018). Altered brain structure in women with premenstrual syndrome. Journal of Affective Disorders. 229: 239-246.
Available from: https://www.sciencedirect.com/science/article/pii/S0165032717314982.

[19] C. Vandeleur, S. Rothen, Y. Lustenberger, J. Glaus, E. Castelao, M. Preisig. (2015). Inter-informant agreement and prevalence estimates for mood syndromes: direct interview vs. family history method. Journal of Affective Disorders. 171: 120-127.
Available from: https://www.sciencedirect.com/science/article/pii/S0165032714005370.

[20] K. Jansen, T. Cardoso, G. Fries, J. Branco, R. Silva, M. Kauer-Sant'Anna, F. Kapczinski, P. Magalhaes. (2016). Childhood trauma, family history, and their association with mood disorders in early adulthood. Acta Psychiatrica Scandinavica. 134(4): 281-286.

[21] H. Berenbaum, K. Bredemeier, M.T. Boden, R.J. Thompson, M. Milanak. (2011). Affective instability, family history of mood disorders, and neurodevelopmental disturbance. Personality Disorders: Theory, Research, and Treatment. 2(3): 220.

[22] A. Daley, H. Stokes-Lampard, A. Thomas, C. MacArthur. (2014). Exercise for vasomotor menopausal symptoms. Cochrane Database of Systematic Reviews. (11).
Available from: https://doi.org//10.1002/14651858.CD006108.pub4

[23] M.S. Hashim, A.A. Obaideen, H.A. Jahrami, H. Radwan, H.J. Hamad, A.A. Owais, L.G. Alardah, S. Qiblawi, N. Al-Yateem, M.e.A.-I.E. Faris. (2019). Premenstrual syndrome is associated with dietary and lifestyle behaviors among university students: a cross-sectional study from Sharjah, UAE. Nutrients. 11(8): 1939.

[24] H. Sakai, K. Ohashi. (2021). Effects of past environmental tobacco smoke exposure on the menstrual cycle and menstrual phase-related symptoms: A cross-sectional study. Journal of Obstetrics and Gynaecology Research. 47(1): 243-253.

[25] C. Delpierre, J. Lepeule, S. Cordier, R. Slama, B. Heude, M.-A. Charles. (2016). DOHaD: epidemiological researches. Medecine Sciences: M/S. 32(1): 21-26.

[26] J. Guo, P. Tian, Z. Xu, H. Zhang. (2021). Introduction to Environmental Harmful Factors. Environment and Female Reproductive Health. 3-19.
Available from: https://doi.org/10.1007/978-981-33-4187-6_1.

[27] C.-H. Ko, C.-Y. Long, S.-Y.C.I.-J. Chen, T.-H. Huang, J.-Y. Yen. (2013). Depression, irritability, and anxiety in women with premenstrual dysphoric

disorder. The International Journal of Psychiatry in Medicine. 46(1): 39-55.
Available from: https://doi.org/10.2190/PM.46.1.d.

[28] L. Riven. (1983). Premenstrual syndrome: A psychological overview. Canadian Family Physician. 29: 1919.

[29] A.J. Rapkin, A.L. Akopians. (2012). Pathophysiology of premenstrual syndrome and premenstrual dysphoric disorder. Menopause international. 18(2): 52-59.
Available from: https://doi.org/10.1258/mi.2012.012014.

[30] J.N. Kues, C. Janda, M. Kleinstäuber, C. Weise. (2016). How to measure the impact of premenstrual symptoms? Development and validation of the German PMS-Impact Questionnaire. Women & health. 56(7): 807-826.
Available from: https://doi.org/10.1080/03630242.2015.1118734.

[31] M. Janssen, J.S. Edgar, E. Golan, Treatment of menstrual cycle-induced symptoms. In Google Patents: 2023.
Available from: https://lens.org/066-153-061-277-567.

[32] S. Hofmeister, S. Bodden. (2016). Premenstrual syndrome and premenstrual dysphoric disorder. American family physician. 94(3): 236-240.

[33] A. Goyal. (2014). Breast pain. Vol. BMJ Clinical Evidence.

[34] J. Scurr, W. Hedger, P. Morris, N. Brown. (2014). The prevalence, severity, and impact of breast pain in the general population. The Breast Journal. 20(5): 508-513.

[35] K. Winther, J. Campbell-Tofte, A.M. Motawei, F. Pedersen, S.B. Roos, A.S.V. Hansen, G.G. Fornitz, M. Killi, G. Gerhardsen. (2018). A double-blinded, randomized, placebo controlled, parallel study of pollen pistil extract (Sèrèlys) on women reporting irritability as predominant PMS symptom. Journal of Herbal Medicine. 12: 23-32.
Available from: https://www.sciencedirect.com/science/article/pii/S2210803318300101.

[36] C. Costanian, Z. Akiki, Z. Rabah, S. Daou, S. Assaad. (2018). Factors associated with premenstrual syndrome and its different symptom domains among university students in Lebanon.

[37] A. Antai, A. Udezi, E. Ekanem, U. Okon, A. Umoiyoho. (2004). Premenstrual syndrome: prevalence in students of the University of Calabar, Nigeria. African journal of biomedical research. 7(2).

[38] G. Moy, V. Gupta. (2022). Menstrual Related Headache. Stat Pearls Publishing.
Available from: https://www.ncbi.nlm.nih.gov/books/NBK557451/?report=classic.

[39] G. Allais, I. Castagnoli Gabellari, C. Burzio, S. Rolando, C. De Lorenzo, O. Mana, C. Benedetto. (2012). Premenstrual syndrome and migraine. Neurological Sciences. 33: 111-115.
Available from: https://doi.org/10.1007/s10072-012-1054-5.

[40] J. Kiesner, V.T. Martin. (2013). Mid-cycle headaches and their relationship to different patterns of premenstrual stress symptoms. Headache: The Journal of Head and Face Pain. 53(6): 935-946.
Available from: https://doi.org/10.1111/head.12082.

[41] P.-C. Lin, C.-H. Ko, Y.-J. Lin, J.-Y. Yen. (2021). Insomnia, inattention and fatigue symptoms of women with premenstrual dysphoric disorder. International Journal of Environmental Research and Public Health. 18(12): 6192.

[42] M. Begum, S. Das, H.K. Sharma. (2016). Menstrual disorders: causes and natural remedies. Journal of Pharmaceutical, Chemical and Biological Sciences . 4(2): 307-20.
Available from: http://jpcbs.info/2016_4_2_20_Monawara.pdf.

[43] S. Sivadasan, A.N. Ali, K. Marimuthu, Z.A. Nazer, S. Chigurupati, R. Veerasamy. (2014). Menstrual disorders among students–an overview. Research Journal of Pharmacy and Technology. 7(6): 704-711.

[44] D. Choi, D.-Y. Lee, P. Lehert, I.S. Lee, S.H. Kim, L. Dennerstein. (2010). The impact of premenstrual symptoms on activities of daily life in Korean women. Journal of Psychosomatic Obstetrics & Gynecology. 31(1): 10-15.

[45] S. Stolla, A.R. Shalita, G.F. Webster, R. Kaplan, S. Danesh, A. Penstein. (2001). The effect of the menstrual cycle on acne. Journal of the American Academy of Dermatology. 45(6): 957-960.
Available from: https://www.sciencedirect.com/science/article/pii/S019096220123641X.

[46] M. Meers, J.L. Bower, C.A. Alfano. (2020). Poor sleep and emotion dysregulation mediate the association between epressive and premenstrual symptoms in young adult women. Archives of Women's Mental Health. 23: 351-359.
Available from: https://doi.org/10.1007/s00737-019-00984-2.

[47] A. Labrum. (1983). Hypothalamic, pineal and pituitary factors in the premenstrual syndrome. The Journal of Reproductive Medicine. 28(7): 438-445.

[48] J.W. Bailey, L.S. Cohen. (1999). Prevalence of mood and anxiety disorders in women who seek treatment for premenstrual syndrome. Journal of women's health & gender-based medicine. 8(9): 1181-1184.

[49] E.W. Freeman, S.M. Halberstadt, K. Rickels, J.M. Legler, H. Lin, M.D. Sammel. (2011). Core symptoms that discriminate premenstrual syndrome. Journal of Women's Health. 20(1): 29-35.

[50] M.A.B.S. Jami, R. Sultana, M.M. Hasan, I.J. Ananna. (2023). Menstrual health and prevalence of menstrual disorders among modern society females in Dhaka, Bangladesh: a cross-sectional study.

[51] S.K. Padhy, S. Sarkar, P.B. Beherre, R. Rathi, M. Panigrahi, P.S. Patil. (2015). Relationship of premenstrual syndrome and premenstrual dysphoric disorder with major depression: Relevance to clinical practice. Indian journal of psychological medicine. 37(2): 159-164.

[52] S. Kumari, A. Sachdeva. (2016). Patterns and predictors of premenstrual symptoms among females working in a psychiatry hospital. Scientifica. 2016. Available from: https://doi.org/10.1155/2016/6943852.

[53] D. Kustriyanti, H. Rahayu. (2020). Prevalence of premenstrual syndrome and quality of life among health science college student. International Journal of Public Health Science (IJPHS). 9(1): 15-19.

[54] N. Nisar, N. Zehra, G. Haider, A.A. Munir, N.A. Sohoo. (2008). Frequency, intensity and impact of premenstrual syndrome in medical students. Journal of College of Physicians and Surgeons Pakistan. 18(8): 481-4.

[55] S. Alshayeb, F. Kahal, O. Al Helwani, A. Al Helwani, A. Torbey, S. Kadri, A. Aldarra, A. Alsaadi, S. Al-Habal, M. Moufti. (2022). The prevalence of various menstrual disorders and its association with psychological stress in medical faculties students. A Cross-sectional study.

[56] E.J. Frackiewicz, T.M. Shiovitz. (2001). Evaluation and management of premenstrual syndrome and premenstrual dysphoric disorder. Journal of the American Pharmaceutical Association (1996). 41(3): 437-447.

[57] E.W. Freeman, S.M. Halberstadt, K. Rickels, J.M. Legler, H. Lin, M.D. Sammel. (2011). Core symptoms that discriminate premenstrual syndrome. Journal of Women's Health. 20(1): 29-35. Available from: https://doi.org/10.1089/jwh.2010.2161.

[58] D.E. Rizk, M. Mosallam, S. Alyan, N. Nagelkerke. (2006). Prevalence and impact of premenstrual syndrome in adolescent schoolgirls in the United Arab Emirates. Acta obstetricia et gynecologica Scandinavica. 85(5): 589-598.

[59] F.A. Quintana-Zinn, B.W. Whitcomb, A.G. Ronnenberg, C. Bigelow, S.C. Houghton, E.R. Bertone-Johnson. (2017). Premenstrual symptom patterns and behavioral risk factors in young women: a cross-sectional study. Journal of Women's Health. 26(10): 1099-1105. Available from: https://doi.org/10.1089/jwh.2016.5921.

[60] R.L. Robinson, R.W. Swindle. (2000). Premenstrual symptom severity: impact on social functioning and treatment-seeking behaviors. Journal of women's health & gender-based medicine. 9(7): 757-768. Available from: https://doi.org/10.1016/S0020-7292(00)82807-6.

[61] R. Kroll, A.J. Rapkin. (2006). Treatment of premenstrual disorders. Journal of Reproductive Medicine. 51(4 Suppl):359–70.

[62] Y. Khelemsky, A. Malhotra, K. Gritsenko. (2019). Academic Pain Medicine: A Practical Guide to Rotations, Fellowship, and Beyond. Springer: pp. Available from: https://doi.org/10.1007/978-3-030-18005-8_13.

[63] E.C. Yiannakopoulou. (2015). Aspirin and NSAIDs for breast cancer chemoprevention. European Journal of Cancer Prevention. 24(5): 416-421. Available from: https://journals.lww.com/eurjcancerprev/fulltext/2015/09000/aspirin_and_nsaids_for_breast_cancer.7.aspx.

[64] W. Marcason. (2012). What Is the FODMAP Diet? Journal of the Academy of Nutrition and Dietetics. 112(10):1696. Available from: https://doi.org/10.1016/j.jand.2012.08.005.

[65] L. Hooper, C. Bartlett, G.D. Smith, S. Ebrahim. (2002). Systematic review of long term effects of advice to reduce dietary salt in adults. Bmj. 325(7365): 628. Available from: http://www.bmj.com/content/325/7365/628.1.abstract.

[66] S.K. Pandit. (2022). Role of meditation and yoga in treating Stress,Anxiety &Depression. Indian Journal of Psychiatry. 64(Suppl 3). Available from: https://journals.lww.com/indianjpsychiatry/fulltext/2022/64003/role_of_meditation_and_yoga_in_treating.271.aspx.

[67] J.F. Mortola. (1992). Issues in the diagnosis and research of premenstrual syndrome. Clinical obstetrics and gynecology. 35(3): 587-598. Available from: https://journals.lww.com/clinicalobgyn/Fulltext/1992/09000/Issues_in_the_Diagnosis_and_Research_of.19.aspx.

[68] J.F. Mortola. (1994). A risk-benefit appraisal of drugs used in the management of premenstrual syndrome. Drug Safety. 10(2): 160-169. Available from: https://doi.org/10.2165/00002018-199410020-00005.

[69] L. Scheffers, I. Vos, E. Utens, G. Dieleman, S. Walet, J. Escher, L. van den Berg, R.E. Team. (2023). Physical training and healthy diet improved bowel symptoms, quality of life and fatigue in children with inflammatory bowel disease. Journal of Pediatric Gastroenterology and Nutrition. Available from: https://journals.lww.com/jpgn/fulltext/2023/08000/physical_training_and_healthy_diet_improved_bowel.16.aspx.

[70] K. Gemesi, S.L. Holzmann, B. Kaiser, M. Wintergerst, M. Lurz, G. Groh, M. Böhm, H. Krcmar, K. Gedrich, H. Hauner. (2022). Stress eating: an online survey of eating behaviours, comfort foods, and healthy food substitutes in German adults. BMC Public Health. 22(1): 391. Available from: https://doi.org/10.1186/s12889-022-12787-9.

[71] M. Kabakibi, K.A. Macauley. (2019). A Web-based Stress Reduction Program for Occupational Health. The International Journal of Health, Wellness and Society. 9(2): 29.

[72] Z. Ubaidillah, R.K. Rosul, R. Ilmiasih. (2023). Benson's Relaxation Techniques to Improve Sleep Quality in Diabetes Mellitus Patients. KnE Medicine. 343–356-343–356.

Available from: https://knepublishing.com/index.php/KnE-Medicine/article/view/13069.
[73] H.T. Pham, H.-L. Chuang, C.-P. Kuo, T.-P. Yeh, W.-C. Liao. (2021). In Electronic device use before bedtime and sleep quality among university students, Healthcare. MDPI. p 1091.
[74] S. Li, X. He, Z. Zhang, X. Zhang, Y. Niu, A. Steel, H. Wang. (2023). Efficacy and safety of a facial serum and a mask containing salicylic acid and lipohydroxy acid in acne management: A randomized controlled trial. Journal of Cosmetic Dermatology.
Available from: https://doi.org/10.1111/jocd.15746.
[75] G. Kosmoski, D. Miller, C. Coret, E. Atillasoy. (2022). A Topical Combination Regimen of Benzoyl Peroxide and Retinol Moisturizer for Mild to Moderate Acne. Journal of Drugs in Dermatology: JDD. 21(12): 1340-1346.
[76] Y. Funakami, E. Itoh, T. Hata, T. Wada, S. Ichida. (2010). Specific alternation of rhythm in temperature (SART) stress-induced irritable bowel syndrome-like changes in mice and effects of drugs. Biological and Pharmaceutical Bulletin. 33(9): 1545-1549.
[77] M.R. Lappin, A. Zug, C. Hovenga, J. Gagne, E. Cross. (2022). Efficacy of feeding a diet containing a high concentration of mixed fiber sources for management of acute large bowel diarrhea in dogs in shelters. Journal of Veterinary Internal Medicine. 36(2): 488-492.
Available from: https://doi.org/10.1111/jvim.16360.
[78] M.G. Puoti, A. Assa, M. Benninga, I.J. Broekaert, F.J.M. Carpi, M.D. Saccomani, J. Dolinsek, M. Homan, E. Mas, E. Miele. (2023). Drugs in focus: Domperidone. Journal of Pediatric Gastroenterology and Nutrition. 77(2): e13-e22.
Available from: https://journals.lww.com/jpgn/fulltext/2023/08000/drugs_in_focus__domperidone.4.aspx.
[79] B. Das, D. Pal, A. Haldar. (2019). Premenstrual syndrome: a review of the literature. Gynecology. 21(2):38–43.
Available from: https://gynecology.orscience.ru/2079-5831/article/view/33475.
[80] J.M. Ferguson. (2001). SSRI antidepressant medications: adverse effects and tolerability. Primary care companion to the Journal of clinical psychiatry. 3(1): 22.
[81] A. Davis, J. Robson. (2016). The dangers of NSAIDs: look both ways. Vol. 66, The British journal of general practice:The journal of the Royal College of General Practitioners. England. p. 172–3.
[82] J.C. De Jong, P.B. Van Den Berg, H. Tobi, L.T. De Jong. (2003). Combined use of SSRIs and NSAIDs increases the risk of gastrointestinal adverse effects. British journal of clinical pharmacology. 55(6): 591-595.
[83] R. Srivastava, A. Singh, S. Shukla. (2013). Chemical investigation and pharmaceutical action of *Cyperus rotundus*-a review. Journal of Biologically Active Products from Nature. 3(3): 166-172.
[84] A.M. Peerzada, H.H. Ali, M. Naeem, M. Latif, A.H. Bukhari, A. Tanveer. (2015). *Cyperus rotundus* L.: Traditional uses, phytochemistry, and pharmacological activities. Journal of ethnopharmacology. 174: 540-560.
Available from: http://dx.doi.org/10.1016/j.jep.2015.08.012.
[85] N. Nuning, J. Jamsari, H.T. Djong, B. Hendr. (2016). Skeleton Development Of Mice (Mus Musculus L) Threated With Nutgrass (*Cyperus rotundus*) Extract. In: The USR International Seminar On Food Security. Bandar Lampung, Lampung, Indonesia. p. 245–52.
Available from: http://repository.lppm.unila.ac.id/2528/1
[86] N. Singh, B. Pandey, P. Verma, M. Bhalla, M. Gilca. (2012). Phyto-pharmacotherapeutics of *Cyperus rotundus* Linn.(Motha): an overview.
Available from: https://api.semanticscholar.org/CorpusID:45868376.
[87] P.B. Shamkuwar, A.H. Hoshamani, I.D. Gonjari. (2012). Antispasmodic effect of *Cyperus rotundus* L.(Cyperaceae) in diarrhoea. Der Pharmacia Lettre. 4(2): 522-524.
[88] S. Uddin, K. Mondal, J. Shilpi, M. Rahman. (2006). Antidiarrhoeal activity of *Cyperus rotundus*. Fitoterapia. 77(2): 134-136.
[89] F.G. Rocha, M. de Mello Brandenburg, P.L. Pawloski, B. da Silva Soley, S.C.A. Costa, C.C. Meinerz, I.P. Baretta, M.F. Otuki, D.A. Cabrini. (2020). Preclinical study of the topical anti-inflammatory activity of *Cyperus rotundus* L. extract (Cyperaceae) in models of skin inflammation. Journal of ethnopharmacology. 254: 112709.
Available from: https://doi.org/10.1016/j.jep.2020.112709.
[90] E.S. Fernandes, E.S. Ferro, G. Simão, G. Alves de Góis, J. Arbiser, S.K. Pereira Costa. (2022). Current challenges in inflammation and pain biology: The role of natural and synthetic compounds. Frontiers in Physiology. 13: 1008538.
[91] B. Das, D. Pal, A. Halder. (2015). A review on *Cyperus rotundus* as a tremendous source of pharmacologically active herbal medicine. International Journal of Green Pharmacy (IJGP). 9(4).
[92] M.Z. Imam, C.D. Sumi. (2014). Evaluation of antinociceptive activity of hydromethanol extract of *Cyperus rotundus* in mice. BMC complementary and alternative medicine. 14(1): 1-5.
[93] N. Singh, B. Pandey, P. Verma, M. Bhalla, M. Gilca. (2012). Phyto-pharmacotherapeutics of *Cyperus rotundus* Linn.(Motha): an overview.
[94] N. Singh, V. Kulshrestha, M. Gupta, K. Bhargava. (1970). A pharmacological study of *Cyperus rotundus*. The Indian journal of medical research. 58(1): 103-109.
[95] F. Wang, S. Zhang, J. Zhang, F. Yuan. (2022). Systematic review of ethnomedicine,

phytochemistry, and pharmacology of Cyperi Rhizoma. Frontiers in pharmacology. 13: 965902.

[96] G.-f. Hao, M.-q. Tang, Y.-j. Wei, F.-y. Che, L.-j. Qian. (2017). Determination of antidepressant activity of *Cyperus rotundus* L extract in rats. Tropical Journal of Pharmaceutical Research. 16(4): 867-871.

[97] A.E. Al-Snafi. (2016). A review on *Cyperus rotundus* A potential medicinal plant. International Organization of Scientific Research : Journal of Pharmacy. 6(7): 32-48.

[98] F. Shoaee, M. Pouredalati, S. Dadshahi, P. Parvin, M. Bolourian, A. Kiani, A. Tavakolian, F. Vafisani. (2020). Evaluation of non-pharmacological strategies, therapeutic and cognitive-behavioral interventions in the treatment of premenstrual syndrome: a review study. International Journal of Pediatrics. 8(2): 10929-10939.

[99] P. Basnet, N. Skalko-Basnet. (2011). Curcumin: an anti-inflammatory molecule from a curry spice on the path to cancer treatment. Molecules. 16(6): 4567-4598.

[100] A. AloK, I.D. Singh, S. Singh, M. Kishore, P.C. Jha. (2015). Curcumin–pharmacological actions and its role in oral submucous fibrosis: a review. Journal of Clinical and Diagnostic Research: JCDR. 9(10): ZE01.

[101] K. Shimizu, M. Funamoto, Y. Sunagawa, S. Shimizu, Y. Katanasaka, Y. Miyazaki, H. Wada, K. Hasegawa, T. Morimoto. (2019). Anti-inflammatory action of curcumin and its use in the treatment of lifestyle-related diseases. European Cardiology Review. 14(2): 117.
Available from: https://doi.org/10.15420/ecr.2019.17.2.

[102] N.S. Tabari, M. Kheirkhah, F. Mojab, M. Salehi. (2020). An investigation of the effect of curcumin (turmeric) capsule on the severity and duration of dysmenorrhea in students of Iran University of Medical Sciences. Journal of evolution of medical and dental sciences. 9(46): 3444-3451.

[103] L. Arabnezhad, M. Mohammadifard, L. Rahmani, Z. Majidi, G.A. Ferns, A. Bahrami. (2022). Effects of curcumin supplementation on vitamin D levels in women with premenstrual syndrome and dysmenorrhea: a randomized controlled study. BMC complementary medicine and therapies. 22(1): 19.

[104] N. Maleki-Saghooni, F.Z. Karimi, Z.B. Moghadam, K.M. Najmabadi. (2018). The effectiveness and safety of Iranian herbal medicines for treatment of premenstrual syndrome: A systematic review. Avicenna journal of phytomedicine. 8(2): 96.

[105] A. Talebpour, M. Mohammadifard, R. Zare Feyzabadi, S. Mahmoudzadeh, H. Rezapour, M. Saharkhiz, M. Tajik, G.A. Ferns, A. Bahrami. (2023). Effect of curcumin on inflammatory biomarkers and iron profile in patients with premenstrual syndrome and dysmenorrhea: A randomized controlled trial. Physiological Reports. 11(13): e15763.

[106] Sheba MD, S N V. (2021). Exploring the Pharmaco-Therapeutic Efficacy of Kumari (*Aloe Vera* L.) on the Reproductive System. World Journal of Pharmacy and Pharmaceutical. 10(4):1593.
Available from: www.wjpr.net.

[107] A. Manouchehri, S. Abbaszadeh, M. Ahmadi, F.K. Nejad, M. Bahmani, N. Dastyar. (2023). Polycystic ovaries and herbal remedies: A systematic review. JBRA assisted reproduction. 27(1): 85.

[108] S. Sardashti, T.S.H. Abadi, S.S.H. Abadi, R. Raznahan. (2020). Investigation the effect of oral Aloe Vera gel pills supplementation on the intensity of primary menstrual pain (Dysmenorrhea). Balneo Research Journal. 11(2): 120-124.

[109] S. Khazaiyan. (2012). The effect of oral aloe vera gel on the intensity of primary dysmenorrhea. Medical-Surgical Nursing Journal. 1(1): 49-54.

[110] J. Nai, C. Zhang, H. Shao, B. Li, H. Li, L. Gao, M. Dai, L. Zhu, H. Sheng. (2021). Extraction, structure, pharmacological activities and drug carrier applications of *Angelica sinensis* polysaccharide. International Journal of Biological Macromolecules. 183: 2337-2353.

[111] P. Zeng, J. Li, Y. Chen, L. Zhang. (2019). The structures and biological functions of polysaccharides from traditional Chinese herbs. Progress in molecular biology and translational science. 163: 423-444.

[112] W.-L. Wei, R. Zeng, C.-M. Gu, Y. Qu, L.-F. Huang. (2016). *Angelica sinensis* in China-A review of botanical profile, ethnopharmacology, phytochemistry and chemical analysis. Journal of ethnopharmacology. 190: 116-141.

[113] M.S. Butt, M.T. Sultan. (2011). Ginger and its health claims: molecular aspects. Critical reviews in food science and nutrition. 51(5): 383-393.

[114] J. Shen, J. Zhang, M. Deng, Y. Liu, Y. Hu, L. Zhang. (2016). The antidepressant effect of *Angelica sinensis* extracts on chronic unpredictable mild stress-induced depression is mediated via the upregulation of the BDNF signaling pathway in rats. Evidence-based complementary and alternative medicine. 2016.

[115] W. Gong, S. Zhu, C. Chen, Q. Yin, X. Li, G. Du, Y. Zhou, X. Qin. (2019). The anti-depression effect of angelicae sinensis radix is related to the pharmacological activity of modulating the hematological anomalies. Frontiers in pharmacology. 10: 192.

[116] T.-S. Yeh, C.-C. Huang, H.-L. Chuang, M.-C. Hsu. (2014). *Angelica sinensis* improves exercise performance and protects against physical fatigue in trained mice. Molecules. 19(4): 3926-3939.

[117] Q. Liu, Y. Li. (2018). Anti-fatigue Effects of Polysaccharide from *Angelica sinensis*. IOP Conference Series: Materials Science and Engineering. 392(5).

[118] J.M. Bokelmann. (2022). Dong Quai (*Angelica sinensis*): Root. Medicinal Herbs in Primary Care. Editor. Elsevier. p. 309–15. Available from: https://www.sciencedirect.com/science/article/pii/B9780323846769000404.

[119] H. Chang, H. Han, P. Tu. (1999). Chemical constituents and pharmacological effects of

safflower. Xiandai Yaowu Yu Linchuang. 14: 201-203.

[120] J. Dhanik, N. Arya, V. Nand. (2017). A review on *Zingiber officinale*. Journal of Pharmacognosy and phytochemistry. 6(3): 174-184.

[121] Q.-Q. Mao, X.-Y. Xu, S.-Y. Cao, R.-Y. Gan, H. Corke, T. Beta, H.-B. Li. (2019). Bioactive compounds and bioactivities of ginger (*Zingiber officinale* Roscoe). Foods. 8(6): 185.

[122] S. Khayat, M. Kheirkhah, Z. Behboodi Moghadam, H. Fanaei, A. Kasaeian, M. Javadimehr. (2014). Effect of treatment with ginger on the severity of premenstrual syndrome symptoms. International Scholarly Research Notices.

[123] Z. Mahmoudpour, J. Shokri, M. Kamalinejad, N. Meftah, S. Khafri, S.A. Mozaffarpur, H. Shirafkan. (2019). The efficacy of a Persian herbal formulation on functional bloating: A double-blind randomized controlled trial. Journal of Integrative Medicine. 17(5): 344-350. Available from: https://www.sciencedirect.com/science/article/pii/S2095496419300731.

[124] A. Giacosa, D. Guido, M. Grassi, A. Riva, P. Morazzoni, E. Bombardelli, S. Perna, M.A. Faliva, M. Rondanelli. (2015). The effect of ginger (Zingiber officinalis) and artichoke (Cynara cardunculus) extract supplementation on functional dyspepsia: a randomised, double-blind, and placebo-controlled clinical trial. Evidence-based complementary and alternative medicine. 2015. Available from: https://doi.org/10.1155/2015/915087.

[125] W. Tianthong, V. Phupong. (2018). A randomized, double-blind, placebo-controlled trial on the efficacy of ginger in the prevention of abdominal distention in post cesarean section patients. Scientific reports. 8(1): 6835. https://doi.org/10.1038/s41598-018-25200-6.

[126] M. Yuki, Y. Komazawa, Y. Kobayashi, M. Kusunoki, Y. Takahashi, S. Nakashima, G. Uno, I. Ikuma, T. Shizuku, Y. Kinoshita. (2015). Effects of Daikenchuto on abdominal bloating accompanied by chronic constipation: a prospective, single-center randomized open trial. Current Therapeutic Research. 77: 58-62. Available from: https://www.sciencedirect.com/science/article/pii/S0011393X15000065.

[127] C.D. Black, M.P. Herring, D.J. Hurley, P.J. O'Connor. (2010). Ginger (*Zingiber officinale*) reduces muscle pain caused by eccentric exercise. The journal of pain. 11(9): 894-903.

[128] P. Rahnama, A. Montazeri, H.F. Huseini, S. Kianbakht, M. Naseri. (2012). Effect of *Zingiber officinale* R. rhizomes (ginger) on pain relief in primary dysmenorrhea: a placebo randomized trial. BMC complementary and alternative medicine. 12: 1-7.

[129] F. Kashefi, M. Khajehei, M. Tabatabaeichehr, M. Alavinia, J. Asili. (2014). Comparison of the effect of ginger and zinc sulfate on primary dysmenorrhea: a placebo-controlled randomized trial. Pain Management Nursing. 15(4): 826-833.

[130] S. Bagheri, L. Kashani. (2021). Therapeutic Application of Saffron for Improvement of Women's Health: A Review of Literature. Journal of Iranian Medical Council.

[131] M. Irani, A. Rahmanian, N. Soltani. (2023). Efficacy of Saffron (*Crocus sativus* L.) in Premenstrual Syndrome, Labor, Childbirth, and Menopause: A Systematic Review of Clinical Trials. Modern Care Journal. 20(3).

[132] S.F. Omidkhoda, H. Hosseinzadeh. (2022). Saffron and its active ingredients against human disorders: A literature review on existing clinical evidence. Iranian Journal of Basic Medical Sciences. 25(8): 913.

[133] A. Hosseini, B.M. Razavi, H. Hosseinzadeh. (2018). Saffron (*Crocus sativus*) petal as a new pharmacological target: A review. Iranian Journal of Basic Medical Sciences. 21(11): 1091.

[134] M. Agha-Hosseini, L. Kashani, A. Aleyaseen, A. Ghoreishi, H. Rahmanpour, A. Zarrinara, S. Akhondzadeh. (2008). *Crocus sativus* L.(saffron) in the treatment of premenstrual syndrome: a double-blind, randomised and placebo-controlled trial. BJOG: An International Journal of Obstetrics & Gynaecology. 115(4): 515-519.

[135] H. Fukui, K. Toyoshima, R. Komaki. (2011). Psychological and neuroendocrinological effects of odor of saffron (*Crocus sativus*). Phytomedicine. 18(8-9): 726-730.

[136] S.P. Beiranvand, N.S. Beiranvand, Z.B. Moghadam, M. Birjandi, S. Azhari, E. Rezaei, A.N. Salehnia, S. Beiranvand. (2016). The effect of *Crocus sativus* (saffron) on the severity of premenstrual syndrome. European Journal of Integrative Medicine. 8(1): 55-61.

[137] A. Noorbala, S. Akhondzadeh, N. Tahmacebi-Pour, A. Jamshidi. (2005). Hydro-alcoholic extract of *Crocus sativus* L. versus fluoxetine in the treatment of mild to moderate depression: a double-blind, randomized pilot trial. Journal of ethnopharmacology. 97(2): 281-284.

[138] A.A. Basti, E. Moshiri, A.-A. Noorbala, A.-H. Jamshidi, S.H. Abbasi, S. Akhondzadeh. (2007). Comparison of petal of *Crocus sativus* L. and fluoxetine in the treatment of depressed outpatients: a pilot double-blind randomized trial. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 31(2): 439-442.

[139] M. Mazidi, M. Shemshian, S.H. Mousavi, A. Norouzy, T. Kermani, T. Moghiman, A. Sadeghi, N. Mokhber, M. Ghayour-Mobarhan, G.A. Ferns. (2016). A double-blind, randomized and placebo-controlled trial of Saffron (*Crocus sativus* L.) in the treatment of anxiety and depression. Journal of Complementary and Integrative Medicine. 13(2): 195-199.

[140] K. Nahid, M. Fariborz, G. Ataolah, S. Solokian. (2009). The effect of an Iranian herbal drug on primary dysmenorrhea: a clinical controlled trial. Journal of midwifery & women's health. 54(5): 401-404.

[141] M. Umadevi, R. Rajeswari, C.S. Rahale, S. Selvavenkadesh, R. Pushpa, K.S. Kumar, D. Bhowmik. (2012). Traditional and medicinal uses of *Withania somnifera*. The pharma innovation. 1(9, Part A): 102.

[142] L.-C. Mishra, B.B. Singh, S. Dagenais. (2000). Scientific basis for the therapeutic use of *Withania somnifera* (ashwagandha): a review. Alternative medicine review. 5(4): 334-346.

[143] G.L. Gupta, A. Rana. (2007). PHCOG MAG.: Plant review *Withania somnifera* (Ashwagandha): A review. Pharmacognosy Reviews. 1(1): 129-136.

[144] M. Adiga, S. Kumar. (2022). Management Of Pre Menstrual Syndrome With Combined Ayurveda Interventions (Ashwagandha Vati And Satvavajaya Chikitsa)-An Open Label Single Arm Clinical Study. Annals of Ayurvedic Medicine. 11(1): 48-48.

[145] H. Kour, I. Kaur. (2017). International Journal of Ayurveda and Pharmaceutical Chemistry. 7(3):15–21.

[146] A. VACHASPATI. (2017). Clinical Study on Efficacy of Ashwagandha Vati and Satvavajaya Chikitsa in the Management of Chittodvega in Pre Menstrual Syndrome. Available from: https://search.proquest.com/openview/10bfa16e177e7cb4eeb06515d35d6220/1?pqorigsite=gscholar&cbl=2026366&diss=y.

[147] A.K. Sinha. (2020). Chemical Analysis Of Ashwagandha With Its Applications Especially As Antioxidant & Anti Stress Agent. 7(10):3191–6.

[148] J. Salve, S. Pate, K. Debnath, D. Langade, D.G. Langade. (2019). Adaptogenic and anxiolytic effects of ashwagandha root extract in healthy adults: a double-blind, randomized, placebo-controlled clinical study. Cureus. 11(12).